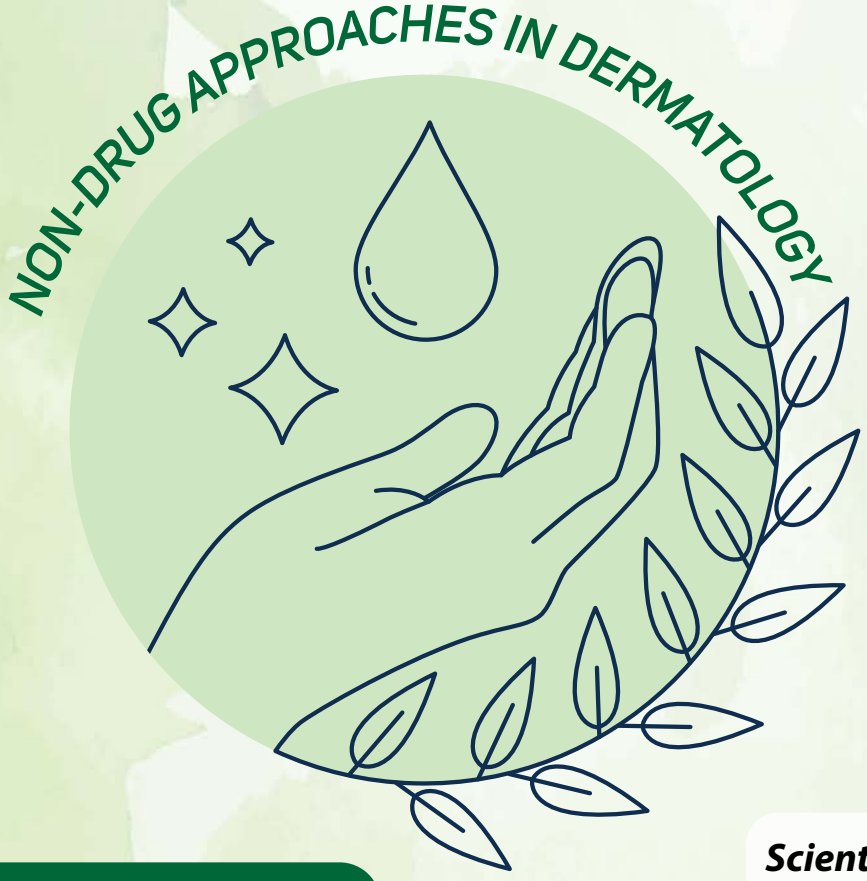
8th INDERCOS

International Dermatology and Cosmetology Congress

09-12 March 2023

Radisson Blu Şişli Hotel - İstanbul, Türkiye



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INVITATION

Dear Colleagues,

On behalf of the Scientific Committee, it is our great pleasure to invite you to join the 8th International Dermatology & Cosmetology Congress- INDERCOS, which will be held from March 09 to 12, in Istanbul, Türkiye.

For 7 consecutive years, INDERCOS has hosted an annual meeting attracting a growing number of national and international attendees from around the world that shared their knowledge, research, and best clinical practices, shaping the present and future of our specialty.

We hope that the 2023 meeting will be conducted in person, and preparations are already in progress to receive you in the beautiful city of Istanbul.

The program will highlight Non-Drug Approaches In Dermatology, and the lectures and courses will be delivered by a team of world experts.

Topics will include the newest aspects in Non-Drug Approaches In Dermatology.

We look forward to welcoming you to the 8th INDERCOS, and we hope you will have an unforgettable and joyful experience.

Sincerely,

Prof. Dr. Ümit Türsen	**Prof. Dr. Kemal Özyurt**	**Prof. Dr. Ayşe Serap Karadağ**	**Prof. Dr. Katlein Franca**
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*Listed alphabetically

SCIENTIFIC PROGRAM

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09 MARCH 2023, Thursday

10:30-14:40	**SESSION: DERMOSCOPY COURSE** ***Chairs: Fezal Özdemir, Mustafa Turan Şahin***	
	Principles in dermatoscopy	*Verce Todorovska*
	Dermatoscopic structures and their histological correlates	*Ömer Faruk Elmas*
	Dermatoscopy of melanoma	*Fezal Özdemir*
	Discussion	
	Sequential digital dermatoscopy: When and how?	*Raimond Karls*
	Dermatoscopy in non melanoma skin cancer	*Mustafa Turhan Şahin*
	Inflammoscopy	*Pawel Pietkewicz*
	Discussion	
	Onychoscopy	*Abdullah Demirbaş*
	Mucoscopy	*Cüneyt Soyal*
	Trichoscopy	*Haitam Donia*
	Entemodermatoscopy	*Tuğba Kevser Uzunçakmak*
	Dermatoscopy in common and specific types of nevi	*Ercan Arca*
	Discussion	
14:40-16:30	**COFFEE BREAK**	
16:30-18:00	**ULTRASOUND-GUIDED AESTHETIC DERMATOLOGY PROCEDURE** ***Chairs: Aslı Tatlıparmak, Feyza Sönmez Topçu***	AG Healthcare Technology
	Overview of facial anatomy	*Erdinç Terzi*
	Ultrasonography basic principles	*Feyza Sönmez Topçu*
	Ultrasonographic views of normal anatomical structures	*Aslı Tatlıparmak*
	Ultrasonographic characters of fillers	*Aslı Tatlıparmak*
	Vascular mapping	*Feyza Sönmez Topçu*
	Ultrasound-guided procedures	*Erdinç Terzi*
	Hands on course	*Aslı Tatlıparmak, Fatih Gülşen*
18:00-18:30	**Autologous Adipose-Tissue Derived Stromal Vascular Fraction (AD-tSVF) for Aesthetic Dermatology**	*Emre Tayfun*

10 MARCH 2023, Friday

08:00-09:00 ORAL PRESENTATION - 1
Chairs: Selami Aykut Temiz, Asude Kara Polat

OP-01	Update and transmission factors of the HIV/AIDS epidemic in Ukraine	*Larissa Burruano*
OP-02	Radıotherapy For Squamous Cell Carcınomas Of The Skın: A Sıngle Institution Experıence From North East Turkey	*Mustafa Kandaz*
OP-03	Arising molloscum contagiosun in an adult patient treated with fingolimod and review of the literature	*Selami Aykut Temiz*
OP-04	Herpetiform lesions of the oral mucosa in a patient diagnosed with COVID-19	*Kadir Kaya*
OP-05	Investigation of the Relationship between Frailty, Dermatological Quality of Life and Depression in Geriatric Patients	*Işıl Göğem İmren*
OP-06	Efficacy of Topical Dapsone 5% Gel for the Treatment of Erythematotelangiectatic Rosacea	*Işıl Göğem İmren*
OP-07	Retrospective Evaluation of Clinicoepidemiologic Profile of Pregnant Patient who applied to the Dermatology Outpatient Clinic	*Işıl Göğem İmren*
OP-08	Immunogenicity of Biologic	*Zuhal Metin*
OP-09	Hyperprolactinemia and Gynecomastia Development During Systemic Isotretinoin Treatment	*Zuhal Erçin*
OP-10	The relationship between monocyte to HDL cholesterol ratio and inflammation in patients with Seborrheic Dermatitis	*Abdullah Demirbaş*

09:00-09:30 OPENING SPEECH & LECTURE
Chairs: Belma Türsen, Katlein Franca

Advances in psychoneurocutaneous medicine: Exploring non-pharmacological treatments	*Katlein Franca*
The heart and the skin: A cardiodermatology talk	*Rafle Fernandez*

09:30-10:20 SESSION: HAIR AND SEBACEOUS GLAND DISEASES
Chairs: Ayşe Serap Karadağ, Deniz Yücelten

Acne: Nondrug therapy approach	*Ahu Birol*
Alopecia: Nondrug therapy approach	*Aslı Bilgiç*
HS: Lights and shadows	*Laura Atrozi*

10:20-10:35 COFFEE BREAK

10:35-11:15 SATELLITE SYMPOSIUM

The Diagnosis of Scabies and Oral Ivermectin Treatment
Moderators: *Ümit Türsen, Ayşe Serap Karadağ*
Speaker: *İlkay Can*

Humanis

11:15-12:45 SESSION: GENERAL DERMATOLOGY: NON DRUG APPROACHES FOR SKIN DISEASES - 1 *(In Memory of Dr. Ebru Gündüz)*
Chairs: Sibel Alper, Algün Polat Ekinci

Cryo-immunotherapy in dermatology: An update	*Paola Pasquali*
Standarizing medical photography	*Paola Pasquali*
Skin diseases in shift workers	*Ayşenur Botsalı*
Chronotherapy in dermatology	*Habib Aktaş*
Teledermatology and dermoscopy: The perfect combination	*Paola Pasquali*
Weight control for skin diseases	*Aylin Türel Ermertcan*

12:45-13:30 LUNCH

10 MARCH 2023, Friday

13:30-14:20	**SESSION: DERMATO-ALLERGY - 1** ***Chairs: Rafet Koca, Necmettin Akdeniz***	
	Nondrug treatments in allergic skin diseases	*Zafer Türkoğlu*
	Urticaria and microorganisms: Myths and facts	*Ragıp Ertaş*
	Wet wrap therapy in allergic skin diseases	*Pelin Ertop*
	Post-scabietic pruritus: What is new?	*Nazime Bensu Önentaşçı*
	Jak inhibitors and atopy: What is new?	*Rafet Koca*
14:20-15:00	**SATELLITE SYMPOSIUM**	
	FROM DIAGNOSIS TO THERAPY MYCOSIS FUNGOIDES ***Moderator:*** *Rafet Koca* **Clinical Diagnosis and Differential Diagnosis in Mycosis Fungoides** ***Speaker:*** *Tuğba Atcı* **Treatment and Follow-up & Real Life Experience with Cases in Mycosis Fungoides** ***Speaker:*** *Mehmet Melikoğlu* **Discussion**	TOBIO®
15:00-16:00	**SESSION: MYTHS AND FACTS IN DERMATOLOGY** ***Chairs: Serap Öztürkcan, İlkin Zindancı***	
	Acne isotretinoin therapy	*Ivana Binic*
	Gluten free diet	*Simin Ada*
	PDT for NMSCs: Does it work?	*Laura Atzori*
	Diet and inflammatory skin disease	*Gökşen Ertuğrul*
	Topical calcineurin inhibitors and cancer risk	*Serap Öztürkcan*
	Ivig treatment in dermatology: Does it work?	*Seray Külcü Çakmak*
16:10-16:30	**COFFEE BREAK**	
16:30-17:30	**SESSION: WHAT IS NEW IN BIOLOGICS - 1** ***Chairs: İlknur Altunay, Kemal Özyurt***	
	Biologic treatment response according to HLA types	*Ömer Kutlu*
	Real life data of biologics for psoriasis	*Filiz Topaloğlu Demir*
	Immunogenicity of biologics	*Zuhal Metin*
	Mycosis fungoides: Bexarotene experiences in Turkey	*Mahmut Sami Metin*
	DLQI improvements after anti-HS biologics	*Cahit Yavuz*
	Comorbidities of Behçet's Disease	*Mehmet Melikoğlu*
17:30-18:00	**LECTURE** ***Chair: Kemal Özyurt***	
	What is new in WHA Publishing?	*Torello Lotti*
	Tips and tricks for hair transplantation	*Roxanna Sadoughifar*

11 MARCH 2023, Saturday

08:30-09:30 ORAL PRESENTATION - 2
Chairs: Burçe Can Kuru, Seçil Vural

OP-11	Mechanical dermabrasion of the upper lips for "bar code " wrinkles: technic, expected results and pitfalls	*Laurent Dupoirieux*
OP-12	Reliability and quality of YouTube videos as a source of information on alopecia areata	*Muazzez Çiğdem Oba*
OP-13	Autologous Micrografting for genetic hair loss	*Naeem Jamal Assaf*
OP-14	A rare case; pemphigus erythematosus in a turkish male and treatment with rituximab	*Semanur Çakır*
OP-15	Evaluation of Invers Approach's Specifity And Sensitivity in Dermoscopic Differential Diagnosis of Lentigo Maligna	*Ece Gokyayla*
OP-16	Baclofen-Induced Dyshidrosiform Bullous Pemphigoid in a Tetraplegic Patient	*Neslihan Deniz*
OP-17	Pediatric Patients with Morphea: A Single-Center Retrospective Study	*Elif Nur Ozler*
OP-18	Efficiency Of Squaric Acid Dibutyl Ester Therapy In Treatment Resistant Cases Of Verruca Vulgaris And Verruca Plantaris	*Sertaç Sever*
OP-19	Peristomal localized pemphigoid: Is it a relatively common presentation of bullous pemphigoid with good prognosis?	*Tugba Atci*
OP-20	Complete healing of alopecia areata in an eleven year old girl with diphencyprone treatment	*Zuhal Erçin*

09:30-10:30 SESSION: DERMATO-ALLERGY - 2
Chairs: Oktay Taşkapan, Ragıp Ertaş

Importance of nocturnal moisturizations in allergic skin diseases	*Andaç Salman*
Approaches to the patient with atopic dermatitis	*Oktay Taşkapan*
Dupilumab: What is new?	*Yılmaz Ulaş*
Omalizumab: What is new?	*Ragıp Ertaş*

10:30-11:00 COFFEE BREAK

11:00-11:40 SATELLITE SYMPOSIUM

FOR YOU FROM YOU:
New generation stem cell technology with GCELL
Speaker: *İrem Hengirmen Acu*

GLOBAL BİYOMEDİKAL

11:40-12:30 SESSION: AESTHETIC DERMATOLOGY - 1
Chairs: Kenan Aydoğan, Şirin Yaşar

Sclerotherapy and Nd-Yag laser in the removal of vascular changes	*Predrag Stilet*
Offlabel RF uses in aesthetic dermatology	*Meltem Önder*
Fractional laser resurfacing of the skin	*Andrej Petrov*

12:30-13:30 LUNCH & WORKSHOP: SVF experience with GCELL new generation stem cell technology
Ulaş Güvenç

11 MARCH 2023, Saturday

13:30-14:10	**SESSION: RATIONAL DRUG USES SESSION (CDC RECOMMENDATIONS)** ***Chairs: Belma Türsen, Mihael Skerlev***	
	Guideline for prevention of surgical site infection	*Amor Khachemoune*
	Guidelines and recommendations for HPV infections	*Mihael Skerlev*
	CDC recommendations for parasitic skin diseases	*Semahat Alp Erdal*
	CDC recommendations for herpes virus infections	*Bilal Doğan*
14:10-14:50	**SATELLITE SYMPOSIUM**	
	Evaluation and Preparation of Superior PRP, FAT Grafting and Mechanical SVF by T-LAB For Better Clinical Outcomes ***Speaker:*** *Timur Veysel Doğruok*	
14:50-16:00	**SESSION: WHAT IS NEW IN BIOLOGICS - 2** ***Chairs: Recep Dursun, Ümit Türsen***	
	New topicals for psoriasis	*Emel Bülbül Başkan*
	Guselkumab	*Serhat İnalöz*
	Adalimumab as a treatment of choice - when and how?	*Monika Fida*
	Secukinumab	*Fatma Aslı Hapa*
	Ixekizumab	*Nida Kaçar*
	Risankizumab	*Zeynep Topkarcı*
16:00-16:30	**COFFEE BREAK**	
16:30-18:00	**SESSION: GENERAL DERMATOLOGY- 2** ***(In Memory of Dr. Murat Harbutluoğlu)*** ***Chairs: Özlem Su Küçük, Arzu Kılıç***	
	Personalizing dermatology	*Burhan Engin*
	The ethics of medical marijuana in dermatology	*Mustafa Tunca*
	Drug/medical erros in dermatology	*Pelin Eşme*
	How to increase patient adherence to dermatologic treatment	*Pelin Üstüner*
	Imiquimod uses in dermatology	*Zoran Nedic*
	Non-drug treatments in vitiligo	*Sanan Kerimov*

12 MARCH 2023, Sunday

08:00-09:00 ORAL PRESENTATION - 3
Chairs: İlteriş Oğuz Topal, Tuğba Özkök Akbulut

OP-21	Demographic, clinical, and histopathological features of Merkel cell carcinoma: A single-center retrospective study	*Özge Sevil Karstarlı Bakay*
OP-22	A case of skin manifestation of richter's transformation in a patient with chronic lymphocytic leukemia	*Saffet Burak Başak*
OP-23	Efficacy of omalizumab in elderly patients with chronic spontaneous urticaria: a multicenter observational study	*Berke Caner Kızmaz*
OP-24	Botulinum Toxin Induced Prolonged Blepharoptosis Lasting 6 Months: A Case Report	*Pınar Özdemir Çetinkaya*
OP-25	Clinical polymorphism and treatment of patients with lichen planus	*A. Sh. Inoyatov*
OP-26	Is relapse prediction in pemphigus vulgaris patients possible? Preliminary results of a retrospective study	*Ecem Güreler Sirkeci*
OP-27	Basic Principles of Ultrasound	*Feyza Sönmez Topcu*
OP-28	The Frequency of Sexual Dysfunction and Its Effect on the Quality of Life In CSU Patients Treated with Omalizumab	*Rabia Öztas Kara*
OP-29	The study of cytokine status and immunological changes in patients with non-segmental form of vitiligo	*Jahongir Narziyev*
OP-30	Low IgE Levels And High Systemic Inflammation Response Index Predict Omalizumab Response	*Özge Sevil Karstarlı Bakay*

09:00-10:30 SESSION: AESTHETIC DERMATOLOGY - 2
Chairs: Zehra Aşiran Serdar, Gülşen Tükenmez Demirci

Hyaluronic acid applications in dermatology	*Şükran Sarıgül Güdük*
Sunscreens: FDA regulations, enviromental and health impact	*Zahide Eriş*
Tips and tricks for lower face botulinum toxin injections	*Filiz Kuşak*
Botulinum toxin tricks for upper face	*Filiz Canpolat*
UV, sugar and smoking in skin aging	*Victor Clatici*
Danger zones for soft tissue filler injections	*Zekai Kutlubay*
Nano- and micro-fat grafts for anti-aging	*Şule Güngör*
PRP or PRF: Which one is better?	*Ayşe Akman Karakaş*

10:30-10:50 COFFEE BREAK

10:50-11:30 COURSE
Sağlık Profesyonelleri İçin 3 Adımda Etkili Sosyal Medya Kullanımı
Speaker: *Gamze Nurluoğlu*

L'ORÉAL Aktif Kozmetik

11:30-12:50 SESSION: AESTHETIC DERMATOLOGY - 3
Chairs: Ayşin Köktürk, Tamer İrfan Kaya

Ogee curve and aesthetic dermatology	*Sadiye Kuş*
Skin antiaging strategies	*Demet Akpolat*
Copper and skin health	*Deniz Demirseren*
Off_label uses of HA fillers in dermatology	*Özgür Gündüz*
The path to a beautiful chin-non-invasive double chin removal	*Medhat Abdelmalek*
Ultrasonography guided aesthetic dermatology procedures	*Aslı Tatlıparmak*

12 MARCH 2023, Sunday

12:50-13:50	**SESSION: AESTHETIC DERMATOLOGY - 4** ***Chairs: Mustafa Atasoy, Gaye Sarıkan***	
	EBD for HPV infections	*Belma Türsen*
	Tips and tricks for HA filler procedures in face	*Hüray Hügül*
	What's the difference between hot and cold laser-lipolysis	*Zennure Takcı*
	Uses of focused ultrasound therapy in dermatology	*Zehra Aşiran Serdar*
	Hair follicle stem cells for vitiligo treatment	*Bobur Toirov*
13:50-14:10	**CLOSING SPEECH** ***Kemal Özyurt, Ümit Türsen***	

LECTURE SUMMARIES

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PRINCIPLES OF DERMOSCOPY

Verce Todorovska

Skin examination was based only on visual inspection with or without a magnifying glass for a long time. Since the late nineties a new diagnostic method emerged, the epiluminescence microscopy (ELM), also known as skin-surface microscopy or dermatoscopy. It is a non-invasive method that makes subsurface structures of the skin accessible for in-vivo examination. Initially designed to be used with massive microscopic equipment, dermatoscopy can now be easily used in any dermatology setting with an inexpensive hand-held microscope-dermatoscope. The dermatoscope is similar to an otoscope, it is a small, mobile device, that can fit in a pocket, is easy to use, and is affordable. Its optical system has monocular observation, magnification X10, and an illumination system.

There are two types of illumination: polarized and non-polarized light. In the beginning, dermatoscopes used only nonpolarized light which requires a liquid interface and direct contact between the scope and the skin with refractive index closer to the one of the stratum corneum It reduces the reflection of the light from the skin, and enhances refraction so light can penetrate into the stratum corneum and make visible structures that are not seen with the naked eye. Unlike nonpolarized light, polarized light dermoscopy allows visualization of deep skin structures without the necessity of a liquid interface or direct skin contact. The depth that polarized light penetrates before undergoing 10 scattering events is approximately 60 to 100 µmThese physics explain the differences between PD and NPD observations and account for the depth of the skin each light can visualize. NPD is better able to visualize the superficial layers of the skin, thus allowing for the easy identification of structures such as milia-like cysts and the blue-white veil associated with orthokeratosis. In contrast, a PD allows for a better appreciation of deeper structures such as the vessels and collagen alterations seen as white shiny lines which can sometimes be the only clue for malignancy.

NPD makes millia-like cysts in SKs more visible, which is extremely helpful when facing clinically suspicious lesions, for example.an asymmetric palpable pigmented lesion on the leg of a middle-aged woman, or a large flat variegated lesion on the face of an elderly.

PD makes WSL visible and enhances our diagnostic abilities even in difficult-to-recognize melanomas, SK-like melanoma, nevoid, spitzoid, and hypomelanotic. Nota bene! WSL are angle dependent so always rotate your dermatoscope while examining the lesions, if you place it only in one direction you can miss the WSL

PD facilitates detection of superficial non-pigmented BCC, which is clinically and even dermoscopically inconspicuous. The same applies to amelanotic flat melanoma which is fortunately a very rare entity.

Dermatoscope can work in two modalities: non-contact and contact dermatoscopy.

1. Non-contact dermatoscopy can be done only with polarized light, it is great for the initial screening, does not require immersion, and saves time. It is practical for bleeding ulcerated lesions, and lowers the possibility of infection. In nodular non-pigmented lesions allows us to avoid compression and better visualization of the vessels. It is helpful in difficult areas like the lips, auricula, periocular area, umbilicus, interdigital…

2. Contact dermatoscopy requires immersion, it can be used in the polarized mode too, for obtaining better image quality. and is indispensable for the nonpolarized mode.

There are various immersion fluids: plain water,70% alcohol liquid or gel, oil, US gel…One of the best for me is the alcohol spray, it disinfects the plate and the skin, is easy to apply, and a very small quantity is needed, is not messy, and does not enter your dermatoscop plate. Ultrasound gel is best and irreplaceable for onychoscopy, mucoscopy and nodular lesions working like a cushion between the dermatoscope and the lesion to avoid compression and better visualisation of the vessels.

Dermatoscopy is used not only for diagnostic purposes but also for monitoring the treatment in general dermatology and in dermatooncology.

The field of dermatoscopy application is constantly widening, although started with skin tumors only, now it is used for examination of the skin appendages, nails-onychoscopy, hair- trichoscopy and for every type of skin lesion, inflammatory-inflamoscopy, infestations-entomodermoscopy.

Basic equipment consists of a handheld dermatoscope, When attached to the smartphone we can easily capture dermatoscopy

images, run documentation for every case, and later correlate with the histology reports. Then we have digital cameras with very high resolution and incorporated optical system, Last in the line of technological improvement are the state of art systems for detailed analysis and follow-up of skin lesions over time, even with incorporate artificial intelligence, the latest models offer a total body dermoscopy or 3D body mapping, for complete coverage of every inch of the patient skin.

Dermatoscopy is the most dynamic and rapidly evolving part of dermatology, Since recently there is UV reflectance dermatoscopy and OSHMD (optical super high magnification dermoscopy) which will open new dimensions and improve our diagnostic capabilities even further.

Dermatoscopy as a bridge between clinical and histopathology is getting stronger and tends to maybe one day completely replace the invasive excisional biopsies for obtaining an accurate diagnosis.

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DERMOSCOPY of MELANOMA

Fezal Özdemir, MD

Knowing the dermoscopic criteria of melanoma, and having more or less some experience with this method, it's not hard to diagnose melanoma. However when the melanoma is thin (Breslow thickness <1mm), and the clinical picture is similar to nevi, one should be more cautious. Actually, this is the exact point where dermoscopy should help to save lives. In situ or microinvasive melanomas should be the ones that we should never miss.

On the other hand melanomas hard to diagnose such as nodular, apigmented, desmoplastic, Spitzoid, and regressive ones should be handled carefully recognizing the special dermoscopic signs and clues.

Pediatric and adolescent cases need particular attention also, because of the underestimation of this age group.

In addition, melanomas localized in special locations like facial skin, acral area, nails, and mucosal sites have unique features that should be remembered to reach the correct diagnoses.

There are also many dermoscopic simulators of melanoma and the mostly encountered cases worth discussing.

In this presentation, summarizing the dermoscopic criteria of melanoma quickly, the emphasis will be given to these critical points of the mentioned scenarios. with plentiful examples of original cases.

DERMOSCOPY OF NON-MELANOMA SKIN CANCERS

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INTRODUCTION

Dermoscopy is a widely used non-invasive technique for diagnosing skin tumors. In melanocytic tumors, the effectiveness of dermoscopic examination has been fully established over the past two decades. In addition to this, dermoscopy has been used to diagnose non-melanocytic tumors. Here, we review novel findings from recent reports concerning dermoscopy of non-melanoma skin cancers mainly including BCC, and squamous cell carcinoma (SCC).[1]

BASAL CELL CARCINOMA

The value of dermoscopy of basal cell carcinoma (BCC) has been extensively demonstrated over the past few decades. The sensitivity of diagnostic criteria for pigmented BCC was reported as 97%. The dermoscopic criteria associated with BCCs include the absence of a pigment network and the presence of specific features, e.g., arborizing vessels, large blue-gray ovoid nests, multiple blue-gray globules, leaf-like areas, spoke wheel areas, and ulceration. In some reports, arborizing vessels, large blue-gray ovoid nests, multiple blue-gray globules, leaf-like areas, spoke wheel areas, and ulceration were dermoscopically observed in pigmented BCCs. Additional features have been reported recently, specifically multiple small erosions, shiny white streaks, and concentric structures. Altamura et al. It was also reported that multiple small erosions were seen in 14.1% of non-pigmented BCCs, whereas shiny white streaks have been seen only in polarized dermoscopy. Moreover, vascular patterns such as short fine telangiectasias (SFTs), arborizing microvessels, and milky-pink backgrounds have been reported, and these patterns may be useful particularly for non-pigmented BCCs. SFTs are small vessels without branches. SFTs were the second most common vascular pattern found in BCCs. These telangiectasias were significantly more common in superficial BCCs than in nodular BCCs (20). Additionally, it was reported that arborizing microvessels, short, bright red, sharply focused, fine-caliber branching vessels, were seen in 62% of superficial BCCs. Reports on milky-pink backgrounds indicated that they were more common in superficial BCCs Dermoscopic characteristics for each BCC subtype have been described. Some reports differentiated between superficial BCC and other subtypes by dermoscopy. In superficial BCC, maple leaf-like areas, spoke wheel areas, SFTs, multiple small erosions, and concentric structure were frequently observed. Ahnlide et al., summarized dermoscopic features in the common subtype of BCC, including superficial BCC, nodular BCC and infiltrated BCC. Based on their reports, both in nodular and infiltrated BCCs, arborizing vessels were the most common, while ulcerations were the second most common findings. Moreover, Lallas et al. reported that blue-gray ovoid nests may be predictors for non-superficial BCCs. According to their findings, both arborizing vessels and ulcerations would exclude superficial BCC.[2-12]

SQUAMOUS CELL CARCINOMA

Dermoscopic criteria for squamous cell carcinoma (SCC) include the presence of keratin/scales, blood spots, white circles, white structureless areas, hairpin vessels, linear-irregular vessels perivascular white halos, and ulceration. Keratin and scales are homogeneous opaque yellow to brown structures corresponding to hyperkeratosis and parakeratosis. Blood spots are the multiple red to black dots in the keratin mass, corresponding to small crusts or hemangiomas. White circles are the bright white circles surrounding a dilated infundibulum corresponding to acanthosis and hypergranulosis of the infundibular epidermis. White structureless areas are the whitish areas covering large areas of tumors, corresponding to large targetoid hair follicles. Among the criteria discussed above, keratin and white circles reached the sensitivity and specificity for SCC diagnostic at a rate of 79 and 87%, respectively. The presence of vessels in more than half and bleeding significantly increased the possibility of poorly differentiated SCC. Conversely, keratin/scales are a potent predictor of well- and moderately differentiated SCC. However, Pyne et al. reported that moderately and poorly differentiated SCC displayed more branched and serpentine vessels than well-differentiated SCC and that moderately and poorly differentiated SCC displayed larger numbers of vessel types than well-differentiated SCC. Regarding lip SCC, it has been recently reported that scales, white structureless areas, and white halos were observed in the majority of the cases .[13-19]

CONCLUSION

We summarized recent reports of novel findings related to dermoscopy of non-melanoma skin cancers. Dermoscopy is presently thought to be effective and helpful for diagnosing non-melanoma skin cancers. However, it is important to consider that dermoscopy is just one of several means, others being clinical history, age and gross appearance, that can be utilized in cancer diagnosis. Therefore, dermoscopist should not hesitate to do a biopsy in cases in which a diagnosis cannot be reached clearly through dermoscopy

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INFLAMMOSCOPY: DON'T LET THE DERMATOSCOPE BE AN OFFICE DECORATION.

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ABSTRACT

Dermatoscopy, or epiluminiscence microscopy, is an in-vivo auxiliary diagnostic method complementary to medical history, clinical examination and pathology. Although initially aimed at early skin cancer diagnosis it has become indispensable in general dermatology. This easy to apply, inexpensive and rapid tool requires basic training in order to interpret the dermatoscopic clues: clues of scale (including colour and distribution), vascular clues (including vessel morphology and arrangement), follicular clues, other clues and specific clues (particularly useful as associated with just one diagnosis) [1,2]. This presentation focuses on clusters of clinical differentials commonly seen in clinical practice.

It should be kept in mind that dermatoscopy should always follow clinical differential diagnosis, as a secondary step verifying the initial clinical impression based on lesion's morphology and distribution. Moreover, in some scenarios it can be used to assess the clinical stage of the disease (age of the lesions), predict the evolution, and clinical outcome of the treatment as well as monitor the effectiveness or side effects of the implemented treatment [3]. Additional modifications of the method – optical super-high magnification dermatoscopy and ultraviolet reflectance dermatoscopy can increase the diagnostic accuracy [4-6].

There are numerous benefits of inflammoscopy that relate to the patient, the physician and the whole healthcare system. The method saves the patient from diagnostic error, prolonged diagnostic process, unnecessary biopsies resulting in cosmetic defects (particularly, in skin of colour), money lost for initial, variably effective treatment before confirmed diagnosis and stress related to the disease/diagnostic or therapeutic uncertainty. The benefits for the physician are fast and reliable verification of tentative diagnosis, better reception of the professional commitment and expertise, resulting in higher confidence in the clinician, higher patient's compliance, and avoiding clinical/therapeutic pitfalls. For the healthcare system the method means shortening the diagnostic path, lower costs of care, better outcomes through higher adherence to the treatment and avoiding medical errors leading to possible legal claims.

Keywords: inflammoscopy, monitoroscopy, inflammatory diseases, dermatoscopy, ultraviolet reflectance dermatoscopy

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ONYCHOSCOPY

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Onychoscopy is the dermoscopic examination of the nail matrix, nail bed, nail plate, and nail plate's proximal and distal ends. The primary purpose of onychoscopy is to evaluate nail pigmentation, and early detection of melanoma is crucial.

Nail Plate Dermoscopy: Onychoscopy is also helpful in diagnosing and following nail diseases, subclinical nail plate surface anomalies, onychomycosis, anomalies of nail bed vascular structures, diagnosis of non-pigmented nail tumors, and the differential diagnosis of linear melanonychia.

Dermoscopy of the Proximal Nail Fold: Proximal nail fold dermoscopy is very important in the diagnosis and follow-up of connective tissue disorders. In normal conditions, the proximal nail fold capillaries flow parallel to the skin surface, and each capillary vessel resembles a hairpin, being formed by two arms that make a distal convex loop. They have a regular distribution, even with large intra- and inter-individual variability. Capillary loss and capillary enlargement are not observed in healthy people. However, in connective tissue diseases, especially dermatomyositis, and scleroderma, the capillaries are enlarged, tortuous, and avascular areas are observed, while small hemorrhages and infarcts are observed in the cuticle.

Periungual pigmentation is crucial for melanoma, particularly the distinction between Hutchinson and pseudo-Hutchinson, which is essential. Dermoscopy can distinguish the Hutchinson's sign from the pseudo-sign, Hutchinson's in which the cuticle appears pigmented because of its transparency.

Dermoscopy of the Hyponychium : It provides information regarding the increase or decrease in the number of vessels, anomalies in vessel shape, and vessel distribution. In nail psoriasis, the vessels of the hyponychium are coiled and twisted.

Dermoscopy of the nail plate's distal ends: This area is important for understanding the region where melanin is produced. If the pigmentation is located in the ventral region of the nail plate, the lesion originates from the distal matrix, and if it is located in the dorsal region of the nail plate, it originates from the proximal matrix. This is useful for us in choosing the excision area.

Intraoperative Onychoscopy; It is a procedure performed during the operation after the avulsion of the nail plate. Intraoperative dermoscopy provides direct visualization of the pigmented lesion.

Onychoscopy in Psoriatic Nail: Polarized tools reveal nail plate surface abnormalities. Dermoscopy shows scales around and inside psoriatic pits, which are large and irregular. Dermascopy demonstrates the erythematous border of psoriatic onycholysis. In the distal nail bed, splinter hemorrhages appear as red-brown linear or filamentous lines. A Dermoscopy of the hyponychium can confirm nail psoriasis in uncertain cases by showing irregularly distributed, dilated, tortuous, and twisted capillaries like those on the scalp. Twisted, enlarged capillaries are also seen in Hallopeau's acrodermatitis.

Onychoscopy in Nail Lichen Planus: Dermoscopy is only useful for the better visualization of nail plate fissures, nail fragmentation, and other nail plate surface abnormalities in lichen planus.

In alopecia areata, dermoscopy enables the better visualization of the nail plate surface. Pits are the most common abnormality: they are small, regularly distributed, and surrounded by scales.

Dermoscopy of the subungual hematoma: Hematomas are usually black, brown, or red on dermoscopy. As phagocytes convert hemoglobin into hemosiderin, its color depends on its duration. Old lesions show red coloring, likely due to nail trauma. Dermatoscopes show the lesion's red and purple colors. A "filamentous" distal end and/or round, dark red periphery suggest this diagnosis. Splinter hemorrhages and peripheral fading are also common.

Dermoscopy of the distal subungual onychomycosis:

- Ragged proximal margin
- White–yellow streaks and patches
- Dermoscopy establishes a proximal progression
- White superficial onychomycosis: Pseudo-leukonychia
- Proximal subungual onychomycosis: Proximal true leukonychia

Dermoscopy of the Onychomatricoma:

- Benign nail matrix tumor that develops within the nail plate.
- Longitudinal thickening and xanthonychia.
- Dermoscopy: Longitudinal white lines, proximal splinter hemorrhages, and distal splinter hemorrhages.
- Dermoscopy of the distal edge: Woodworm-like cavities

Dermoscopy of the Onychopapilloma

- Benign neoplasm of the distal matrix and the nail bed
- Longitudinal erythronychia, leukonychia, and melanonychia
- Dermoscopy: Single or multiple splinter hemorrhages within the band
- Dermoscopy of the distal edge: Subungual keratotic mass

Dermoscopy of the nail Bowen's Disease/ Squamous cell: Dermoscopy shows dotted vessels, islands of scales, and hyperkeratotic, targetoid structures in Bowen's disease. White circles appear in squamous cell carcinoma.

Dermoscopy of the nail nevi: Dermoscopy: Adults: brown–black bands, sharp lateral borders, and thin, regular, longitudinal parallel lines; children: brown–black bands, irregular lines of different colors and thicknesses, dots and globules, and brushy pigmentation across skin marks.

Dermoscopy of the nail melanoma: Dermoscopy: Blurred lateral margin, longitudinal lines of different thicknesses and colors with disruption of parallelism, very dark homogeneous pigmentation, and parallel ridge pattern in the hyponychium.

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MUCOSCOPY

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Lips, oral cavity, and genital skin (perianal, penil, vulvar) are mucosal areas of human body. There is increasing evidence that dermoscopy may also be helpful to differentiate benign from malignant or suspicious lesions arising in the mucosa. Dermoscopic examination of mucosal lesions, namely Mucoscopy, reveals structural, color and pattern characteristics of these lesions. This presentation will review the dermoscopic clues for the diagnosis and differential diagnosis pf pigmented and nonpigmented mucosal lesions

DERMATOSCOPIC IN COMMON AND SPECIFIC TYPES OF NEVI

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Different types of nevi do exist in relation to their epidemiology, morphology, evolution, and associated melanoma risk. The introduction of dermoscopy opened a new dimension of the morphologic universe of nevi and allowed clinicians to observe colors and structures within nevi that are otherwise not visible to the unaided eye. In consequence, a new nevus classification has been proposed, subdividing nevi into 7 categories, which are as follows: (1) globular/cobblestone nevi, (2) reticular nevi, (3) starburst nevi, (4) homogeneous blue nevi, (5) nevi on special body sites, (6) nevi with special features, and (7) and unclassifiable melanocytic proliferations.

Notably, the prevailing morphological pattern of melanocytic nevi is influenced by the body site, age and pigmentary trait. As such, globular (clod) nevi are typically located on the head/neck or upper trunk and are particularly commonly seen in children, while reticular nevi are more commonly observed on the trunk and extremities after the second decade of life.

Moreover, it has been shown that persons with a fair skin type exhibit large (>6 mm), orange/light brown nevi with a central structureless and peripheral reticular pattern. Histopathologically, these nevi are mainly compound with a significant dermal component with or without atypia. Instead, persons with a dark pigmentary trait tend to develop small (<5 mm) dark brown/black reticular nevi with a central hyperpigmentation, which correlate histopathologically with junctional nevi. Finally, it is well documented that individuals with multiple nevi harbor a so-called signature pattern among all of their nevi.

The main characteristic features of the seven melanocytic nevi are as follows:

Globular (Clod) nevi — characterized by aggregated, differently sized, brown to gray-blue globules is a commonly observed dermoscopic pattern in congenital, compound and dermal nevi typically located on the head, neck and upper trunk.

Reticular nevi —It is characterized by a regular pigment network, which may also show areas of hypopigmentation and/or structureless brown/black colour. They present as brown/black, flat/slightly elevated, monomorphous nevi, commonly small in size at less than 5 mm^2.

Spitz nevi — are considered the "stars" within the melanocytic garden because of their highly variable morphology. Spitz nevi may exhibit the following six dermoscopic patterns: (i) starburst (peripheral lines) pattern characterized by thick radially arranged lines or pseudopods; (ii) globular with variable large brown, gray and black globules; (iii) structureless black and (iv) reticular as well as dot pattern, typified by (v) dotted vessels and (vi) white lines in hypo-/non-pigmented variants.

The dermoscopic morphology shows alterations over a lifetime: during the phase of growth, they present with peripheral regular streaks, finger-like and globule-like pigmentation in a radiating pattern (starburst) which disappear after a few months, resulting in a homogeneous dermoscopic pattern with structureless brown/black pigmentation and finally spontaneous involution. Reticular depigmentation and dotted vessels are commonly observed in non-pigmented lesions

Blue nevi — The most classic pattern of blue nevi is a structureless blue color. However, the structureless blue may also be associated with white, brown or other colors. They are congenital or acquired melanocytic lesions usually persisting throughout a patient's lifetime, macroscopically presenting as rather flat or elevated, blue/black plaques. Dermoscopic criteria for blue nevi, which allow a better correlation and subdivision regarding the underlying histopathological features: (i) blue-blue nevi (common); (ii) white-blue nevi (hypochromic); (iii) black-blue nevi (compound); (iv) brown-blue nevi (combined); and (v) polychromatic-blue nevi (deeply infiltrating).

Site related nevi –.

Acral nevi; present as brown/black, flat/slightly nevi. With the exception of congenital nevi, they usually do not exceed a size of more than 7 mm. Eight different dermoscopic patterns in nevi located on soles, fingers and palms have been described so far: (i) the most common being the parallel furrow pattern (Fig. 3a), followed (ii) by the lattice-like, (iii) non-typical, (iv) fibrillar, (v) homogeneous, (vi) globular/clod, (vii) reticular and (viii) transition pattern (combination of brown-black network and parallel furrow or latticelike).

Nevi of the nail unit: These nevi arise from the nail matrix and present as small bandlike, light to dark brown pigmentation, extending from the primal to the distal nail. Small pigmented band composed by parallel lines of uniform color and width.

Facial nevi; in children present as brown, flat/slightly elevated, symmetrical lesions of less than 15 mm with a structureless brown-gray pattern that is intermingled with numerous hypopigmented follicular openings. In striking contrast, facial nevi in adults are elevated, flesh-colored lesions showing comma vessels and remnants of pigment. Dermoscopy reveals pseudo-network pattern intermingled by hairs.

Mucosal nevi: Mixed pattern composed of prominent network structures and/or gray-blue globules and/or homogeneous blue-gray pigmentation.

Nevi of the nipple: There are a few differential diagnoses regarding pigmented lesions on the nipple: melanocytic nevi, nevoid hyperkeratosis, reactive hyperkeratosis, melanosis of the areola, melanoma and Paget's disease.

Scalp nevi: Recently, a new dermoscopic classification of scalp nevi was proposed: (i) common nevi (flat/slightly elevated/nodular, domeshaped, symmetrical); (ii) papillomatous nevi; (iii) eclipse nevi (central hypopigmentation with a pigmented rim); (iv) congenital nevi (present since birth or the first 2 years of life); (v) blue nevi; and (vi) atypical nevi (presenting with at least one of the following features: asymmetry, uneven borders, >three colors, >6 mm diameter).

Nevi with special features —

Combined nevi: Combined nevi are defined as congenital or acquired nevi presenting with two areas of different color and size and show at least two of these four dermoscopic patterns: (i) globular/clod; (ii) reticular; (iii) starburst; and (iv) homogeneous. The most stereotypical appearance of a combined nevus is that of a reticular or globular (clod) nevus in association with a blue (structureless blue) nevus

Recurrent nevi are benign melanocytic nevi that regrow after incomplete surgical excision or trauma. Most RN originate from 'ordinary' or common acquired nevi removed for cosmetic reasons by means of a shave biopsy; less often, recurrences may arise from incomplete excision of congenital, Clark and blue nevi. Dermoscopic pattern is round scar exhibiting a central irregular pattern composed of atypical network, streaks, and globules.

Sclerosing nevi with pseudomelanomatous features present a recently classified entity simulating regressing melanoma induced by minor trauma on preexisting nevi.39-41 These nevi are typically found on the convex area of the back of young to middle-aged men.

Cockade nevi is characterized by a central pink to darkly pigmented, often papular portion, which is surrounded by an inner de-pigmented and outer, pigmented rim. Dermoscopic pattern of cockade nevus has been described only in a few cases according to the literature. All cases occurred in adolescents, revealing a darker, central globular or homogeneous pattern, lighter homogenous inner ring and a peripheral darker reticular ring.

Sutton nevi (Halo nevi) are congenital/acquired, monomorphous, brown to gray nevi surrounded by a depigmented ring (halo), dermoscopically presenting with a globular pattern and blue pepperlike granules and additionally white scar-like regions.

Meyerson's nevi (eczematous nevi) is defined as an eczematous halo surrounding a melanocytic nevus.42 Eczematous nevi show a predilection for young healthy adults Targetoid hemosiderotic nevi Targetoid hemosiderotic nevi are due to trauma and present as elevated nevi surrounded by an asymptomatic, ecchymotic, violet halo.42 They most frequently occur on the upper thorax of children and adolescents.

Desmoplastic nevi: Desmoplastic nevi present as flesh-colored or slightly pigmented papules/nodules of less than 1 cm, commonly located on young adults' extremities.

Balloon cell are histopathologically diagnosed due to their typical large, vesicular, clear melanocytes. They most commonly present as brown papules or polypoid lesions on the head/neck, trunk and extremities during the first three decades of life. Dermoscopically, numerous white globular/clod structures correlate with the balloon cells in histopathology

Unclassifiable melanocytic lesions - This category refers to equivocal melanocytic lesions, for which a confident diagnosis between surely benign or malignant cannot be made and which cannot be classified into one of the categories described above. These are lesions in the gray zone benign–malign from a clinical, dermoscopic and histopathological point of view.2 Common terms used for these lesions are superficial atypical melanocytic proliferations of uncertain significance, melanocytic tumors of uncertain malignant potential, atypical Spitz tumors, or spitzoid tumors of uncertain malignant potential

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ACNE: NON DRUG THERAPY APPROACH

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Acne vulgaris is a skin disorder affecting more than 85% of young individuals worldwide. It is not uncommon in adults either. Current first line treatment of acne vulgaris is the conventional pharmacological therapy including; keratolytics, topical or oral antibiotics, retinoids, and hormonal agents; but the use of this pharmacological therapy is not always satisfactory because of poor compliance of the patients, occurrence of side effects of drugs. Therefore, non-pharmacological treatment is developed as safe and effective options for treating acne vulgaris. They are applied either as independent treatment modality, an adjunct to pharmacological therapy, or as maintenance therapy. However sufficient evidence based support in the efficacy and safety of several non pharmacological therapies is lacking

The most commonly applied non-pharmacological therapies are diet control, counseling dermocosmetics, comedo extraction, chemical peels, platelets rich plasma (PRP), botulinum neurotoxin A (BoNTA), light-based therapy, laser and fractional microneedling radiofrequency. The most frequently reported sıde effects for non pharmacologıcal therapıes ınclude erythema, tolerable pain, purpura, edema, hyperpigmentation which were in most cases mild and transient.

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ALOPECIA: NON-DRUG THERAPY APPROACH

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Firstly, as we all know alopecias are generally divided into two groups: non cicatricial alopecias and cicatricial alopecias. Luckily non-cicatricial alopecias are more common and the most common is androgenetic alopecia. However, although it is less common, cicatricial alopecias are important and in a sense urgent as they cause irreversible alopecia. Medical treatments currently available for alopecias have their own limitations including need of continuous use, non-compliance of patients, possibility of relapse and possible side effects.

Thus, in my presentation I will try to mention some of the non-drug therapeutic approaches for alopecia. I will especially focus on low-level light therapy (LLLT), lasers and other light sources, platelet rich plasma (PRP) injections, microneedling, mesotherapy and nutritional supplements.

LLLT devices have been used to induce a variety of benefits for skin diseases. The reported biological effects include anti-inflammation, pain reduction, wound healing, anti-edema, immunomodulation, and increased local blood circulation. It has been proposed that LLLT increases the number of the hair follicles and hair tensile strength through improved microvascular circulation, reduced inflammation, and increased cell energy. Furthermore, LLLT can stimulate anagen re-entry in telogen hair follicles, prolong the duration of the anagen phase, increase the rates of proliferation in active anagen hair follicles and prevent premature catagen development. The wavelength used in most of the studies fall between 630 nm and 660 nm. According to the recent meta-analysis LLLT can improve hair density in both men and women with no significant difference between genders. Both the helmet-type and comb-type LLLT devices were effective. The effect of hair growth in long-term course treatment (> 20 weeks) versus short-term course treatment (16–20 weeks) was not significantly different, suggesting a treatment duration of 16 weeks by LLLT is sufficient to produce a therapeutic effect. Also their analysis showed that in contrast to high treatment frequency (> 60 min/week), low treatment frequency (<60 min/week) had a more significant improvement in hair density. It has been also tried in scarring alopecias recently (1,2).

The 308-nm excimer laser/light (EL) treatment emits high-energy monochromatic light of wavelength similar to that of the NBUVB peak. Therapeutic effects are due to cutaneous immunosuppression (like NBUVB) and anagen induction (activation of the β-catenin pathway) for hair disorders. In the studies examining excimer laser in alopecia areata: Hair regrowth was observed in all patients with partial AA, but not in those with AU or AT. Hair regrowth occurred only on the irradiated patches, ruling out the possibility of spontaneous remission. Excimer lasers have limited efficacy for AA affecting the beard and extremities similar to the severe forms (AT, AU). Treatment was well-tolerated, with side effects limited to mild peeling of skin, erythema, hyperpigmentation, and itching (3).

PRP is a preparation of concentrated platelets of plasma obtained by the centrifugation of the venous blood. We know that different alopecia types includes modifications to two sorts of hair stem cells, which are the hair follicle stem cells (HFSCs) and the dermal papilla cells (DPCs). PRP is suggested to show its efficacy via its indirect effects on these stem cells. PRP stimulates extracellular signal-regulated kinase (ERK) and Akt signaling and upregulate the FGF-7 and Beta-cathenin. These molecules then prevent apoptosis, facilitate cell growth and prolong survival of hair folliciles and promotes faster telogen to anagen transition with increased proliferation of dermal papilla cells. In the literature, PRP is effective in treating AGA, especially in men. It increases hair density in men and increases hair diameter both in men and women. It is more effective in early stages of AGA (<IV on the Hamilton-Norwood scale) and more effective when the alopecia is recent. Recent metaanalysis recommended having 2 to 4-times platelet concentration in PRP, minimizing red and white blood cells, and

suggested subdermal injections of 3 to 4 sessions of PRP at 1-month intervals followed by a maintenance regimen of 2 to 4 times per year. The authors also recommend 0.3 to 0.5-mL injection volume, and 1 to 2.5-cm space between injections in the affected area, depending on the volume of PRP (4). PRP does not provide persistent results in alopecia areata. Recently there has been also some reports regarding PRP use in scarring alopecia. PRP might be offered in scarring alopecia especially if other conventional therapies have failed. Physicians should consider to examine the patient for the presence of autoimmune markers, exclude an existing autoimmune disease and careful follow-up is needed for any exacerbation (5).

Microneedling is a minimally invasive procedure involving the induction of percutaneous wounds with medical

grade needles. Releases of PDGF and VEGF to promote wound-healing responses, improving angiogenesis, and attenuating or partially reversing fibrosis are the main mechanism of action for microneedling.

It also enhances transdermal delivery of topical drugs, promote anagen-initiating Wnt/bcatenin signaling, and improve dermal papillae stem cell proliferation when used for alopecias. It could be used as a standalone and adjunct therapy for hair loss disorders (6).

Nutritional supplements; given the limited regulation of the supplement industry, it is utmost importance that physicians educate patients about the difference between evidence-based treatments and marketing claims. The recent systematic review published in JAMA Dermatology suggested that highest-quality evidence was only shown with some brands and nutritional supplements such as Viviscal, Nourkrin, Nutrafol, Lamdapil, Pantogar, capsaicin and isoflavone, omegas 3 and 6 with antioxidants, apple nutraceutical, total glucosides of paeony and compound glycyrrhizin tablets, zinc, tocotrienol, and pumpkin seed oil. Kimchi and cheonggukjang, vitamin D3, and Forti5 showed low-quality evidence for disease course improvement. Thus, physcians should be careful regarding their suggestion of supplements.

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CHRONOTHERAPY IN DERMATOLOGY

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Chronotherapy is the administration of a treatment at a certain time to increase the effectiveness of the treatment by both increasing the effect of drugs and reducing their side effects.

It is generally based on the circadian rhytm. The circadian rhythm is described as the body's endogenous 24-hour physiologic, metabolic, and behavioral actions that repeats regularly .

Drug therapy is affected by circadian rhytm in terms of its absorption, distribution, target expression, drug metabolism, additional mechanisms of drug resistance, and drug elimination.

Physical, mental, and behavioral changes that happen in the body consitute the components of circadian rhytm that could influence the drug metabolism positively or negatively.

The specific timing of administration of a drug may more positively affect drug availability, increase the desired therapeutic effect, or reduce the likelihood of adverse side effects, through the action of these circadian components (1).

The first chronotherapy experiments were published in the 1970s. Haus et al found that, instead of giving equal doses , chemotherapeutic treatment given in sinusoidally increasing and decreasing 24-hour courses, the largest amount being given at times of peak host resistance to the drug, prolonged the survival in leukemic mice. (2).

Later studies have found that chronotherapy is effective not only in cancer but also in many other diseases. (3).

In laboratory animals, researchers have shown that the tolerability of many cancer drugs varies by up to 50% depending on the time of administration in relation to the circadian rhythm, and that the dose can be increased at certain times without increasing side effects. (4).

In a Lancet article, an interesting finding has been published by researchers in France . Patients who require heart surgery due to aortic valve replacement were randomly selected to undergo surgery either in the morning or in the afternoon. Major adverse cardiac events were found to be lower in the afternoon surgery group than in the morning group (5). This finding showed that even intervention time dramatically affected treatment success.

As an another striking observation, statins used to reduce cholesterol levels have been shown to be more effective in they are taken in the evenings . This finding was attributed to the fact that an enzyme working against statin metabolism is in peak level during the nighttime hours (6). It seems logical to deliver drug when the targets around are abundant.

Drug doses are already adjusted according to the body weight of the patient. In fact, the timing of drug administration is an important issue that needs to be addressed (6)..

In one of the early studies that addressed the chronotherapy in dermatological diseases, Yosipovitch et al pointed out that topical medications and skin care products should be recommended at optimal times of the day.

Sunscreen products should be given during the day whereas DNA repair enzyme agent at night , compatible with circadian rhythm of the body clock. A regular and adequately long sleep is particularly important in preventing DNA damage to the skin cells as DNA repair mechanism works best during sleep where melatonin secretion is high (7).

Skin permeability is higher in the evening than in the morning,thereby causing more transepidermal water loss.This can explain why itching is more common during evenings as itching is often related to dry skin (7,8).

Thus, many topical agents including moisturizers and topical steroids might be more beneficial when used in evenings. Discovery of this finding could lead to better results in the treatment of steroid-responsive dermatoses and skin conditions that need moisturizer.

Late afternoon and night are the hours when the blood flow is relatively higher and therefore the passage of drugs increases. The possibility of systemic effects in the treatments applied during these hours is also high (9).

It has been reported that psoriasis is more common in night workers, and melatonin levels are also found to be low in patients with psoriasis . Moreover, circadian oscillation of vascular endothelial growth factor A (VEGF-A) in epidermal keratinocytes has been proposed in the pathogenesis of psoriasis.This novel approach offers a chronotherapeutic potential based on the VEGF-A rhythmicity (10).

It's like we've just started the game in terms of the chronotherapeutic approach in medicine, including dermatological diseases.

There is still a long way to go for this. Because, how distinct tissues in each individual will react to the components that constitute the circadian rhythm should be determined by gene studies.

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URTICARIA AND MICROORGANISMS: MYTHS AND FACTS

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Urticaria is a hard challenge to dermatologists and allergists because of the complexity of etiologic factors.

The relationship between urticaria and microorganisms has often been examined, and some specific bacteria, viruses, and parasites have been found in previous studies. While the infectious agents in acute urticaria are more acute infections, those in chronic urticaria are more insidious and chronic infectious agents. Prominent among these are H. pylori, streptococci, mycoplasma Salmonella Brucella, and borelia from bacterias, Anisakis, Ancylostoma, Strongyloides, Filaria, Echinococcus, Trichinella, Toxocara, and B. hominis from parasites, and picornavirus, coronavirus, respiratory syncytial virus, Hepatitis A, C, HIV, Coronavirus and vaccines from viruses.

Another important reason may be changes in the gut microbiota. Gut microbiome consists of a core microbiome and a variable microbiome. An imbalance in the composition, or loss of function is called dysbiosis. The relationship between dysbiosis and CSU has been examined in the literature. The studies on CSU patients showed predominantly beneficial bacteria was decreased (Firmicutes, actinobacteria and bacteroides), while that of opportunistic bacteria was increased (Enterobacteria and Proteobacteria). There is limited number of studies about skin microbiome

A study from Russia, they found High frequency of S. aureus on both affected and non- affected skin areas in children with acute urticaria is a predictor of the disease severity.

WET WRAP THERAPY IN ALLERGIC SKIN DISEASES

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Wet Wrap therapy (WWT), is generally defined as a treatment modalitiy using layers of tubular bandages, cotton clothing together with a topical medication. There are several treatment protocols regarding these topicals. Emollients only or diluted or non-diluted topical corticosteroids are either applied on lesional skin or the entire body surface(1, 2). After application of these topicals, two layers of cotton bandages or garments; a wet inner layer and dry outer layer are used to cover body surface(3).

Wet dressings have been utilized since the 1930's for pruritic dermatoses in Mayo Clinic (1). However a detailed case series regarding wet therapy was first published in 1991 by Goodyear et.al. in pediatric patients with Atopic dermatitis (AD) claiming wet wrap as an effective treatment method for acute eczematous dermatitis(4).

WWT, has antiinflammatory, cooling and antipruritic properties on the skin. Pruritus is reduced by cooling through vasoconstriction(2). However exact mechanism of action of WWT is not yet well studied. In a study investigating mechanism of action of the WWT which only wet wrap without any emollient or topical corticosteroid was applied to patients with AD, it was shown that WWT was associated with the recovery of epidermal barrier. This effect of WWT was occurred by the release of lamellar body together with the restoration of intercellular lipid lamellar structure(5). Another proposed mechanism of action is whether there is an increased absorption of steroids by WWT, however future studies should be done to assess this effect(1). Also it acts as a barrier against scratching.

It is utilized to treat various pruritic conditions including atopic dermatitis, non-specific dermatitis, psoriasis, cutaneous T cell lymphoma, prurigo nodularis and pityriasis rubra pilaris(1, 2). WWT is mostly used in severe and/or refractroy AD patients(1-3, 6). According to European guidelines for AD, WWT is recommended for the moderate AD in addition to other treatment modalities including topical tacrolimus, topical class II or class III glucocorticosteroids or phototherapy(6). Patients with acute, oozing and erosive lesions and who do not tolerate standart topical application or whom systemic treatment can not be used, can be treated with WWT until the oozing stops(6). It can be used up to 14 days with diluted topical corticosteroids but mostly preferred 3 days for acute critical lesions. However, WWT protocol is not standardized yet. There are wide variations in WWT methodology from center to center or country to country. It includes using water or not, applying topical corticosteroids or nonsteroidal topical preparations including topical calcineurin inhibitors, difference in the potency of the topical corticosteroids, applying only emollients and using only a wet wrap without either topical medication or moisturizer(2).

There are various studies comparing the efficacy of WWT with standart regimens. A recent metaanalysis revealed that there is only low quality evidence that WWT is more effective than standart treatment with topical steroids(3).

Possible side effects related to WWT were evaluated in 3 categories in the literature. These include expected discomfort including chills due to using moist bandages, skin infections and possible systemic effect of topical corticosteroids(1, 3, 7). There is conflicting data regarding increased skin infection due to occlusion. Mostly folliculitis, impetigo, furunculosis, pseudomonas infection and herpes virus infections are reported as cutaneous infections(1-3). According to a metaanalysis, increase in these mild infections is nonsignificant(3). In a study investigating the effect of short contact WWT with topical steroid on the hypothalamic-pituitary-adrenal axis, temporary adrenal supression was shown which eventually resolve even with ongoing topical steroid use(7).

In conclusion WWT, can be considered as a treatment option ahead of systemic therapies for patients who do not respond conventional topical therapy.

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ACNE ISOTRETINOIN THERAPY

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Acne vulgaris is one of the most common skin diseases in the world, affecting more than 80% of adolescents and young adults. (1) It is a chronic inflammatory disease of the pilosebaceous unit and can have a different clinical picture. In many cases, acne leaves scars, which is a big problem for patients and the doctors who treat them.

Also, like many other skin diseases, acne significantly impacts sufferers' quality of life, affecting their self-confidence, daily activities, social life, and interpersonal relationships due to its visibility.

Acne therapy depends on the clinical picture and severity of symptoms. It can be divided into topical treatment (retinoids, benzoyl peroxide, and antibiotics) in mild cases and systemic therapy (oral antibiotics, hormones, and isotretinoin) in moderate to severe cases. Each type of therapy is directed toward different pathogenetic mechanisms of acne.

Current European guidelines (2) strongly recommend oral isotretinoin in moderate or severe papulopustular/nodular acne at lower doses and in acne conglobata at a dose of ≥ 0.5 mg/kg/day. Systemic therapy, including isotretinoin, is not usually recommended for mild-to-moderate papulopustular acne (3).

The U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) both approved oral isotretinoin (13-cis retinoic acid), a natural vitamin A metabolite, for the treatment of acne vulgaris in 1982 and 1983, respectively. Strong biological activity and low binding affinity for retinoid receptors are two characteristics of isotretinoin, which converts quickly inside cells to all-trans retinoic acid. In addition to reducing Propionibacterium acnes, inflammation, and hyperkeratinization in the pilosebaceous unit, it suppresses sebocyte proliferation, differentiation, and lipid production in vivo and in vitro. (4).

According to the extensive systematic review (5) that comprised 11 randomized controlled trials published up to 2016, oral isotretinoin for acne is effective and safe. Compared to the control group (placebo, systemic antibiotics, or another control arm), there was a clinically significant reduction in acne lesions with isotretinoin in all investigations. According to reports, the frequency of adverse events associated with isotretinoin was twice as high as for the control group. More than half of the negative side effects had to do with the skin and were linked to xerosis. Stevens-Johnson syndrome, cheilitis, xerosis, acne flare-up, photophobia, an increase in liver enzymes, a decrease in appetite, headaches, and depression were among the side effects that prompted the withdrawal of isotretinoin.

Although this drug has been used for many years, various questions are still being asked about it today. (6). There are many algorithms and guides for the use of isotretinoin. However, there are still different opinions regarding the daily dosage, cumulative dose, time of mandatory laboratory monitoring, the age at which you start therapy, and the duration of treatment. There are also concerns about the association of isotretinoin with depression, inflammatory bowel disease, and other conditions. As the drug exhibits teratogenic properties, there are also questions related to the duration of contraception and possible pregnancy after therapy. When many aesthetic procedures exist, there is also the question of whether they are possible during isotretinoin therapy and, if so, which ones to choose and at what time.

Given the need for more consistency in the recommendations made by different standards, it is impossible to make a firm conclusion on the indication of isotretinoin for acne. The inconsistent application of classification methods for acne is a significant drawback. According to European and US recommendations, the daily dose is between 0.3 and 0.5 mg/kg and up to 1 mg/kg. Only the European recommendations and the consensus of Gollnick et al. (7). prescribe a defined length of treatment of 16–24 weeks and at least six months. All recommendations state that rigorous pregnancy prevention methods are necessary. The European, French, and AAD recommendations advise monitoring for depressive symptoms. The age indication, the proposal for a cumulative dose, the timing of procedures, the connection between isotretinoin and IBD, the guidance for preventing acne flare-ups, and appropriate laboratory monitoring are all essential clinical questions inconsistently addressed in guidelines. Since these issues are frequently mentioned explicitly in routine clinical practice, they should be included in the guidelines' recommendations.

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DIET AND INFLAMMATORY SKIN DISEASES

Gökşen Ertuğrul

Diet has a vital role in the maintenance of particular skin pathologies. A well-balanced diet can reduce the costs of chronic disease care while also reducing the risks of complications (1).

Acne

Its shown that the intake of a low glycemic index diet in adolescents and young adults resulted in a significant improvement in acne severity (2). The incidence of acne has been found to be low in cultures with a Paleolithic diet. The Mediterranean diet, rich in vegetables, fruits, antioxidants, unsaturated fatty acids (FAs), and low GI foods, has a protective effect against the development of acne. Regular fish intake has also been reported to reduce acne (1). Studies have shown that acne patients may have a significant deficiency of vitamin D and zinc as compared with controls who have healthy skin. It has been shown that vitamin B12 supplementation in patients reduces the expression of vitamin B12 synthesis genes in Propionibacterium acnes, causes changes in the skin microbiome, and ultimately leads to porphyrin production and triggers acne (2).

Rosacea

Hot foods, alcohol, spices containing capsaicin, pepper, hot sauce, and foods such as tomatoes, citrus fruits, cinnamon, and chocolate containing cinnamaldehyde may cause clinical exacerbation. In a randomized, controlled trial in patients with ocular involvement, supplementation with 325 mg of eicosapentaenoic acid (EPA) and 175 mg of docosahexaenoic acid (DHA) twice daily for six months resulted in objective improvement in ocular symptoms (1).

Hidradenitis Suppurativa (HS)

Dietary habits may contribute to increased obesity, a preventable risk factor, which may trigger and exacerbate HS lesions. Dairy and high-glycemic foods have a role in triggering the androgen-mediated follicular obstruction underlying the pathogenesis of HS. Therefore, restriction of dairy products provides an improvement in HS symptoms (3). Fruits, vegetables, chicken meat, and fish seem to improve the symptomatology of HS. It has been reported by observational and case-control studies that the severity of the disease is lower in HS patients following a Mediterranean diet. Supplementation of vitamin D, riboflavin, turmeric, and zinc gluconate has been associated with improvement in HS symptoms. Omega-3 FAs are thought to play a role in reducing inflammation in HS. Saccharomyces cerevisiae is an important yeast species used in making beer, wine, cakes, and bread. Of 37 patients on the yeast exclusion diet, 26 (70%) reported an improvement in HS symptomatology without further treatment. In a multicenter study investigating the effect of intermittent fasting during Ramadan on HS patients, a statistically significant decrease was found in the severity of the disease, although there was no significant change in body weight (4).

Psoriasis

Dietary saturated FAs represent a major risk factor for psoriasis exacerbation. In psoriasis patients, the serum levels of free FAs were associated with disease severity. The diet for patients with psoriasis should be rich in omega-3 FAs, while omega-6 FAs should be limited. Low intake of dietary fiber is associated with the development of psoriasis. In addition, a high-fiber diet reduces the severity of skin scores in patients with psoriasis. The Mediterranean diet is an effective anti-oxidant diet, which was inversely correlated with inflammatory markers and psoriasis severity. It is recommended that patients with psoriasis choose food products with a low glycemic index or load. It is known that a diet rich in vegetables and fruit may significantly contribute to improving the clinical condition of persons suffering from psoriasis. Some authors draw attention to the positive impact of a vegetarian diet on the course of the disease in patients with psoriasis. Recent reports indicate that a low-calorie ketogenic diet can reduce the severity of clinical symptoms and even inhibit psoriatic disease triggering (5). The gluten-free diet appears to be definitively beneficial in patients with psoriasis and confirmed celiac disease. The Medical Board of the National Psoriasis Foundation suggested a 3 months trial of a gluten-free diet as an adjunct to standard medical therapy in adults with psoriasis who test positive for serologic markers of gluten sensitivity (6). There are studies reporting clinical improvement with vitamin D treatment in psoriasis (5). Reliable data on nutritional supplementation, which has prompted doctors to recommend supplements such as fish oil, selenium, and vitamin B12 for psoriasis, is still absent (6).

Atopic Dermatitis (AD)

If there is a food allergy that can be tested by skin prick test and serum IgE values, food avoidance behavior should be adopted. An elimination diet in infants and children under age three is most effective. By elimination diet, significant reductions in food-specific IgE levels and a reduction in symptoms are seen when patients avoid foods they are allergic to. In adult people, it is recommended to investigate food allergies only with severe or resistant AD. In children, non-specific food restriction could lead to growth alteration without benefit to AD (6). In a systemic review maternal consumption of the Mediterranean diet, was associated with a lower risk of allergic disease in their children. In a meta-analysis study, it was reported that evening primrose oil supplementation containing linoleic and linolenic acids showed beneficial effects on AD (7). Although ω-3 and ω-6 FAs appear to be ineffective in preventing disease, they may provide some benefit when used to reduce disease severity alongside vitamin A and C supplementation in selected populations (6). In a study of adult 118 patients with recalcitrant AD, drinking oolong tea three times daily after meals were associated with a marked-to-moderate improvement in 63% of participants (8).

Dermatitis Herpetiformis (DH)

As a specific manifestation of coeliac disease, a lifelong gluten-free diet, is the first-choice treatment for DH. However, months or even years are needed before diet alone can control the dermatologic manifestations, especially itching. Iodine is a mineral found in seaweed, fish, and dairy products and added to table salts, and is among the triggering factors for DH (9).

Vitiligo

Gluten elimination may be beneficial in patients with both vitiligo and celiac disease, but further and more robust studies are currently needed to consider it as a treatment option. Patients with vitiligo consume more saturated FAs and less polyunsaturated fat than unaffected patients, increased fat intake has been associated with the onset of vitiligo (10). In one study, repigmentation developed in 94.7% of patients treated with UVA combined with 50 mg/kg/day l-phenylalanine. A superior improvement was observed in vitiligo patients treated with topical corticosteroid combined with 440 mg oral zinc daily compared to those treated with topical corticosteroid alone. Antioxidant-acting alpha-lipoic acid, vitamins C and E were used in combination in vitiligo patients receiving NB-UVB phototherapy and provided superior benefit compared to placebo (6).

Alopesi Areata (AA)

The Mediterranean diet, rich in raw vegetables and fresh herbs, or a high protein diet is a potential treatment for AA. Low serum ferritin and zinc are more prevalent in patients with AA. A gluten-free diet may be a beneficial treatment for AA patients with celiac disease. Some components of the metabolic syndrome are more frequently encountered in patients with AA. The risk of developing AA was found to be less in people following a soy-based oriental diet (11).

Pemphigus

The main foods that trigger pemphigus are garlic, leeks, onions, chives, and shallots, which are vegetables containing thiol and allium. In addition, foods containing polyphenols, black pepper, cherry, mango, cashew, red wine, tea, vanilla, cocoa, and tomato containing cinnamic acid have also been reported to trigger pemphigus (9).

Seborrheic Dermatitis (SD)

In a study conducted on 4300 SD patients, it was shown that the risk of disease decreased with a fruit-rich diet and increased with a Western diet. Biotin deficiency is commonly implicated in hair and nail disorders, including seborrhoeic dermatitis (1).

Allergic Contact Dermatitis

Contact dermatitis and nickel allergy are more common in patients with non-celiac wheat sensitization than in subjects with functional gastrointestinal disorders. Nickel can be found in wheat and results in systemic nickel allergy syndrome. Nickel allergy should be evaluated in patients with cutaneous manifestations after wheat ingestion. Other nickel-rich foods include chocolate, legumes, shellfish, nuts, and canned foods (12).

Urticaria

In a study conducted with 79 children with chronic urticaria, celiac disease was detected in 4 children. It was reported that

remission of urticaria developed in 5-10 weeks in these children with gluten-free diets and serological markers disappeared in 5-9 months (13).

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IVIG TREATMENT IN DERMATOLOGY: DOES IT WORK?

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Intravenous immunoglobulin (IVIg) is a solution of human plasma-derived IgG, salt, sugars and solvents. It has been used to treat a multitude of dermatological diseases safely and successfully in which immune system plays a prominent role. It is generally used in 2 g/kg doses, over 3-5 consecutive days in dermatological indications.

Main Indications of Intravenous immunoglobulins in Dermatology

Kawasaki disease

IVIg is indicated in children with Kawasaki disease to prevent coronary artery anormalies. It improves the severity of coronary lesions but does not protect from long term development of coronary artery lesions.

Dermatomyositis

Dermatomyositis is one of the conditions in which there is the highest level of evidence for IVIg use. It is generally used as a second line treatment if corticosteroid therapy had failed or could not be used because of the side effects. But it can be used as a first line therapy in patients with a fulminant course, severe myoliysis or paralysis. Also it is particularly of use in patients who have an associated malignancy to reduce the need for an immunosuppressive medication.

Autoimmune Blistering Diseases

IVIg has been used in pemphigus vulgaris and foliaceus, bullous pemphigoid, epidermolysis bullosa acquisita and mucous membrane pemphigoid patients with good therapeutic response. It has also been used in linear IgA disease, IgA pemphigus and paraneoplastic pemphigus. It is used generally in severe forms and forms refractory to systemic corticosteroids in combination with immunosuppressants. It is also a good option in pregnant patients beacuse of the therapeutic limitations associated with pregnancy

Toxic Epidermal Necrolysis/Stevens Johnson Syndrome

In some recent metaanalyses of patients with toxic epidermal necrolysis and Stevens Johnson syndrome IVIg therapy in combination with systemic corticosteroids were found to reduce the mortality predicted by SCORTEN**.** A total dose of 3 g/kg is generally recommended in the early course of disease in order to prevent epidermal detachment.

Scleromyxedema

IVIg is recommended as a first line treatment in severe scleromyxedema because of the unsatisfactory response and associated morbidity of alternative treatments.

Other Dermatological Indications

Other possible treatment indications of IVIg therapy in dermatology includes atopic dermatitis, autoimmune urticaria, garft-versus-host disease, pyoderma gangrenosum, cutaneous lupus, systemic vasculitis and livedoid vasculopathy.

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BIOLOGICAL TREATMENT RESPONSE ACCORDING TO HLA TYPES

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Psoriasis is a chronic, inflammatory skin disease, characterized by scaly plaques. Numerous genes have been implicated in pathogenesis of psoriasis to date. These genes include different functions that can be sorted as antigen presentation (HLA-Cw6, ERAP1, ERAP2, MICA), the IL-23 axis (IL12Bp40, IL23Ap19, IL23R, JAK2, TYK2), T-cell development and T-cells polarization (RUNX1, RUNX3, STAT3, TAGAP, IL4, IL13), innate immunity (CARD14, c-REL, TRAF3IP2, DDX58, IFIH1), and negative regulators of immunity (TNIP1, TNFAIP3, NFKBIA, ZC3H12C, IL36RN, SOCS1).

Within antigen presentation-related genes, HLA-Cw6 encodes a major histocompatibility (MHC) I and is located at PSORS1 at chromosomal position 6p21.3. There are three major MHC class I genes in HLA: A, B, and C. The class I HLA gene HLA-C In particular, the HLA-C*06:02 allele (about %50 increased risk) has a strong relationship with vulnerability to psoriasis.

Considering the information above, it has been proposed that specific genes can influence the treatment response of biological agents. In this context, it has been reported that there is a better response of the anti-IL-12/ IL-23p40 drug ustekinumab and anti-IL-17 agents with HLA-Cw6 allele. Similarly, it has been reported that anti-TNF agents were more effective in HLA-Cw6-positive patients, even though there are some conflicting results. Moreover, Dand N et al. found that HLA-Cw6-negative patients better respond to adalimumab than to ustekinumab. Lastly, a recent study reported that IL-23 inhibitors are highly effective in treating plaque-type psoriasis regardless of the HLA-cw6 genotype. These aforementioned results show us certain genes may play an important role in the prediction of treatment response. Further studies are required in order to find the exact association between HLA gene polymorphism and the treatment response of psoriasis.

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REAL LIFE DATA OF BIOLOGICS FOR PSORIASIS

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Randomized controlled trials are appropriate designs to evaluate the efficacy, safety, correct dose, and duration of dose intervals of treatments. They are the golden standard for evaluating new therapeutic molecules as confounding factors are removed. However, patients encountered in clinical practice are mostly those who do not meet the inclusion criteria in randomized controlled trials due to many factors such as age distribution and comorbidities. Real-life evidence's importance has been increasing in recent years, as real-life data evaluate the efficacy and safety of the drug in these more heterogeneous groups rather than a selected, relatively homogeneous population in clinical trials (1) They complement information on both the efficacy and safety of biologic therapy.

A variety of biologics are currently available for the treatment of psoriasis. Since anti-TNF agents and ustekinumab are biologic agents that have been used in the treatment of psoriasis for many years, a large number of real-life data are available, including efficacy, safety, drug survival rates, and long-term outcomes. In addition, after Secukinumab's license approval in 2015, researchers have published several real-life evidence studies of secukinumab from major national registries, and an increasing number of independent real-life studies (2) Real-life data on the efficacy, safety, and drug survival of Ixekizumab, another IL-17 inhibitor approved for the treatment of psoriasis in 2016, have been increasing (3). Since guselkumab was the first approved IL-23 inhibitor, there have been several real-life data on its efficacy and safety (4). Risankizumab, on the other hand, does not have enough long time real-life data yet, as it is the last approved IL-23 inhibitor.

Interleukin(IL)-17 and IL-23 inhibitors showed higher efficacy than TNFi and IL-12/23i in clinical trials, increasing the treatment goal from psoriasis area severity index (PASI) 75 to PASI 90 and even to PASI 100. Although real-life data support these findings, studies with high populations that directly compare the therapeutic efficacy, safety, and drug survival of these biologics are still needed (5)

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IMMUNOGENICITY OF BIOLOGIC

Zuhal Metin

introduction

Biologics are substances whose active component is derived from a biological source using biotechnology by recombinant DNA techniques. They have pharmacological effects to mimic normal human proteins or interact with circulating proteins or cellular receptors for treatment. They hold a great deal of promise among the therapeutic interventions for a wide range of disorders, including cancer and inflammatory diseases.We will be focus on biogenicity of biologıc agents in this chapter.

Material and Metods

The immunogenetics of biological agents were searched and compiled from literature review from pubmed,clinical key, up to date and comprehensive drug therapy dermatological textbook sections.

Discussion

Biological agents are divided into 3 groups in terms of structure content non-human origin, partial human-sequence, complete human-sequence. Structures and antigenicity of biological agents can trigger immunologic reactions. Immunogenicity is defined as the propensity of the therapeutic biologics to generate immune responses to itself and to related proteins or to induce immunologically related non clinical affect or adverse clinical events. It is complex phenomenon that depends on the interplay between several drug- and patient-related factors (including sex, comorbid conditions, and ethnicity). Repetitive administration of these protein-based therapeutics to immunocompetent patients elicit immune responses and trigger the production of anti-drug antibodies (ADA) or cell-based immune responses.

According to studies in the literature, immune reaction to an exogenous version of an endogenous human protein or failure of immune tolerance to self-antigens are also trigger the development of ADA. Antigen recognition and biological presentation are important aspects in the development of biological agent immunogenicity. Evidence from many studies of biologic agents demostrate that immunosuppressive/anti-proliferative therapy (Combining methotrexate, azathioprine, leflunomide or mycophenolate) reduces ADA levels and immunogenicity due to the immunosuppressive effect of these drugs.

Result

The presence of ADAs may be associated with some clinical consequences: reduction in therapeutic efficacy, increased risk of adverse events, hypersensitivity reaction, IgE-independent anaphylactic reactions.

Conclusion

To know more about biological agents and their immunogenicity may provide essential information to clinicians that can potentially improve treatment, reduce risks and costs.

Keywords: ADA, immunogenicity, biologics

MYCOSIS FUNGOIDES: BEXAROTENE EXPERIENCES IN TURKIYE

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Mycosis Fungoides

Extranodal, insidious T-cell non-Hodgkin lymphoma.The primary disease is in the skin,

but in advanced stages, lymph node, blood and visceral spread may be present.

Staging

Early stage (IA- IIA); papule, plaque, plaques, visceral involvement ϕ

Stage IA

Less than 10% of the total body area is macular, plaque and papular MF lesion, and there is no lymph node and visceral involvement. However, if there are more than 5% Sezary cells, histopathologically folliculotropic and large cell transformed variant, more aggressive treatment is required. At this stage, skin-focused treatment is performed.

Stage IB/IIA

Stage IB Disease: Presence of macules, plaques and papules exceeding 10% of the total skin surface and absence of L.N or internal organ involvement.

Stage IIA Disease: Any size reactive palpable L.N. (N1) to macul, plaque and papular lesions of any size or isolated scattered L.N. Despite the neoplastic cell histology (N2), the nodal structure is preserved and the visceral tissue is not involved. More aggressive treatment is applied in stage IB/IIA patients if more than 5% of atypical Sezary cells (B1 disease), histological folliculotropic variant, or large cell transformed MF are present. Stage IB/IIA diseases are commonly treated alone or in combination with generalized skin-focused therapies.

Skin-focused treatments

Topical corticosteroids, Topical chemotherapy (nitrogen mustard or carmustine), **Topical retinoids**, Topical imiquimod, Local radiation (X-ray or electron beam), Phototherapy (UVB or PUVA)

Topical bexarotene

Bexarotene is a synthetic retinoid that selectively activates the retinoid X receptor subfamily of retinoid receptors. Topical bexarotene (1% gel) has been shown to be effective and generally well-tolerated treatment. Topical bexarotene response rates vary between 45-65% and provide complete remission in 20% of patients. Complete remission may take 12-16 weeks, with a median response time of approximately 2 years on continuous or maintenance therapy. Since topical bexarotene is a skin irritant, it is generally used in patients with less than 15% involvement.Retinoids can be used as a combination regimen agent or adjuvant therapy in primary refractory or advanced patients.In the phase 3 study, bexarotene-resistant or persistent early-stage disease was 62% and 50% successful in stage IA or IB patients, respectively, and stage IIA or IIB 3 patient did not respond to bexarotene treatment. Bexarotene gel has been approved by the FDA in the topical treatment of stage IA and IB CTCL in patients who are resistant or persistent or who cannot tolerate other treatments. Tazarotene gel was also used in the MF pilot study, but it could not get FDA approval because its effectiveness was not proven in clinical studies.

Application: 1% formulation. The dose intensity is changed by the frequency of administration. In general, bexarotene is applied to the lesions once at night for the first week and twice a day thereafter. If tolerated, it can be taken up to 4 times a day.

Toxicity: Topical bexarotene is generally well tolerated. It most commonly causes mild to moderate irritant dermatitis, itching, burning and skin inflammation. Systemic and topical forms are absolutely contraindicated in pregnancy. All retinoids are sun sensitive. Sun protective clothing and/or SPF creams should be recommended, especially if patient will be in the sun for a long time.

Bexarotene Studies

Topical bexarotene studies in Türkiye

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The Importance of Early Treatment in MF

In clinical studies, it is observed that bexarotene gel is effective in the typical treatment of stage IA-IB MF patients and is an important option in patients who are resistant-chronic and cannot tolerate other treatments.Topical bexarotene gel is generally well tolerated and can be added to conventional treatments with a flexible application regimen.It may be first-line therapy in patients with early MF. Further studies should be conducted on its combination with other therapeutic agents.It may be a new skin-focused drug that provides great convenience to both the patient and the dermatologist in early stage MF patients.

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DLQI IMPROVEMENTS AFTER ANTI-HS BIOLOGICS

Cahit Yavuz

Hidradenitis suppurativa (HS), also known as acne inversa, is a chronic inflammatory disease, characterized by recurrent painful nodules, abscesses and draining sinus tracts in primarily intertriginous areas. The prevalence of HS was estimated 0.4%, which varies among different geographic regions with a female preponderance in North America and Europe but a male preponderance in Asia. The pathogenesis of HS is multifactorial and not fully understood yet. HS has a devastating impact on quality of life (QoL). Patients suffer from social stigma, poor mental health, substance use disorders, relational issues and higher suicide rates compared with the general public.

Hidradenitis suppurativa can affect QoL in many ways and has consistently been shown to score very high on different health-related quality-of-life instruments. Patients with uncontrolled disease often suffer from pain, pruritus and odour production, which can lead to interference of daily functions and disutility. Pain and pruritus may impair sleep quality and duration, contributing to daytime dysfunction. As mentioned above, mental health issues, such as loneliness, low self esteem, anxiety and depression, also contribute to poor QoL for HS patients. Training of resilience has been suggested to help protect patients against worsening QoL due to progressive depression. Moreover, HS may have profound impacts on patients' sexual health, another crucial QoL aspect. Aside from sexual dysfunction, patients have reported lack of partner intimacy and sadly, even sexual assault. Pain is a challenging chronic symptom of HS, and studies show that it is still under-treated. It is both nociceptive and neuropathic in origin and might be influenced by HS severity, anxiety and depression. Friction, heat and psychological stress are common triggers.

Six retrospective controlled trials assessed the mean improvement of DLQI score in HS patients treated by adalimumab, with five showing significantly better improvement of DLQI score compared with placebo. Bimekizumab, guselkumab, and infliximab also showed similar results, while anakinra, apremilast, etanercept, and IFX-1 did not significantly differ from placebo. Tthe meta-analysis found adalimumab (RR 3.97; 95% CI 1.70–9.28, I2 = 0%, three RCTs) and bimekizumab (RR 15.23; 95% CI 0.95–242.79, one RCT) were both superior to placebo in achieving DLQI 0/1 but only adalimumab reached significant difference.

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APPROACH TO THE PATIENT WITH ATOPIC DERMATITIS

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Atopic dermatitis (AD), characterized by eosinophilic/spongiotic inflammation of the skin with characteristic age-dependent distribution patterns and morphology of lesions, is a chronically relapsing and intensely pruritic, Th2-driven skin disease often occurring in families with atopic diseases (AD, food allergy, bronchial asthma or allergic rhinoconjunctivitis). Its complex pathophysiology is based on several factors including genetic background, environmental factors, allergens, skin barier defects and reduced microbial diversity. Since the disease negatively affects patients' and families' quality of life, causes pshycosocial problems and an increased cost in healthcare, a holistic approach is necessary in the management of AD. The important steps in the evaluation of an AD patient is summarized below:

- History (age of onset, family history, treatment history, seveity, information on exacerbation periods etc.)
- Detailed physical examination
- Evaluation of phenotypic and morphologic features
- Etiologic and/or triggering factors
- Assessment of disease activity (scoring)
- Evaluation of atopic / non-atopic co-morbidities (and associated systemic diseases)
- Treatment plan

Phenotypic and morphologic features of AD patients should be rgarded for a reasonable therapeutic approach. These are as follows:

- *Acute vs. chronic AD*
- *Early onset, severe / persistent AD* with ichthyosis, keratosis pilaris and palmar hyperlinearity (FLG null genotype)
- *Intrinsic vs. extrinsic AD*
- *Adult onset AD*
- *Morphological variants:* Nummular eczema, atopic prurigo, lichen planus-like, pityriasis alba
- *Localized variants:* Hand eczema, head and neck dermatitis (HND), juvenile palmar and plantar dermatitis, eyelid dermatitis, cheilitis, nipple dermatitis, periorificial dermatitis.

It is well known that AD is associated with atopic comorbidities such as bronchial asthma, allergic rhinoconjunctivitis and food allergy. Recent findings have also revealed increased frequency of nonatopic comorbidities, including anxiety, depression, infections and cardiometabolic diseases. It is clear that atopic /nonatopic comorbidities should be incorporated into the evaluation and therapeutic management of all AD patients:

- *Atopic comorbidities*: Asthma, rhinitis, food sensitivity (severity of AD seems correlated with increased likelihood of atopic comorbidities)
- *Ocular comorbidities*: Allergic conjunctivitis, eye pruritus
- *Psychiatric comorbidities*: Depression, anxiety, suicidality and ADHD (depression: Particularly in moderate-to-severe AD /higher prevalance of parental depression)
- *Autoimmune comorbidities:* vitiligo (up to 10 fold), CU, Celiac disease, IBD, SLE and RA
- *Cardiovascular comorbidities*:Increased risk of hypertension and CVD in severe AD
- *Infectious comorbidities*: Increased occurrence of skin infections
- *Contact dermatitis and hand eczema*
- *Osteoporosis and fractures*

A good physician-patient (and family) relationship and frequent follow-ups seem reasonable for "treatment adherence" which is one of the most important points in AD. Structured written plans also may help especially for children and adolescents with AD.

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DUPILUMAB: WHAT IS NEW?

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Dupilumab is a recently developed monoclonal antibody that blocks signaling of IL-4 and IL-13, both of which are crucial cytokines in the T2 response. Dupilumab has been shown to significantly reduce disease severity, symptoms, and improve quality of life in allergic diseases. The safety profile of the drug is very good and the incidence of side effects is low.

Dupilumab is currently approved in the U.S., Europe and other countries around the world for use in specific patients with moderate-to-severe atopic dermatitis (AD) and and other disease in different age populations. Dupilumab has been approved by the U.S. Food and Drug Administration (FDA) for five indications; AD, Asthma, Chronic Rhinosinusitis, Eosinophlic esophagitis and now aprroved prurigo nodularis (PN). Also In dermatology, many disease such as bullous pemphigoid and chronic urticaria, which are resistant to standard treatments, are tried.

Dupilumab has been studied across 60 clinical trials involving more than 10,000 patients with various chronic diseases. In addition to the currently approved indications dupilumab in a broad range of diseases driven by type 2 inflammation or other allergic processes, Including prurigo nodularis and pediatric atopic dermatitis (6 months to 5 years of age), recently these are approved by FDA. Also bullous pemphigoid (Phase 3), chronic spontaneous urticaria (Phase 3), chronic inducible urticaria-cold (Phase 3), and other disease. These potential uses of dupilumab are currently under clinical investigation.

AD is one of the most common skin disorders in children. AD is a prevalence of 19% or greater in children younger than 6 years. AD begins before the age of 5 years in more than 85% of patients and persists into adulthood in half the cases. Although not recommended by multispecialty guidelines, glucocorticoids are the only approved systemic treatment for atopic dermatitis in children younger than 6 years. Dupilumab was approved in June 2022 by the FDA regulator for children in aged 6 months to 5 years with moderate-to-severe atopic dermatitis. The safety results of this pivotal trials were generally consistent with the known safety profile of dupilumab in atopic dermatitis. Infants/ Preschoolers (6 months – 6 years) Dupilumab was well tolerated and showed an acceptable safety profile, similar to results in older children and adults.

PN is a chronic condition that can cause painful, stinging lesions with intense itch mainly on arms, legs, upper back, lower back, chest, and/or abdomen. Although the cause of PN is not entirely understood. Dupilumab may help bring balance by controlling a source of unwanted inflammation under the surface to help keep you one step ahead of PN symptoms. Dupilumab is the first-and-only FDA-approved treatment proven to help reduce PN symptoms, on Semp 2022.

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OMALIZUMAB: WHAT IS NEW?

Assoc. Prof. Dr. Ragıp Ertaş

CSU and Autoimmunity is important on pathogenesis of CSU. There are 2 types Type one and Type IIb. Although the boundary between these two groups is not always clear, it is now known that omalizumab response and response rates are better in type 1.

In patients with CIndUs, the trigger may result in de novo synthesized autoantigen or (autoallergen), which is detected by IgE bound to skin mast cells, resulting in mast cell degranulation. In several subtypes of CIndU, for example, SD, ColdU, and solar urticaria, the disease is passively transferable by transfer of serum, with IgE being the suggested transferable serum factor. Because of these omalizumab should be effective in CINDUs. There are increasing number of publications on efficacy of omalizumab on CINDUs. Also with new publications we can predict the response or resistance to omalizumab treatment using clinical and laboratory characteristics of the patients with CSU.

The recommended and approved dose of omalizumab is 300 mg from the asteria ıstudy. With the 2022 update of the guide, Omalizumab ruitine dose and dose increasing or interval shortening is now in step 2. We know from recent publications about 70-80 % of patients who were AH resistant will be responder to OMA treatment. There are publications about dose can be increase upto 600 mg for 2 weeks . In a recent publication, Oma has protective effect on viral enfections as an indirect action. Recently, in an another study, authors showed during the oma treatment, about 1 of 4 of the patients stopped getting AH. Omalizumab treatment response in those with good response, AH drop-off rates are higher in Isolated CSU patients. Omalizumab is effective for severe allergic asthma. It is also indicated in nasal polyposis, bullous pemphigoid, virally induced asthma exacerbations, mastocytosis and food allergy. SLE may be a potential candidate for anti-IgE treatment. An initial clinical trial showed that patients treated with omalizumab showed significant improvement in disease activity scores. İnterestingly, There is a link between IgE and T reg cells. And recently Lopez Abente et. al. showed Omalizumab restores T reg homeostasis, and that this mechanism is associated with clinical improvement in asthma maybe in CSU. also suggests that anti-IgE therapy may also have a potential role in the treatment of other autoimmune diseases in which Tregs are involved.

SCLEROTHERAPY AND ND-YAG LASER IN THE REMOVAL OF VASCULAR CHANGES

Predrag Stilet

The procedure for removing medium and large capillaries as well as small and medium varicose veins can be treated in two ways: sclerotherapy and Nd-YAG laser.

Sclerosis or sclerotherapy is a suitable form of treatment for capillaries, reticular veins and spider web veins, as well as for the treatment of smaller varicose veins. The intervention is performed by injecting a sclerosing agent into the vein, which irritates the vein wall, leading to spasm of the blood vessel and its permanent closure. The injected solution can be in liquid or foam form

With the Nd-YAG laser, all blood vessels with a diameter of 0.5-2.5 mm are permanently removed so that the laser beam with a wavelength of 1064 nm passes through the skin, without damaging it, and is resorbed by the blood vessels, which leads to their permanent obliteration through the process of photothermocoagulation, which means that the light energy of the laser beam is converted into thermal energy, which causes blood vessel coagulation and permanently removes the treated capillaries

GUIDELINES AND RECOMMENDATIONS FOR THE HPV INFECTIONS

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Anogenital warts (condylomata acuminata) are the most common HPV-genital infections presented in men, however, during the last decade the other HPV-associated exaggerated lesions such as condylomata plana, penile, scrotal, and anal intraepithelial neoplasias, as well as the penile, tonsillar and oropharyngeal cancer have been studied a little bit more extensively. Consistent studies are still sparse for male population. More than 35 types of HPV infect the genital tract; types 16 and 18 inducing about 70% of high-grade intraepithelial genital neoplasias and HPV 6 and 11 causing 90% of anogenital warts. However, the "banality" of anogenital warts should not be underestimated providing that the high risk HPV DNA 16 and 18 can be isolated (PCR) from "benign" HPV-associated genital lesions in 10-20% of patients, i.e. more than it is usually expected. On the other hand, the presence and the recalcitrant course of HPV DNA 6 and 11 associated diseases represent a significant physical and psychological problem for both men and women.

A prophylactic vaccine that targets these types should thus substantially reduce the burden of HPV-associated clinical diseases. Ultimately, within the spectrum of therapeutic options for condylomata, no method is really superior to others; recurrences occurred in 30-70% of cases. However, the proactive sequential treatment representing the combination of the ablative and immunomodulatory treatment (imiquimod, sinecatechins) might be considered as treatment of choice today. We definitely need the HPV vaccination programme to get rid of one of the oldest and up to now unsolved problems of humankind. Managing both partners is necessary in order to eliminate the virus in the population. Approaches to this include prophylactic vaccines such as nonavalent (9-v) HPV vaccine for both men and women. This should be the only way to significantly decrease the numbers of infected persons. Besides, a proper dermatological training is required as the clinical criterion is still very important and the HPV-induced lesions are quite often misdiagnosed unless managed by the skilled professional. It can be thus concluded that the HPV-genital infections represent a significant dermato-venereological issue, and the dermatovenereologists should definitely be the part of the HPV vaccine programme team.

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Drug/ Medical Errors in Dermatology

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Abstract

Dermatology practice has become increasingly varied and complex, with more than 1,000 skin or skin-related conditions. These disorders range from benign, self-limiting dermatoses to fungal diseases, cosmetic skin problems, potentially life-limiting cancers, and chronic inflammatory skin disorders. Due to the recent advances in pathogenesis, the scope of dermatological therapeutics has significantly expanded over the past few decades. Considering the increasing frequency of referral to dermatologists, in addition to complex disease pathogenesis and new treatment modalities, unintentional medical errors can become a situation faced by many physicians. Medical errors are reported as approximately 5% in dermatology clinics, while 10-20% in other visual specialties. Moreover, nearly half of them are preventable.

'Primum non-nocere' describes an essential principle of medical ethics. Patient safety and prevention of harm are the primary focus of all healthcare disciplines. To overcome medical errors in dermatology, we need to understand the underlying causes, including technical/system and cognitive/thinking errors. Technical errors consist of incorrect lateralization (i.e., left vs. right), medication errors in dosage, frequency, route selection, prescription writing errors such as illegible handwriting, ambiguous abbreviations or unintended omissions, missing prescriber information (e.g., signature, license number), inappropriate administration mislabeled specimens with the wrong patient's name, incorrect placement or labeling of tests, and incorrect procedures related to biopsy specimen including staining, sectioning and placement to the medium. Most cognitive/thinking errors are due to cognitive deficiency rather than a lack of knowledge and mainly consists of diagnostic errors.

Overcoming medical errors needs teamwork among all healthcare professionals. First, checklists should be prepared for each medical and surgical procedure to minimize technical errors. During each visit, the visit should progress according to the relevant checklist. Electronic medical systems are also precious in preventing technical errors. Qualified training of the technical team and double-checking algorithm at every step has a critical role in minimizing technical errors. Diagnostic errors could be prevented by clear communication with the patient and the detailed medical anamnesis and by keeping the clinician's dermatological knowledge up-to-date. Clinicians should be able to individualize the treatments, explain the situation to the patient in case of possible undesirable side effects, and be ready for possible complication management.

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IMIQUIMOD - USES IN DERMATOLOGY

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Imiquimod is a local immunomodulator, which belongs to the imidazoquinoline amine family. It was first approved for use in 1997 by the old US Food and Drug Administration. It was first approved for the treatment of external genital and perianal warts, and then for the treatment of superficial basal cell carcinoma and actinic keratosis. The precise mechanism of action has not been clearly established. Imiquimod is thought to activate immune cells, by binding to a membrane receptor similar to the toll-like receptor and it induces the proliferation of B lymphocytes. Imiquimod activates macrophages that produce cytokines, which with imiquimod applied locally activates Langerhans cells, which activate the adaptive immune system.

Therapy should be tailored to each patient separately, taking into account: the type of skin disease, the number and distribution of changes, the morphology of the lesions, and the possibility of application by patients. Based on these facts, as well as the wishes of the patients, we recommend the use of imiquimod, the frequency of its application, and the duration of therapy.

The advantages of imiquimod compared to other methods of therapy are targeted therapy of lesions, simple and easy application, good cosmetic effect, effective treatment, and low recurrence rate.

For condyloma, imiquimod cream is applied three times a week, before bedtime, for up to 16 weeks. Best results after 4-6 weeks of therapy. In the case of basal cell carcinoma, it is applied once a day, 5 days a week, with a two-day break. The cream is left on the skin for about 8 hours. The duration of the application is 6 weeks. For the treatment of Actinic Keratosis, it is applied once a day before going to bed or daily three times a week for up to 4 weeks. If necessary, repeat the treatment for another 4 weeks. In case of side effects, the treatment can be stopped until the reactions subside.

Topical imiquimod should be tried as the first therapy, choice therapy, especially in the case of old patients, patients with other serious diseases, and patients who do not want surgery. Further studies are needed to show how imiquimod can be effective in other diseases.

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SKIN ANTIAGING STRATEGIES

Associate Professor Dr. Demet Akpolat, Clinic of Demet Akpolat

Skin aging is a complex biological process influced by a combination of intrinsic and extrinsic factors. Skin health and beauty are considered one of the principal factors representing overall ‘’well-being’’ and the perception of ‘’health’’ in humans; therefore, anti-aging strategies to combat aging signs and dysfunction have been developed over the last decades.

Preventive aesthetic dermatology might supplement the request of healthy aging, treat or prevent certain cutaneous disorders and delay skin aging combining local and systemic methods of therapy, instrumental devices and invasive procedures[1].

The mainspring of any anti-aging therapy is to achieve; healty, smooth, blemish-free, translucent, resilient skin. In clinical practice, ‘’to look better’’ does not mean to ‘’look younger’’. That is why it is so important to understand patients’ wishes and orientate them to achieve satisfyied outcomes by using all available treatment techniques[2].

Before choosing the strategy for each individual case; the age, previous procedures or surgery, general health status, type of the skin, style of life and many other factors should be taken into consideration[3]. The skin anti-aging strategies attemped to reverse the dermal and epidermal signs of photo and chronological aging can be grouped under the following 5 approaches; Cosmetic care, topical medicine agents or topical agents, systemic agents, invasive procedures and avoiding of exogenous factors of aging, correction of life style and habits.

Aesthetic dermatology should be contribute to ‘ healty aging’ not only in cosmetic means by trying to erase time vestiges in skin but also playing a significant part in prevention, regeneration and delaying pf skin aging combining knowlege of possible local and systemic therapy, instrumental devices and invasive procedures.

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OFF-LABEL USES OF HYALURONIC ACID FILLERS IN DERMATOLOGY

Özgür Gündüz

Hyaluronic Acid (HA), a nonsulfated glycosaminoglycan and one of the main components of the extracellular matrix, can be found throughout connective, epithelial, and neural tissues. It contributes to the lubricating properties of synovial fluid, the resilience of cartilage tissue, and wound repair. It also has critical roles in the formation of granulation tissue, cell migration, and skin healing. Primary medical uses of HA consist of intra-articular injection for osteoarthritis, as a component of artificial tears, and atrophic skin augmentation. In addition, FDA approved the use of hyaluronic acid fillers for the treatment of facial and perioral wrinkles, skin folds, acne scars, lipoatrophy of HIV-positive patients, and augmentation of lips. In recent years, HA fillers have been reported to be successful in treating lipoatrophy associated with various connective tissue disorders such as scleroderma lupus erythematosus and in esthetic procedures such as breast augmentation. In this presentation, these off-label uses of HA fillers are reviewed.

LASERS AND ENERGY-BASED DEVICE FOR HPV INFECTIONS

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Introduction: World-wide the risk of at least one HPV infection in an individual's lifetime is 50-80%. Transmission typically occurs via skin-to-skin and mucosa-to-mucosa contact. Lasers, radiofrequency, electrocautery, HIFU, microwave and photodynamic therapy are important energy-based devices.

Materials and methods: Recalcitrant wart response rates with several different type of lasers, electro-surgery, radio frequency were different. For example, CO2 laser ca reach 50–100%; Er: YAG laser, 72–100%; and Nd: YAG laser, 46–100%. They are an expensive choice and also there is no randomised controlled trials comparing with conventional treatments such as electro-cotery, cryo-therapy etc. Also, we need to know the clear efficacy, risks and safety protocols of energy-based treatments for HPV.

Discussion: By far we came to situation that vast amount of options are in our hands to treat HPV infections. But we still do not know the best treatment strategy cause it changes according to age of the patient; location and size of the lesions and immunity of the patient. We still have the latent virus to handle which is making the recurrences. carbondioxide lasers, erbium yag laser, pulsed dye lasers, electrocotery and cryotherapy will be discussed. But we know that in some patients combinations of different treatment options will work better.

Keywords: Lasers; wart; HPV; treatments;energy-based

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TIPS &TRICKS FOR HA FILLER PROCEDURES IN FACE

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Assos Prof DroOf DermatologyaAnd Venerolo

Soft tissue filler augmentation has become increasingly popular due to its perceived ease and impressive results.Dermal hyaluronic acid fillers are gel like substances that are injected beneath the skin to restore the volume loss, smooth lines and soften creases or enhance facial contours. They can be used as "volumizers" plumping and lifting cheeks, chins, jawlines and temples, filling out thin lips. Mostly hyaluronic acid fillers are using for face rejuvenation. The procedure is easy to apply and can be done in clinical office environment. Its duration period is approximately 8-18 months depending on every patient's own biological features.

Soft tissue filler augmentation has become increasingly popular due to its perceived ease and impressive results. Unfortunately, although the results are impressive, so are the reported complications[1].

Even though it is a comfortable procedure to apply; there are real tips and tricks for hyaluronic acid filler treatment for face. There are dangereous aeras in face so we have to be aware of there areas and we have to apply fillers properly and carefully for our patients.

Filler injection into the glabella is well known to be a highly dangerous procedure due to the high risk of embolism and intravascular injection[2]. A needle or a cannula can be safely used during filler injection procedures to correct a sunken upper eyelid. To date, there are no precise injection points recommended that are based on an anatomical study[3]. Forehead augmentation with filler injection is one of the most dangerous procedures associated with iatrogenic intravascular injection resulting in the severe complications.

This is of particular importance since vascular compromise is one of the most severe adverse events possibly leading to tissue necrosis and in rare cases to loss of vision. We have to be aware of the danger zones in these aesthetic units and provide recommendations how to avoid severe adverse events.

These danger points are on temporal region, glabella and nose, infraorbital region, nasolabial folds and nasal triangle, lips, and chin[4].

It is safe if the facial danger zones are recognized and proper injection techniques and fillers are used. Reported complications arising from facial filler injections include erythema, tissue loss, blindness, stroke, and even death[5]. We describe the anatomically based techniques to minimize risk and maximize safety when injecting in the facial danger zones, including the glabella/eyebrow, temporal region, perioral region, nasolabial fold, nose, and infraorbital region. Complications generally arise secondary to vasculature injury and/or cannulation with filler. Most importantly, the practitioner should be able to recognize complications and address them immediately.

Treatment of the frontonasal angle, the dorsum, the nasolabial angle and the columella may be used to shape and contour the nose. Neuromodulators may be used to treat bunny lines and for elevation of the nasal tip. The midface is considered an advanced area for treatment, and injectors are advised to obtain specific training, particularly when injecting fillers near the nose, because of the risk of serious complications, including blindness and necrosis. Injections made in the midcheek must be performed with caution to avoid the infraorbital artery[6]. Nonpermanent facial fillers are associated with rare but potentially severe complications. Severity and impact of complications depend on the anatomical region of the face and eventually require profound knowledge of facial anatomy[7].

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WHAT IS NEW IN WHA PUBLISHING HOUSE?

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Abstract

The World Health Academy Publishing House (WHAPH) It is an international publishing house founded on the project of the World Academy of Health. It publishes scientific research through journals indexed on Scopus, Pubmed and minor databases in addition to numerous book publications; collaborates with the most prestigious universities in the world

TIPS AND TRICKS FOR HAIR TRANSPLANTATION

Roxanna Sadoughifar

Many people still recall hair transplant with unnatural looking, pluggy grafts from the past. Even many physicians are not aware of the huge progress that has been made in field over the last 50,60 years. But interestingly these days hair transplants are so natural that one can strongly argue that they can be visually undetectable. For achieving that many factors should be considered. Correct diagnosis is fundamental to a proper treatment plan. These factors are worthy of attention in proper case selection:

- ✓ Deliberate consultation including dermoscopy (necessary to omit patients with Alopecies that have contraindication for the surgery like Telogen Effluvium, Alopecia Areata, Active Scarring Alopecies or Trichotillomania). Scaling, Pustules and Erythema should be investigated.
- ✓ Determination and classification of present and expected future hair loss pattern.
- ✓ Assessment of donor area; recognizing the borders of the safe donor area, follicular unit density, hair shaft color, caliber, texture, …
- ✓ Examination of scalp elasticity; tight scalp will limit the width of excised strip, in this case the number of obtained follicular units would be very low. In patients with excessive laxity, we should rule out Ehlers-Danlos variants.
- ✓ Recognizing the underlying causes of hair loss, like thyroid disorders, polycystic ovarian disease, child birth, starting or stopping OCP, taking androgenic hormones or supplements and simple process going through menopause.

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OP-01 [Infectious Diseases, Parasitic Diseases, Infestations]

Update and transmission factors of the HIV/AIDS epidemic in Ukraine

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AIM: On account of the geographic nearness the development is the HIV/AIDS figures in Ukraine also from epidemiological meaning for Europe. The medium-term purpose of Ukraine is the entry in the European Union.The number of newly diagnosed HIV infections in Ukraine ranks second in the WHO European Region after Russia according to the European Centre for Disease Prevention and Control (1). However, because of many unreported cases the actual figures are supposed the official reports considerably. METHODS: Reported HIV/AIDS cases from the official epidemiological register of the Ukrainian Centre for AIDS Prevention between 1987 and 2021 were reviewed and analysed and this information was supplemented with published HIV prevalence and sexually transmitted disease case reporting information. Between 1987 and 2004, 74,856 Ukrainian were registered with HIV. The number of officially registered HIV-infections increased from 16,078 in 2006 to 17,289 in 2021. 5,325 new infections were due to IDU, 9,534 to heterosexual contact and 1,977 to vertical transmissions from HIV infected mothers to their children. DISCUSSION: Despite efforts by government agencies, local governments, non-governmental organizations and international donors, the number of HIV infection with the most rapidly increasing number of newly diagnosed HIV cases mainly transmitted through heterosexual, but also through contact IDU and mother-to-child-transmission still increases in Ukraine over the past few years (2, 3). Mortality in patients with AIDS is high, but still stable over the last years. However, without effective prevention and intervention measures the HIV epidemic can develop in the Ukraine during the coming years for the European Union to a long-term population-medical problem.

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Keywords: HIV infection, AIDS, Ukraine

OP-02 [Cutaneous Oncology]

Radıotherapy For Squamous Cell Carcınomas Of The Skın: A Sıngle Instıtutıon Experıence From North East Turkey

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AİM: Skin cancer patients with non-melanoma skin cancer who have the highest risk of disease-specific death are squamous cell carcinoma (SCC) and keratinocytes. The aim of this study is to determine the characteristics (age, sex), indications and doses of lesions and radiotherapy, Loco-regional control, relapse free survival and overall survival rates in SCC patients treated and followed at our clinic.

MATERİALS AND METHODS: The study was conducted on 161 patients with skin SCC, radiotherapy and followed up in our clinic between January 1996 and December 2021.

RESULTS: 99 (61%) were men and 62 (39%) woman. The mean age was 57.3±14.3 (42-94) years. The mean age of females was 58.36±11.78

years (45–94 years), and the mean age of males was 55.94±11.12 years (42–92) years. The primary tumor sites included the head and neck 139 (86%) (cheek 41 (26%), nose 32 (20%), forehead 23 (14%), lips 6 (4%), neck 4 (2%), peri-auricular 4 (2%) and scalp 29 (18%)), extremity 13 (8%) and body 9 (6%). The three-year loco-regional survival, relapse-free survival, and overall survival rates were 89% [95% confidence interval (CI): 82–98], 87% (95% CI: 80–96) and 92% (95% CI: 88–98), respectively. Kaplan-Meier estimates (with 95% confidence intervals) of cumulative recurrence rates of all tumors at 2 and 5 years were 2.1% (1%-3.2%) and 9.8% (6.9%-13.7%), respectively. Men gender received significantly worse prognosis than female sex (p=0.02). The recurrence-free rate of tumors 2 cm or smaller was significantly lower than tumors larger than 2 cm (p<0.001). Cosmetic results were good in 29% of the patients, acceptable in 50%, and worse in 21%.

CONCLUSİONS: Radiotherapy plays an integral role in the treatment of primary and postoperative squamous cell carcinomas. Definitive radiation is typically recommended for patients who cannot tolerate anesthesia and often for those who are on anticoagulants, for tumors located in cosmetically or functionally sensitive areas of the face, or for patients who prefer radiation. In general, adjuvant local radiation is recommended following excision for patients with high-risk factors, including close or positive margins, perineural invasion, invasion of the bone or nerves, or recurrent disease.

Keywords: Skin tumor, Squamous cell Carcınomas, Radiotherapy.

OP-03 [Allergology and Immunology]

Arising molloscum contagiosun in an adult patient treated with fingolimod and review of the literature

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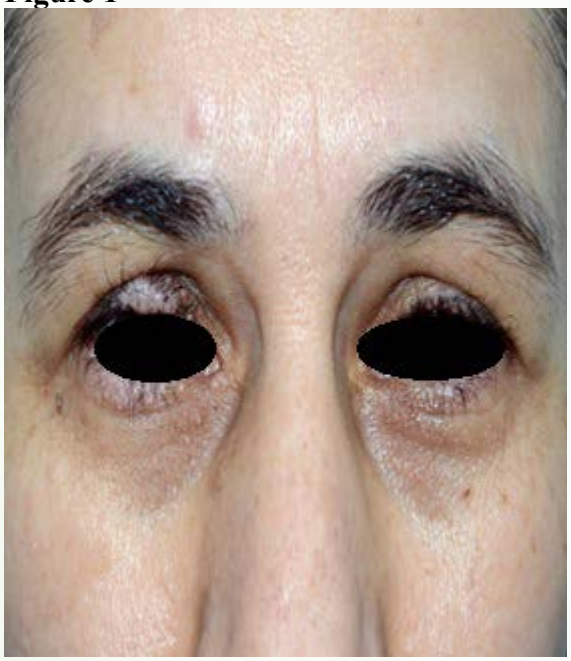
Molluscum contagiosum is a self-limiting viral eruption characterized by umbilical papules on the skin. Extensive, chronic, and larger lesions may occur in case of immunodeficiency. Fingolimod therapy used for Multiple Sclerosis (MS) treatment can also lead to immunosuppression and promote the occurrence of molluscum contagiosum and other opportunistic infections.

Some conditions commonly associated with molluscum contagiosum in adults include acquired immunodeficiency syndrome, solid organ transplantation, systemic lupus erythematosus, sarcoidosis, neoplasms, immunosuppressive and biologic therapies. Diffuse and giant molluscum contagiosum lesions may also occur in DOCK8 deficiency, a genetic disorder that affects dendritic and T cell migration.

In this presentation, we discuss a case of extensive long-term molluscum contagiosum infection in the face of an adult patient treated for Multiple Sclerosis with fingolimod (after the discontinuation of which Molluscum contagiosum regressed), as well as similar cases from the literature.

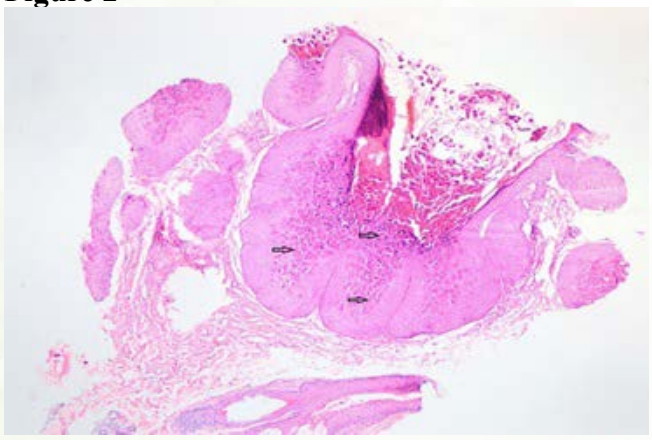
Keywords: Molluscum contagiosum, fingolimod, immunosuppression

Figure 1



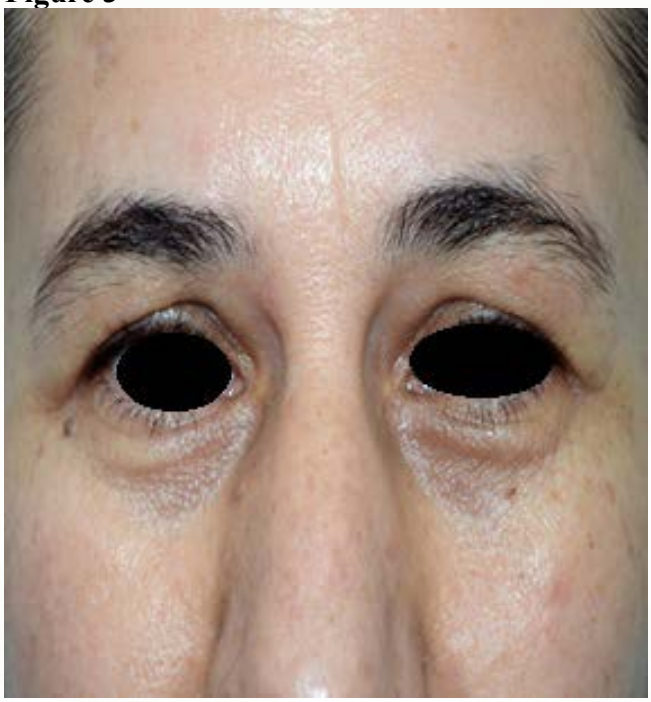
Belly papules on bilateral eyelids

Figure 2



Endophytic hyperplasia of the epidermis and large intracytoplasmic inclusions in keratinocytes

Figure 3



Completely regressed appearance

OP-04 [Infectious Diseases, Parasitic Diseases, Infestations]

Herpetiform lesions of the oral mucosa in a patient diagnosed with COVID-19

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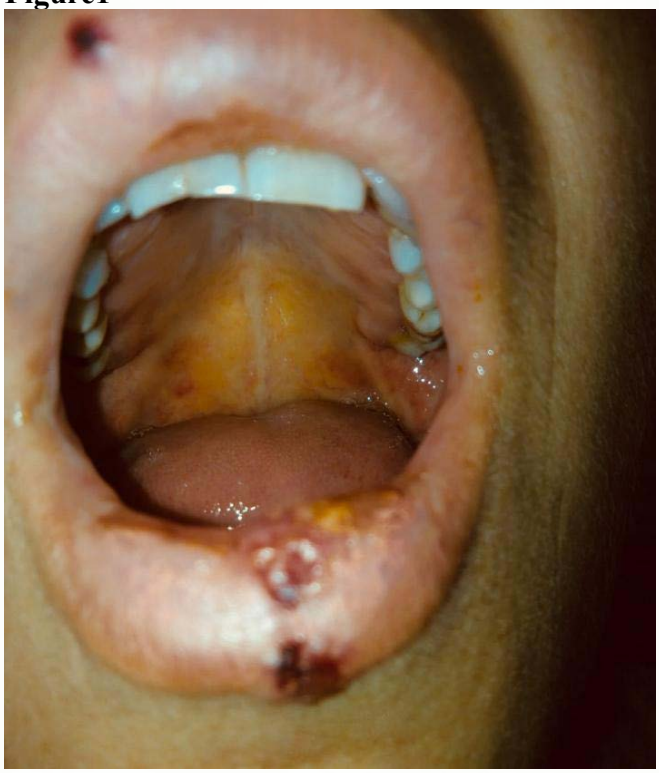
COVID-19 is a viral infection caused by SARS-CoV-2 resulting in numerous symptoms in various organs of the body, mainly in the lungs.(1) The incidence of oral lesions seen in COVID-19 patients is not fully known. (2) The most common oral mucosa finding seen in these patients is herpetiform lesions.(1,2) Here, a COVID-19 patients with herpetiform lesions is presented. Forty two years old female patient applied to our dermatological and venereal diseases clinic for ulcerative lesions that were present in her oral mucosa for more 1 week. The patient was reported to be diagnosed with COVID-19 two weeks before as a result of real-time reverse-transcriptase polymerase chain reaction test that she has taken due to fever and back pain. Systemic paracetamol and hydroxychloroquine treatment was initiated for the patient and ulcerative lesions were reported to occur in the oral mucosa and on the lips one week later. In the dermatological examination, eroded and ulcerative lesions were found to be present on the lower lip and even more in the soft palate of the oral mucosa. (Figure 1) HSV-1 IgM and HSV-2 IgM results of the patient were evaluated to be negative. The patient was considered to manifest lung involvement of COVID-19. Herpetiform lesions are observed in both keratinized and non-keratinized mucosa of COVID-19 patients as multiple, painful, unilateral, round yellowish gray ulcers with erythematous surrounding. These lesions may arise before, simultaneously or after the occurrence of systemic symptoms. (2,3) Herpetiform lesions are determined to arise as painful lesions with irregular margins on the tongue, hard palate and labial mucosa and HSV-1 and HSV-2 tests of these patients were found to be negative.(3) Thrombotic vasculopathy developing secondary to COVID-19 is considered to be the reason for the the development of ulcerative and erosive lesions. (3,4) Indu et al. stated that multiple oral ulcers might be the first finding of COVID- 19.(4) In their study in which they examined 123 cases diagnosed with COVID-19, Favia et al. 1determined that ulcerative lesions(52.8%) were the most common findings observed in the oral mucosa. In 92% of the cases, ulcerative lesions arised simultaneously with systemic symptoms or one week later than.(5) In our patient, ulcerative lesions in the oral mucosa and the tongue occurred 1 week after the systemic symptoms. It should be kept in mind that herpetiform lesions might develop in the oral mucosa of COVID-19 patients and oral mucosa examinations must be performed in these patients.

Keywords: COVID-19, herpetiform, oral

Figure1



OP-05 [Dermatology and Internal Medicine, including Skin Manifestations of Systemic Diseases]

Investigation of the Relationship between Frailty, Dermatological Quality of Life and Depression in Geriatric Patients

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Introduction & OBJECTIVES: Frailty is a geriatric syndrome result of the cumulative decrease in the functions of various systems with aging. Although there are studies showing the relationship between frailty, quality of life and depression, there are few studies examining the effect of dermatological problems on frailty. We aimed to detect the frequency of dermatological diseases in geriatric patients and their relationship with frailty syndrome in terms of dermatological quality of life and depression. Materials & METHODS: This single center, cross-sectional, observational study was approved by the Ethics Committee of Pamukkale University. A total of 264 patients (126 females,138 males) aged ≥65, were included. Clinic and demographic data of the patients were recorded. The dermatological diseases were categorized into 28 groups after diagnostic evaluation were performed. 'Dermatological Quality of Life Index (DLQI)', 'Edmonton Frail Scale(EFS)' for the assessment of frailty levels and 'Geriatric Depression Scale-30 (GDS-30)' for the assessment of depression were applied to the patients. RESULTS: Based on the EFS, 0–4 points as 'not frail, robust', 4–10 points as 'frail' and >11 points were evaluated as 'severely frail' patient group. It was determined that 34 (12.9%,mean age 69.5 ± 5.4) patients were robust, 169(64%, mean age 71.9 ± 5.5) were frail and 61(23.1%, mean age 79.4 ± 8.8) were severely frail. The difference between groups was statistically significant (p< 0.005). The most common dermatological diseases observed in decreasing order of frequency were; photodermatoses (87%), premalignant skin tumors (68%), xerosis (68%), pruritus (52%), fungal skin diseases (48%) and eczema (32%). The increase in the DLQI score with the increase of frailty degrees was statistically significant (p <0.001). In the correlation analysis, fragility degrees, GDS-30 scores and DLQI scores were found to be significant positively correlated with each other(p <0.001). Frailty both increases the possibility of depression and affects the dermatological quality of life. According to the results of multivariate logistic regression analysis on fragility; low educational status (aOR=0.156, 95% CI=0.34-0.714), increased DLQI scores (aOR=1,269, 95% Cl=1.073-1.501), the presence of depressive symptoms (probable depression and depression group) according to GDS-30 (aOR=15.055, 95% CI=3.545) were determined as risk factors for frailty. CONCLUSION: We have obtained data showing that dermatological diseases that affect the quality of life may have an important role in the evaluation of frailty. Considering the close relationship of depression with frailty and DLQI, we think that dermatological diseases may also contribute to depression. In addition to reaching these results in our study, it is difficult to make a definite judgment due to the limited number of publications on the subject in the literature. Therefore, studies including large numbers of patients are needed.

Keywords: Geriatric dermatology, Quality of Life, Frailty, Dermatological Quality of Life Index, Edmonton Frail Scale, Geriatric Depression Scale

Figure 1:The relationship between frailty degrees and DLQI scores

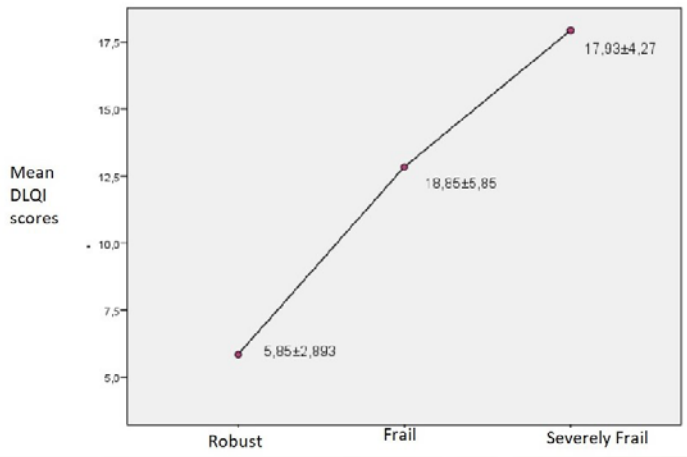

Table 1: Relationship between Frailty status and demographic characteristics of patients

	Total N=264	Robust N=34(%12,9)	Frail N=169(%64)	Severe Frail N=61 (%23,1)	p-value
Sex Female Male	126(%47,7) 138(%52,3)	10(%7,9) 24(%17,4)	80(%63,5) 89(%64,5)	36(%28,6) 25(%19,1)	<0,005
Age (mean, years)		69,52±5,40	71,94±5,48	79,38±8,84	<0,005
Age group 65-75 >75	180(%68,2) 84(%31,2)	29(%16,1) 5(%6)	122(%67,8) 47(%56)	29(%16,1) 32(%38)	<0,001
EFS scores(-mean)		4,11±3,83	7,26±2,57	10,26±1,53	
Mariatal Status Married Single	214(%81,1) 50(%18,9)	32(%15) 2(%0,4)	140(%65,4) 29(%58)	42(%19,6) 19(%38)	0,007
Smoke Yes No	70(%26,5) 194(%73,5)	14(%20) 20(%10,3)	43(%61,4) 126(%64,9)	13(%18,6) 48(%24,7)	0,095
Use of walking aids No Yes	172(%65,2) 92(%34,8)	34(%19,8) 0	119(%69,2) 50(%54,3)	19(%11) 42(%45,7)	0,001
Comorbid diseases No Yes	54(%20,5) 210(%79,5)	15(%27,8) 19(%9)	34(%63) 135(%64,3)	5(%9,3) 56(%26,7)	0,001
Living place Rural Urban	21(%8) 243(%92)	3(%1) 31(%11,8)	13(%5) 156(%59)	5(%2) 56(%21,2)	0,972

Table 3: Edmonton Frail Scale(EFS), 'Dermatological Quality of Life Index (DLQI) and Geriatric Depression Scale-30 (GDS-30) correlation analysis

	EFS Correlation coefficient	p-value
DLQI	0,395	<0,001
GDS-30	0,751	<0,001

Table 3: Multivariable logistic regression analysis of risk factors for frailty

Variables	Univariate OR (95% CI)	p	Multivariate OR (95% CI)	p
Age (y) (>75)	3,034 (1,131-8,145)	0,028	0,820 (0,191-3,511)	0,789
Sex Female	2,242 (1,118-5,336)	0,025	0,969 (0,286-3,279)	0,960
Comorbid Disease	3,866 (1,809-8,264)	<0,001	2,248 (0,724-6,975)	0,161
Low economic status	0,144 (0,067-0,310)	<0,001	1,458 (0,304-6,991)	0,639
Low educational status	0,137 (0,062-0,304)	<0,001	0,156 (0,34-0,714)	0,017
DLQI	1,486 (1,295-1,705)	<0,001	1,269 (1,073-1,501)	<0,005
GDS-30	57,571 (16,685-198,645)	<0,001	15,055 (3,545-65,613)	<0,001

DLQI 'Dermatological Quality of Life Index ', EFS' Edmonton Frail Scale' for the assessment of frailty levels and GDS-30 'Geriatric Depression Scale-30 '

Table 2: Relationship between Frailty status and dermatologic diseases

Dermatologic Diseases	Total N=264	Robust N=34(%12,9)	Frail N=169(%64	Severe Frail N=61 (%23,1)	p
Bacterial Infections	16(%6,1)	2(%0,8)	9(%3,4)	5(%1,9)	0,489
Fungal Infections	126(%47,7)	16(%6,1)	83(%34,3)	29(%11)	0,303
Parasitic Infections	11(%4,2)	1(%0,4)	8(%3,1)	2(%0,8)	0,187
Viral Infections	15(%5,7)	1(%0,4)	10(%3,8)	4(%1,6)	0,035
Bening skin tumors	55(%21,2)	11(%4,2)	33(%12,6)	11(%4,2)	0,678
Premalign skin tumors	119(%45,2)	29(%10,8)	53(%20,17)	47(%17,85)	0,098
Malignant skin tumors	33(%12,5)	3(%1,2)	23(%8,8)	7(%2,6)	0,927
Cutaneous lymphomas	8(%3,1)	2(%0,8)	4(%1,5)	2(%0,8)	0,547
Pruritus	137(%51,9)	13(%4,9)	85(%32,2)	22(%14,8)	0,044
Xerosis	180(%68,2)	16(%6,1)	111(%42)	53(%20,1)	0,001
Physical dermatosis	93(%35,2)	9(%3,4)	63(%23,9)	63(%23,9)	0,479
Papulosquamous disorders	15(%5,7)	2(%0,8)	11(%4,2)	2(%0,8)	0,645
Lichenoid skin disorders	1(%0,4)	0	7(%2,7)	2(%0,8)	0,477
Granulomatous dermatitis	1(%0,4)	0	1(%0,4)	0	0,754
Vesiculobullous diseases	8(%3,1)	0	5(%1,9)	3(%1,2)	0,763
Connective Tissue Disease	9(%3,5)	0	7(%2,7)	2(%0,8)	0,771
Eczema	84(%31,8)	6(%2,4)	51(%19,4)	27(%10,3)	0,030
Urticaria and Angioedema	22(%8,3)	4(%1,5)	14(%5,3)	4(%1,5)	0,678
Cutaneous drug reactions	7(%3,2)	3(%1,2)	2(%0,8)	3(%1,2)	0,043
Cutaneous Vasculitis	5(%1,9)	1(%0,4)	4(%1,5)	0	0,453
Panniculitis	1(%0,4)	0	1(%0,4)	0	0,754
Pigmentary disorders	23(%8,8)	4(%1,5)	13(%4,9)	6(%2,4)	0,680
Stasis Dermatitis and ulcers	55(%21,2)	9(%3,4)	13(%4,9)	12(%4,6)	0,807
Acne vulgaris and Rosacea	20(%7,6)	4(%1,5)	14(%5,3)	2(%0,8)	0,399
Hair disorders	46(%17,6)	9(%3,4)	33(%12,7)	4(%1,5)	0,168
Nail disorders	21(%8)	3(%1,2)	13(%4,9)	5(%1,9)	0,982
Behçet's disease and RAS	3(%1,2)	0	1(%0,4)	2(0,8)	0,189
Photodermatoses	230(%87,1)	28(%10,6)	147(%55,6)	54(%20,5)	0,681

OP-06 [Topical Therapy]

Efficacy of Topical Dapsone 5% Gel for the Treatment of Erythematotelangiectatic Rosacea

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Introduction & OBJECTIVES:

Erythematotelangiectatic rosacea (ETR) is one of the main subtypes of rosacea. Topical dapsone has been reported to be effective in papulopustular rosacea. In this study, we aimed to measure the efficacy of 5% dapsone gel as a new treatment option for ETR.

Materials & METHODS: A total of 35 patients aged >18 years were included in the study who diagnosed with ETR based on National Rosacea Society criteria and received dapsone 5% gel twice a day for 12 weeks. Medical records of patients were retrospectively examined in terms of their clinicoepidemiyologic data and disease related follow-up parameters. Patients with a lack of sufficient data were excluded. Patients' demographic characteristics and week 0 / 2th week / 6th week / 12th week Investigator Global Assessment of ETR Severity (IGA-ETRS) (range, 0-4), visual analogue score (VAS) (range, 0-10) and DLQI scores were analyzed. Data were analyzed with IBM Statistical Package for the Social Sciences (SPSS) for Windows 23.0 (IBM Corp., Armonk, NY). In addition to qualitative statistical methods, the Wilcoxon signed-rank test was used to compare the quantitative data. Logistic regression analysis was used to determine the risk factors to affect the success of therapy. The significance was evaluated at $p<0.05$. Ethics committee approval from Pamukkale University was obtained.

RESULTS: The study included 22 women and 13 men with a median age of 38 years. The mean age at disease onset was 34.3 years. Mean symptom duration was 4 months. The 11(31.4%) patients were current smokers. Sun exposure (97.4%) was found to be the most common triggering factor, followed by psychological stress (77.1%). The most common affected area was malar region in all 35 patients and nose in 24(%68.6) patients. A total of 11 patients(31.4%) with ETR had additional systemic disease. Additionally, 19 patients (54.3%) had dermatologic disease other than rosacea. All 35 patients had a previous history of rosasea treatment. There was a statistically significant difference between the IGA-ETRS, DLQI and VAS scores in the 2nd, 6th and 12th weeks of treatment compared to baseline ($p<0.05$). (Table 1 and 2) Only mild irritation in 3 patients during treatment period was experienced. Patient satisfaction was scored on a four-point scale from 1 least satisfied to 4 very satisfied. While there was no statistically significant difference İN THE 2nd week measurements (p=0,071) COMPARED TO baseline; significant difference WAS FOUND İN the 6th and 12th week measurements ($p<0.05$). Logistic regression analysis revealed that only absence of systemic disease effects treatment success in the 6th (aOR=6,30, %95 CI=1,11-35,67) and 12th weeks (aOR=5,25, %95 CI=1,13-24,42) (p=0,037, p=0,034, respectively). CONCLUSION: In our study, dapsone 5% gel has been shown to be effective and well tolerated for the treatment of ETR. Future studies including more patients with longer periods of follow-up are suggested.

Keywords: Rosacea, Erythematotelangiectatic rosacea, Dapsone, Dermotology quality of life

Figure 1: Investigator Global Assessment of ETR Severity (IGA-ETRS) in 0 / 2th/ 6th / 12th weeks of treatment

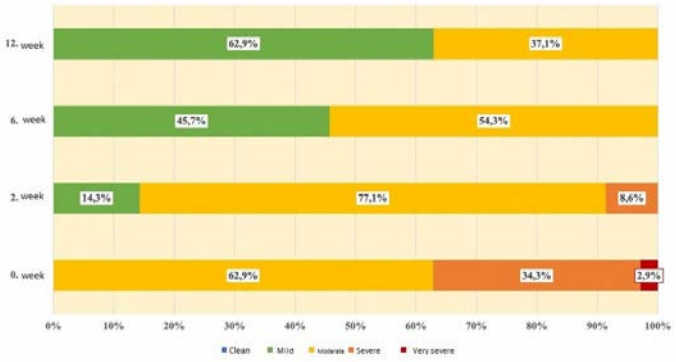

Figure 2: Dapson %5 treatment responses in patients in 0/12th week

Table 1: IGA-ETRS scores in 0 / 2th / 6th / 12th weeks of treatment

IGA-ETRS		0. week	2. week	6. week	12. week
Grade	Score	n (%)	n (%)	n (%)	n (%)
Clean	0	0 (0)	0 (0)	0 (0)	0 (0)
Mild	1	0 (0)	5 (14,3)	16 (45,7)	22 (62,9)
Moderate	2	22 (62,9)	27 (77,1)	19 (54,3)	13 (37,1)
Severe	3	12 (34,3)	3 (8,6)	0 (0)	0 (0)
Very severe	4	1 (2,9)	0 (0)	0 (0)	0 (0)
p-value		-	<0,001	<0,001	<0,001

Table 2. Assesment of Visual Analog Scale (VAS) and Dermatology Life Quality Index (DLQI) scores

	0. week	2. week	6. week	12. week
	Median (Min-Max)	Median (Min-Max)	Median (Min-Max)	Median (Min-Max)
VAS	7 (5-9)	5 (3-8)	4 (3-6)	4 (2-6)
p-value	-	<0,001	<0,001	<0,001
VAS-burning sensation	5 (2-9)	3 (1-7)	4 (1-7)	3 (1-6)
p-value	-	<0,001	<0,001	<0,001
VAS-erythema	6 (4-10)	4 (2-7)	4 (2-6)	3 (2-6)
p-value	-	<0,001	<0,001	<0,001
VAS-pruritus	2 (1-9)	3 (0-6)	2 (0-5)	2 (0-4)
p-value	-	0,232	0,018	0,005
VAS-edema	2 (1-6)	2 (0-6)	2 (0-4)	2 (0-5)
p-value	-	0,080	0,005	0,005
DLQI	8 (6-14)	5 (3-11)	5 (3-11)	4 (2-9)
p-value	-	<0,001	<0,001	<0,001

OP-07 [Pregnancy-related Dermatoses]

Retrospective Evaluation of Clinicoepidemiologic Profile of Pregnant Patient who applied to the Dermatology Outpatient Clinic

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INTRODUCTION & OBJECTIVES: Endocrinologic, vascular, or immunologic modifications during pregnancy may cause skin changes which may range from physiological conditions, to common skin diseases.

In this study, our aim is to analyze the clinicoepidemiologic profile of pregnant patients applying to the dermatology outpatient clinic

MATERIALS AND METHODS: Data from 112 pregnant patients who have applied to the dermatology outpatient clinic from March 2021 to September 2022 were retrospectively examined. Application details about dermatology outpatient clinic such as single or repeated appointment, consultation notes from other clinics, preferred diagnostic methods, prescribed treatment choices and recommended personal care products were analyzed. Ethical permission was obtained from the Pamukkale University Clinical Research Ethics Committee. The collected data were analyzed using Statistical Package for the Social Sciences (SPSS) version 23 (IBM SPSS 23.0, SPSS Inc).

RESULTS: The age of the study population ranged from 18 to 51 years (mean age: 29,07). The study population included 65 (58%) primigravidae and 47(42%) multigravidae. Among the multigravidas, 32(28.6%) were second gravida, 6(5.4%) were third gravida, and 9(8.1%) were fourth or more gravida. Cases seen in the first trimester were 24 (21.4%, mean age: 27,75 years), 2nd trimester were 47 (42%, mean age: 29,96 years) and 3rd trimester were 41 (36.6%, mean age: 28,83 years). Physiological skin changes were seen in 91 (81.25%) cases, with stria gravidarum being more common in 58 (51.8%). Specific dermatoses of pregnancy were observed in 3 (2.7%) cases with atopic eruption of

pregnancy, pemphigoid gestationis and impetigo herpetiformis. Prevalence of infection was found to 38 (33.9%) with fungal infections being the most common 16 (%17.9), scabies being the second common 13 (%11,6). Exacerbations of psoriasis vulgaris, urticaria and atopic dermatitis were observed. Pigmentary changes, striae gravidarum and specific dermatoses of pregnancy were observed in statistically significant proportion in primigravidas and during third trimester (≤0.005). Repeated appointments to outpatient clinics were observed in statistically significant proportion in multigravidas and during third trimester (≤0.005). Distribution of dermatologic diseases (Table 1); preferred diagnostic methods of dermatologic evaluation of pregnant patients (Table 2); preferred treatment methods, prescribed medicines and recommended skin care products to patients (Table 2) were shown in tables.

CONCLUSION: A majority of pregnant women develop physiological skin changes, worsening of preexisting skin conditions, or the appearance of new dermatoses. Therefore, updated reports on drugs and skin care products during pregnancy are crucial for physicians and the patients to wisely choose treatment plan.

Keywords: Physiological skin changes of pregnancy, pregnancy specific dermatoses, skin

Table 1: Distribution of dermatologic diseases observed during pregnancy.

Dermatoses			To-tal	Percentage (n=112)
Physiological Changes			91	81.25%
	Pigmentation	Melasma Linea Nigra Diffuse pigmentation	10 3 1	9% 2.7% 0.9%
	Vascular	Varicose veins Cherry angioma	6 3	5.4% 2.7%
	Connective Tissue	Striae gravidarum Acrochordon	58 3	51.8% 2.7%
	Hair	Hirsuitism Hair loss	2 3	1.8% 2.7%
	Nail	Ingrown nails	2	1.8%
Infectious diseases of the skin			38	33.9%
	Bacterial	Celulitis Paronychia	1 1	0.9% 0.9%
	Fungal	Dermatophyte Tinea versicolor Candidasis	10 4 2	9% 3.6% 1.8%
	Viral	Wart HSV Herpes zoster Molluscum	10 1 2 1	9% 0.9% 1.8% 0.9%
	Parasitic	Scabies Leishmania Pediculosis	13 1 1	%11.6 0.9% 0.9%
Miscellaneous dermatoses				
	Acne and Rosacea		4	3.6%
	Vitiligo		2	1.8%
	Alopecia Areata		3	2.7%
	Psoriasis		7	6.2%
	Seborrheic dermatitis		10	9%
	Urticaria and Angio-edema		3	2.7%
	Panniculitis		1	0.9%
	Lichen planus		1	0.9%
Pregnancy specific dermatoses			3	2.7%
	Pemphigoid gestationis		1	0.9%
	Impetigo herpetiformis		1	0.9%
	Atopic eruption of pregnancy		1	0.9%

Table 2: Preferred diagnostic methods of dermatologic evaluation of pregnant patients

Diagnostic Methods	Total	Percentage (n=112)
Dermoscopic Examination	71	%63,4
Wood Lamp Examination	43	%38,4
KOH preparation	24	%21,4
Tzank smear	5	%4,5
Pathologic Examination	6	%5,35

Table 3: Preferred treatment methods, prescribed medicines and recommended skin care products to patients

Treatment Modalities		To-tal	Percentage (n=112)
	Cryotherapy	15	%13,4
	Electrotherapy	2	%1,8
	Abscess Drainage	3	%2,7
	Intralesional corticosteroid injection	2	%1,8
Prescribed Medicine			
Topical			
	Antibiotics	16	%14,3
	Antifungal	20	%17.8
	Corticosteroids	29	%25,9
	Others	23	%20,5
Systemic			
	Antibiotics	3	%2,7
	Corticosteroids	4	%3,6
	Antihistamines	6	%5,4
	Others		
Skin care products			
	Sunscreen	60	%53,6
	Moisturizer	30	%26,8
	Shampoo and hair care products	12	%10,8
	Others	4	%3,6

OP-08 [Biologics, Immunotherapy, Molecularly Targeted Therapy]

Immunogenicity of Biologic

Zuhal Metin
zuhal metin

Introduction: Biologics are substances whose active component is derived from a biological source using biotechnology by recombinant DNA techniques. They have pharmacological effects to mimic normal human proteins or interact with circulating proteins or cellular receptors for treatment. They hold a great deal of promise among the therapeutic interventions for a wide range of disorders, including cancer and inflammatory diseases.We will be focus on biogenicity of biologic agents in this chapter.

Material and Metods: The immunogenetics of biological agents were searched and compiled from literature review from pubmed,clinical key, up to date and comprehensive drug therapy dermatological textbook sections.

Discussion: Biological agents are divided into 3 groups in terms of structure content non-human origin, partial human-sequence, complete human-sequence. Structures and antigenicity of biological agents can trigger immunologic reactions. Immunogenicity is defined as the propensity of the therapeutic biologics to generate immune responses to itself and to related proteins or to induce immunologically related non clinical affect or adverse clinical events. It is complex phenomenon that depends on the interplay between several drug- and patient-related factors (including sex, comorbid conditions, and ethnicity). Repetitive administration of these protein-based therapeutics to immunocompetent patients elicit immune responses and trigger the production of anti-drug antibodies (ADA) or cell-based immune responses. According to studies in the literature, immune reaction to an exogenous version of an endogenous human protein or failure of immune tolerance to self-antigens are also trigger the development of ADA. Antigen recognition and biological presentation are important aspects in the development of biological agent immunogenicity. Evidence from many studies of biologic agents demostrate that immunosuppressive/anti-proliferative therapy (Combining methotrexate, azathioprine, leflunomide or mycophenolate) reduces ADA levels and immunogenicity due to the immunosuppressive effect of these drugs.

Result: The presence of ADAs may be associated with some clinical consequences: reduction in therapeutic efficacy, increased risk of adverse events, hypersensitivity reaction, IgE-independent anaphylactic reactions.

Conclusion: To know more about biological agents and their immunogenicity may provide essential information to clinicians that can potentially improve treatment, reduce risks and costs.

Keywords: ADA, immunogenicity, biologics

OP-09 [Dermatology and Internal Medicine, including Skin Manifestations of Systemic Diseases]

Hyperprolactinemia and Gynecomastia Development During Systemic Isotretinoin Treatment

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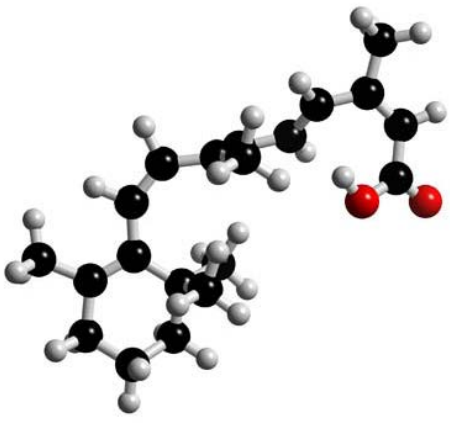
Vitamin A has been first used for the treatment of acne by Straumfjord in the year of 1943. Vitamin A has a narrow therapeutic window. Therefore, in the following years, research has been initiated to develop more effective synthetic retinoids with fewer side effects. Isotretinoin had been produced in 1955. After its production, its use for various dermatologic diseases had been investigated. In 1982, FDA had approved isotretinoin for the treatment of nodulocystic acne. Isotretinoin belongs to the group of first generation retinoids. Retinoids are hormones with small molecular size and exert their effect through regulation of gene transcription by binding to the RAR or RXR retinoid receptors in the nucleus of the cell. Retinoids show off their clinical effect in dermatology through regulation of inflammation, cellular differentiation, apoptosis and sebaceous gland activity. Isotretinoin is indicated for numerous skin diseases along with nodulocystic acne. Frequent side effects of systemic isotretinoin are well known but gynecomastia as a side effect of systemic isotretinoin treatment is not well known. In Litt's Drug Eruption Reference Manual two gynecomastica cases have been mentioned which are published by Flückiger in 1992 and by Shelley in 1994. Also there are three gynecomastia case reports in the literature published by Ustun in 2013, by Gualtieri in 2018 and by Bonifazi in 2020. This is the sixth case of gynecomastia due to the systemic isotretinoin to the best of our knowledge. Our patient was an 18 year old male who was on oral isotretinoin treatment for his nodulocystic acne. He was weighing 63 kg and in the fourth month of his treatment during which he was taking 40 mg isotretinoin daily had noticed an increase in the size of his breasts. He first appealed to the general surgery outpatient clinic and physical examination showed a nodular induration under the areola of his left breast. Bilateral breast ultrasound has been ordered by the general surgeon and the ultrasound showed 5cmx1cm and 18mmx3.5 mm fibroglandular tissue on the the left breast and the right breast respectively. Ultrasound revealed no mass lesion and has been reported as bilateral gynecomastia with explicitness on the left side. We consulted our patient to the endocrinology department and his prolactin level has been found high as 30.32 ng/ml. We determinated his systemic isotretinoin treatment upon his wish and approval. His prolactin level has been checked one month later and has been found normal as 10.54 ng/ml. Systemic isotretinoin can lead to hyperprolactinemia through derangement of pituitary hormones and/or through downregulation of cutaneous androgen receptors. Gynecomastia is a rare side effect of systemic isotretinoin treatment. But it is important that this side effect be well known by the dermatologists so unnecessary cranial radiologic investigations can be avoided and patients can be informed wisely.

Keywords: Isotretinoin, gynecomastia, hyperprolactinemia

Isotretinoin Three Dimensional Molecular Structure



Isotretinoin Two Dimensional Molecular Structure

OP-10 [Inflammatory Skin Diseases]

The relationship between monocyte to HDL cholesterol ratio and inflammation in patients with Seborrheic Dermatitis

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BACKGROUND: Seborrheic dermatitis (SD) is a chronic inflammatory disease. Although the precise etiopathogenesis is unknown, hormones, gender, microorganisms, and immunological factors that cause inflammation and oxidative stress are implicated. In recent studies, monocyte-to-high-density lipoprotein cholesterol ratio (MHR), monocyte-to-lymphocyte ratio (MLR), and neutrophil-to-lymphocyte ratio (NLR) have been shown to reflect inflammation and oxidative stress in chronic inflammatory and autoimmune diseases.

AIM: This study aimed to investigate hematological and inflammatory parameters in patients with SD and evaluate their potential relationship with disease severity.

METHODS: MHR, MLR, and NLR were analyzed retrospectively in patients with SD and healthy control. Disease severity was evaluated using the Seborrheic Dermatitis Area and Severity Index (SDASI) score.

RESULTS: The study included 50 SD patients and 50 age- and gender-matched healthy controls. MHR and MLR values were significantly higher in patients with SD ($p < 0.05$). There was no statistically significant correlation between MHR, MLR, and NLR levels and age, disease duration, and SDASI in the patient group ($p > 0.05$).

CONCLUSION: We believe that MHR, MLR can be used as low-cost and easily accessible markers of inflammation in SD patients.

Keywords: HDL-cholesterol, inflammation, monocyte, seborrheic dermatitis

Table 1. Demographic features of the patients and controls

	Patients (N=50)	Controls (N=50)	P-value
Gender, N (%) Male Female	24 (%48) 26 (%52)	24 (%48) 26 (%52)	1.0
Age, Mean±Sd	27.44±9.31	26.74 ±9.37	0.68
Disease duration (years), Mean±Sd	3.69 ± 3.66	-	-
Seborrheic Dermatitis Area and Severity Index, N(%) Mild Moderate Severe	22 (%53.75) 24 (%36.25) 4 (%5)	-	-

Table 2. The mean values of the laboratory parameters for the patients and controls

	Patients (N=50)	Controls (N=50)	P-value
MN (K/µL),Mean±Sd	0.55±0.13	0.51±0.13	0.19
HDL-C (mg/dl),Mean±Sd	44.99±8.01	50.08±8.23	0.004
NE (K/µL),Mean±Sd	4.14±1.12	4.27±1.36	0.80
LY (K/µL),Mean±Sd	2.12±0.51	2.23±0.57	0.46
MHR,Mean±Sd	0.01±0.004	0.01±0.003	0.005
MLR,Mean±Sd	0.27±0.07	0.23±0.06	0.02
NLR,Mean±Sd	2.02±0.67	2.01±0.79	0.62

MN monocyte, HDL-C high-density lipoprotein cholesterol, NE neutrophil, LY lymphocyte, MHR monocyte to high-density lipoprotein cholesterol ratio, MLR monocyte to lymphocyte ratio, NLR neutrophil to lymphocyte ratio, S.d standard deviation, $P < 0.05$ is defined statistically significant

OP-11 [Corrective, Aesthetic and Cosmetic Dermatology]

Mechanical dermabrasion of the upper lips for "bar code " wrinkles: technic, expected results and pitfalls

Laurent Dupoirieux
Nouvelle Clinique Bel Air (Bordeaux)

In this presentation we present step by step the technique for mechanical dermabrasion of the upper lips wrinkles. The most favorable conditions of this technique will be presented and possible pitfalls will be advanced. Alternative treatments with the cost-efficacy comparison will also be discussed.

Keywords: Dermabrasion, lip, wrinkle, dyschromia.

OP-12 [Hair Disorders/Diseases]

Reliability and quality of YouTube videos as a source of information on alopecia areata

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Introduction & OBJECTIVES: YouTube has become, in the recent years, an important means to communicate medical information. No prior studies have investigated the quality of the content of YouTube videos pertaining to alopecia areata (AA). Our main objective was to make an analysis of the quality and reliability of the most popular videos on YouTube about alopecia areata (AA). Our secondary aim was to compare the quality of the videos uploaded by different sources.

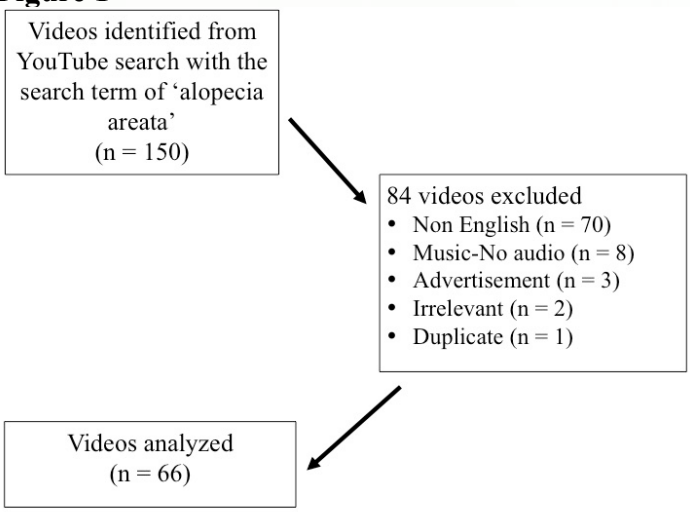
Materials & METHODS: We searched YouTube for the search term "alopecia areata". We rated the videos using the Global Quality Scale (GQS) (1 = poor, 5 = excellent) and reliability score.

RESULTS: Analyzed 66 videos had a total view count of 6759061. 71.2% of videos had a GQS score of ≤2, and 68.2% of them had reliability score of ≤2. Overall the mean number of views (102410 ± 147003) did not correlate with reliability score (p= 0.329) and GQS (p= 0.720). Independent users represented 42.4% of upload source, followed by healthcare providers (30.3%). In comparison with videos including health care providers, videos of independent users were statistically significantly longer (p=0.001), had more likes (p=0.027) and comments (p=0.034), despite having lower reliability scores (p=0.001), and GQS scores (p=0.001).

CONCLUSIONS: We observed that videos on YouTube concerning AA were mostly of low quality and contained misleading and potentially harmful information, most commonly conveyed by independent users.

Keywords: alopecia areata, Global Quality Scale, internet, reliability, social media, quality assessment

Figure 1



Algorithm showing the process of video selection on alopecia areata

Table 1

	Mean± SD	Maximum	Minimum
Length (min:sec)	9:35 ± 9:57	01:04:47	00:40
Duration on YouTube (days)	1596 ± 1096	5100	190
N of views	102410 ± 147004	747357	14388
N of views per day	86 ± 101	433	4
N of dislikes	63 ± 101	8864	5
N of subscribers	330337 ± 993459	612	0
N of subscribers	330337 ± 993459	7300000	136
N of comments	2279 ± 16715	136000	0
Reliability score	2 ± 1	5	0
GQS	2 ± 1	5	1

Characteristics of the analyzed videos

OP-13 [Hair Disorders/Diseases]

Autologous Micrografting for genetic hair loss

Naeem Jamal Assaf
Dr. Naeem Assaf, Board certified Dermatologist, Amman, Jordan

Many people around the world suffer from Androgenetic Alopecia (AGA). There are well-known and approved medications such as Minoxidil and Finasteride, in addition to hair transplant surgery. Recently the use of micrografting technology showed promising results when used for patients with specific conditions. There are constraints when it comes to the benefits of using this technology. Micrografting achieves autologous cell suspension by mechanical fragmentation of subcutaneous and adipose tissue from the occipital area. The use of micrografting technology can stop or slow down hair falling, increase hair density and thickness and moreover, it affects the hair color. After treating over 1400 AGA patients in my clinic using micrografting technology and by applying a specific treatment protocol for each case, which involves the use of topical solutions such as minoxidil along with Concentrated Growth Factor (CGF) and other supplements. Promising results were achieved for male and especially for female patients in which hair transplants were avoided. Furthermore, the use of micrografting technology is a treatment for all parts of the head with minimum to null recovery time.

Keywords: Autologous Micrografting, hair loss, genetic, androgenic, alopecia, regenerative medicine

OP-14 [Autoimmune Bullous Diseases]

A rare case; pemphigus erythematosus in a turkish male and treatment with rituximab

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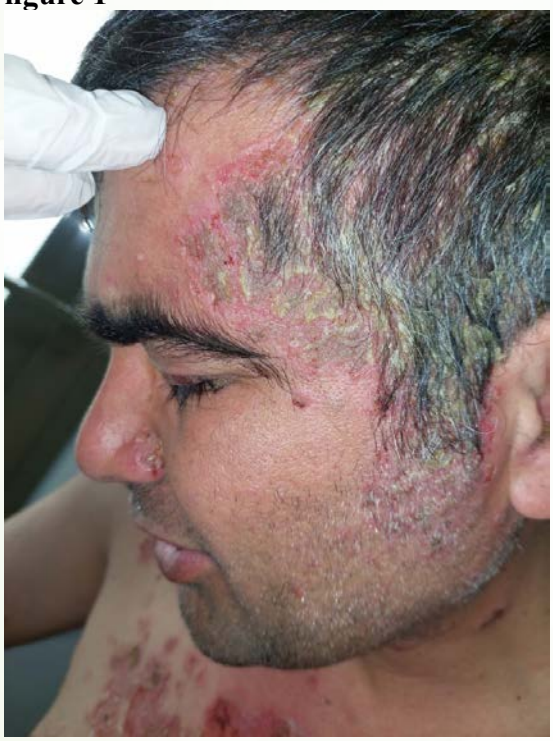
Pemphigus erythematosus, also known as Senear-Usher syndrome, is a rare autoimmune skin condition with overlapping clinical, histopathological, and serological features of lupus erythematosus and pemphigus foliaceus. Patients present with erythematous, scaly and crusted lesions in seborrhoeic distribution. Rash can be triggered by sun exposure. Oral mucosal involvement is not expected. Diagnosis is based on clinical findings, characteristic histopathologic changes, presence of antinuclear antibodies and immunolabelling in direct immunofluorescence test.
We report a middle-aged Turkish male patient, who presented with the complaints of photosensitivity, itchy rash on the cheeks and flaccid blisters and crusted erosions on the chest and back for a few weeks. A diagnosis of pemphigus erythematosus was made on clinical, histological and immunological findings. To our knowledge, this is the first case reported from Turkey.

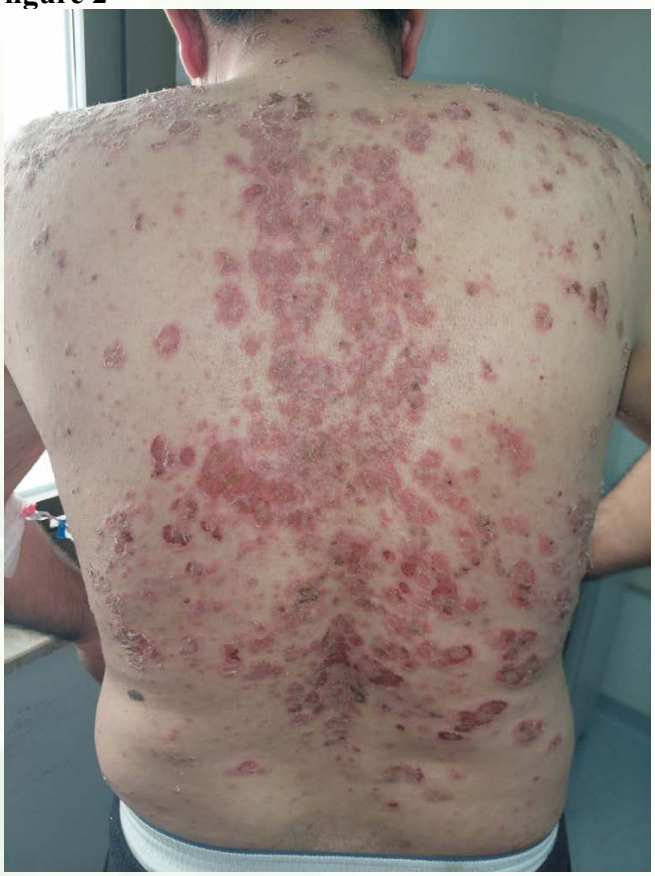
Keywords: Pemphigus erythematosus, Senear-Usher syndrome, Antinuclear Antibody (ANA), Anti-ribosomal P antibody

figure 1



Case Presentation

figure 2



Case Presentation

figure 3

case presentation

OP-15 [Dermoscopy]

Evaluation of Invers Approach's Specifity And Sensitivity in Dermoscopic Differential Diagnosis of Lentigo Maligna

Ece Gokyayla[1], Aylin Türel Ermertcan[2], Peyker Temiz[3]
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[3]Manisa Celal Bayar University, Faculty of Medicine, Department of Pathology

INTRODUCTION: Lentigo maligna is a subtype of malignant melanoma that occurs in chronically sun-exposed skin areas such as the head and neck region. It may be overlooked until the late stages of its progression, especially because of the other signs of sun damage on the skin and its slow growth rate. Therefore, dermoscopic evaluation algorithms are needed to increase diagnostic sensitivity and specificity.

OBJECTIVES: The aim of this study is to prospectively determine the sensitivity of the newly defined inverse approach in the dermoscopic differential diagnosis of lentigo maligna and evaluate its applicability in dermatology practice.

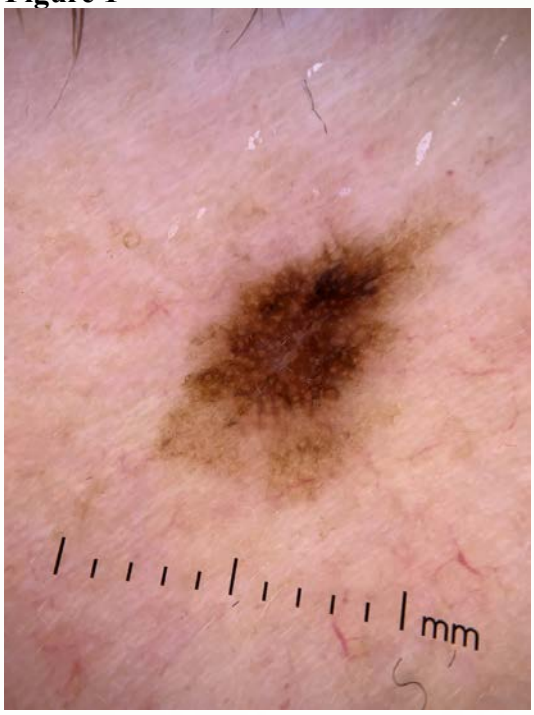
MATERIALS-METHODS: A total of 68 patients with hyperpigmented macules in the head and neck region were included in the study group, and 947 lesions were examined clinically and dermoscopically. The data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 26.0 for Windows.

RESULTS: Out of a total of 947 lesions evaluated in the study, 940 were evaluated dermoscopically as benign. According to the inverse approach, 6 of the 7 lesions were histopathologically diagnosed as lentigo maligna and 1 was diagnosed as atypical lentiginous proliferation. 2 of 6 lentigo maligna were not diagnosed according to classical dermoscopic criteria. The sensitivity of the method was found to be 100% and spesifity of the method was found to be %99,8.

CONCLUSION: According to the results of our study, the inverse approach is an easily applicable diagnostic algorithm in the diagnosis of lentigo maligna with high sensitivity and spesifity. It should be used as an additional algorithm in dermoscopic examinations of patients with chronic sun damage and presenting with multiple hyperpigmented macules in the head and neck region.

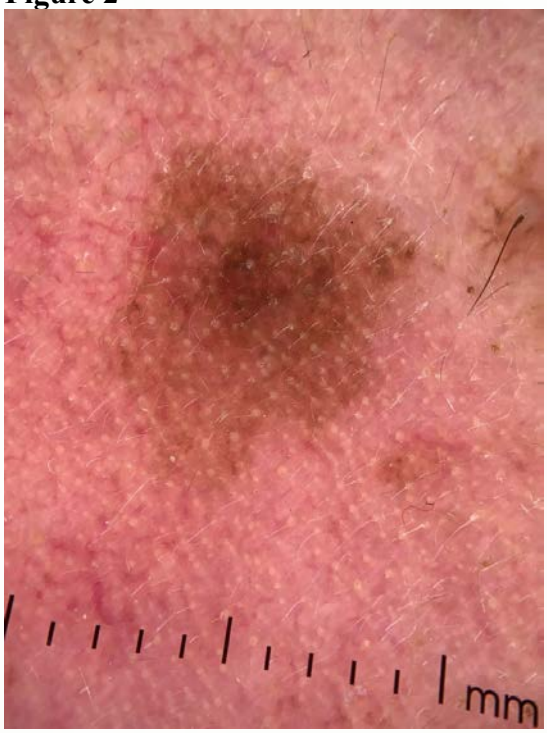
Keywords: lentigo maligna, invers approach, dermoscopy

Figure 1



Asymmetrical follicular pigmentation, rhomboidal structures, homogenous pigmentation with preserved follicular openings. Classical criterias for lentigo maligna are present. Histopathological diagnosis is lentigo maligna.

Figure 2



There is no classical dermoscopic criteria for lentigo maligna. And also the lesion does not have any inverse approach criteria predominantly. Histopathological diagnosis is atypical lentiginous proliferation.

OP-16 [Autoimmune Bullous Diseases]

Baclofen-Induced Dyshidrosiform Bullous Pemphigoid in a Tetraplegic Patient

Neslihan Deniz[1], umit tursen[2]
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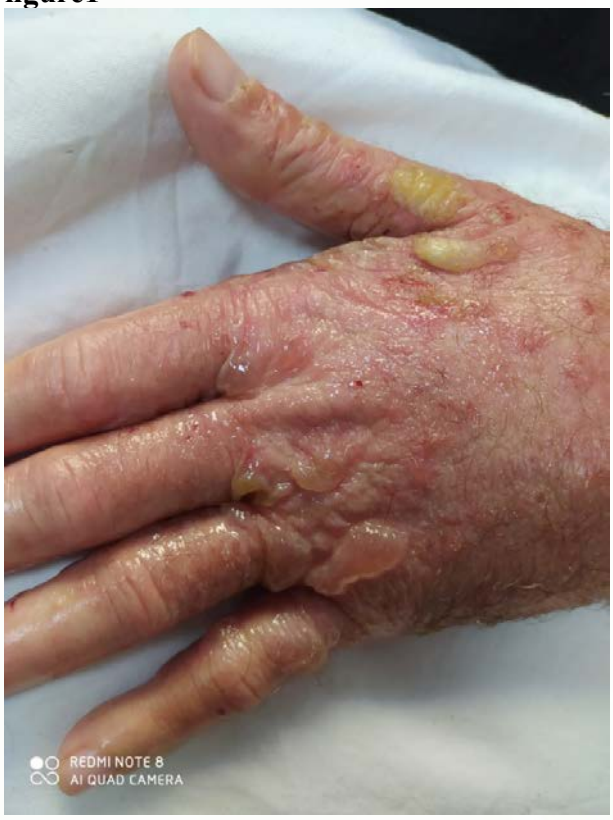
[2]Prof.Dr.Ümiit Tursen,Mersin University, Department of Dermatology,Mersin,Turkey

Dyshidrosiform bullous pemphigoid is a rare variant of bullous pemphigoid, and it usually presents as itchy, potentially hemorrhagic, or purpuric blisters on the palms and soles of elderly individuals; subsequently, typical bullous lesions of bullous pemphigoid appear on other body sites. A 62-year-old tetraplegic male patient presented with a history of tender blisters on the hands and feet for 1 month. Over time, erythema spread all over the body, red itchy lesions on the legs and arms began to form. He had gliclazide, which he had been using for 2 years due to diabetes, and betanecol, which he had been using for 1 month due to neurogenic bladder. Gabapentin was discontinued due to increasing pain and rash, and he was switched to baclofen. He had been using baclofen for 2 months. On skin examination there were hemorrhagic vesiculobullous lesions on the erythematous ground on the hands and feet including the palms and soles. There were also erythematous urticarial plaques on the trunk and extremities, and several hemorrhagic bullous lesions on the arms and legs. In the microscopic examination of the skin biopsies of the lesions in the right ankle there was subepidermal bulla formation and mixed-type inflammatory cell infiltration rich in eosinophil leukocytes in the perivascular and periadnexal area of the dermis. A second biopsy was performed immediately adjacent to the right foot lesion for direct immunofluorescence. Staining for immunoglobulin G (IgG) and C3 showed a flat band of linear immunoreaction deposition at the dermo-epidermal junction. The staining was negative for immunoglobulin A (IgA), immunoglobulin M (IgM), and fibrinogen. Both (direct immunofluorescence) biopsies of the left ankle (hematoxylin and eosin) were diagnostic for bullous pemphigoid. Correlation of clinical history with histopathology and immunopathology diagnosed dyshidrosiform bullous pemphigoid. The patient's eosinophil count was 2900cells/mcl.serum immunoglobulin E (IgE) level was very high at 738 UI/ml (normal: <115 UI/ml). IV methylprednisolone (60 mg/day) and topical clobetasol propionate 0.05% ointment (2 times a day). Betanechol was discontinued with urology consultation. IV prednisone treatment was continued. Azathioprine 50 mg twice a day (after confirming normal thiopurine methyltransferase enzyme activity) was started as a corticosteroid sparing agent. New blisters continued to appear despite the discontinuation of betanechol. Baclofen was discontinued with neurology consultation. The patient's eosinophil count was from 2900 cells/mcl (microliter) to 900 cells/mcl. declined. Within 2 weeks, the lesions on the hands and feet began to regress; There were no new blisters after four weeks. Currently, methylprednisolone and azathioprine treatment continues. Started reducing prednisone by 10mg every other week

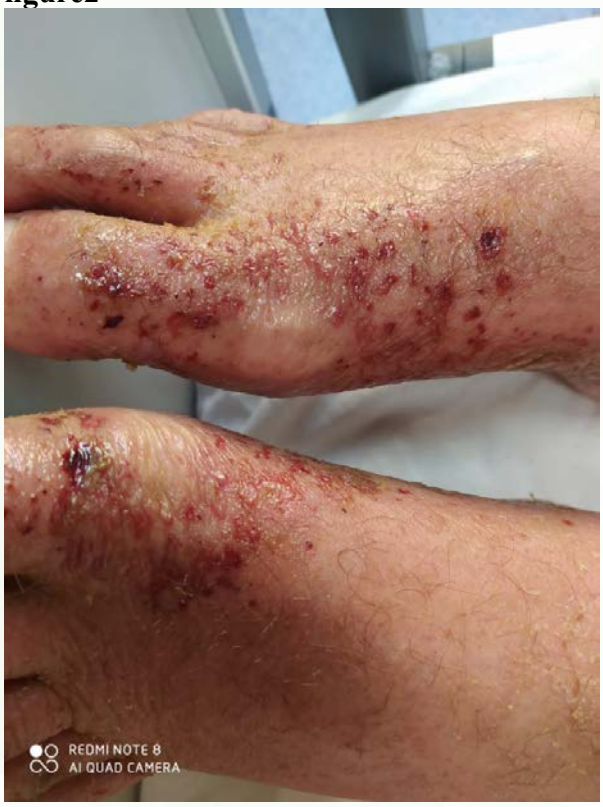
Keywords: Baclofen,blister, bullous, corticosteroid, dyshidrosiform

figure1



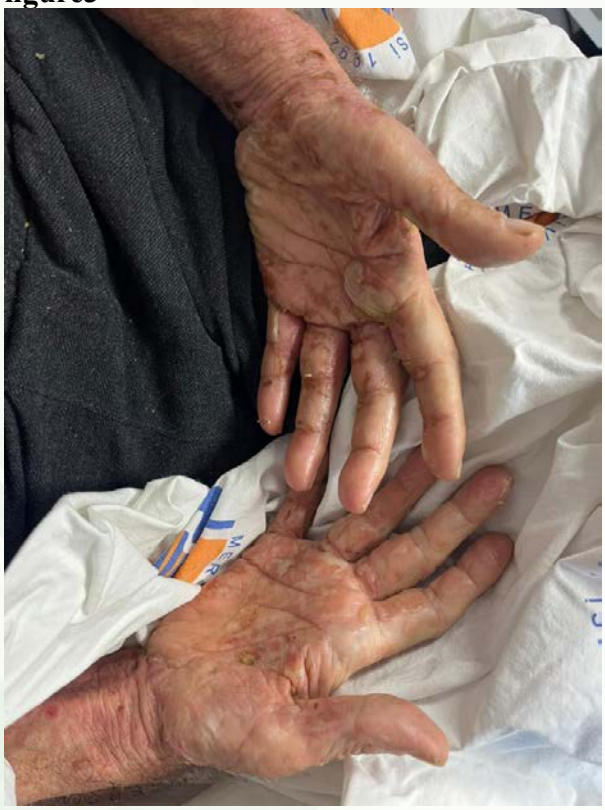
vesiculobullous lesions on the dorsum of the hand

figure2



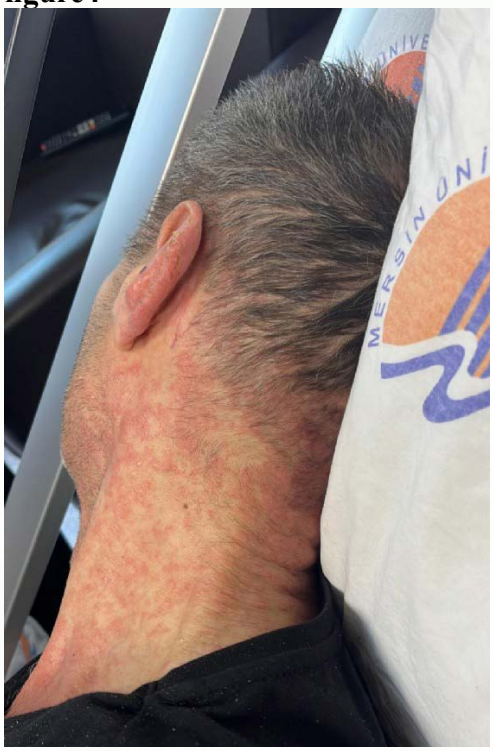
vesiculobullous lesions on the dorsum of the foot

figure3



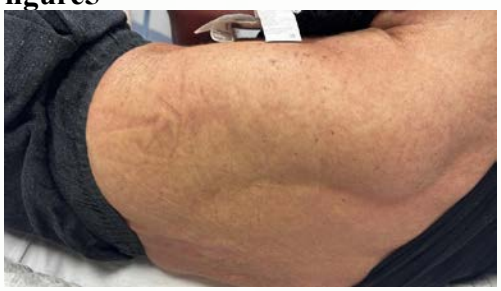
bullous lesions on the palm

figure4



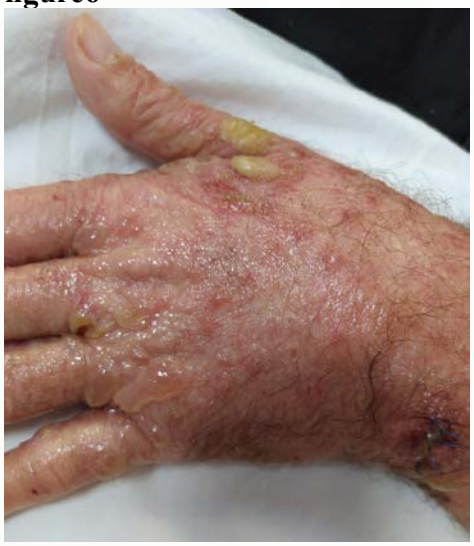
urticarial plaques on the neck

figure5



maculopapular erythema of the back

figure6



veziculobullous lesion on hand

OP-17 [Paediatric Dermatology]

Pediatric Patients with Morphea: A Single-Center Retrospective Study

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INTRODUCTION and OBJECTIVES: Morphea, is a rare sclerosing autoimmune disease. Childhood morphea, also known as juvenile localized scleroderma (JLS), can result in irreversible functional impairments. Data on the clinical and laboratory characteristics and prognosis of pediatric patients with morphea in Turkey are limited. This study aimed to investigate the clinical and demographic features and prognosis of pediatric patients with morphea.

MATERIALS & METHODS: We retrospectively analyzed pediatric patients seen in our outpatient clinics in Istanbul, Turkey, with clinical and histological diagnoses of morphea, between January 2014 and January 2023. Information about each patient's age at disease onset, sites, and distribution of skin lesions, associated systemic manifestations, laboratory results, including antinuclear antibody (ANA) and serology for *Borrelia* IgM and IgG antibodies, treatments, and disease course were evaluated.

RESULTS: A total of 38 patients (27 female and 11 male) with JLS were included in this study. The mean age was 10,18 (range 3-16) years. with a mean disease duration of 2,43 years. The most common type was plaque morphea (n=18); followed by linear type (n=13), generalized type (n=3), mixed type(n=2) and pansclerotic type (n=1). Patients with sclerotic linear lesions with forehead involvement, known as en coup de sabre (ECDS) (n=4), were accepted as the linear type. One patient had progressive hemifacial atrophy (PHA), known as Parry-Romberg Syndrome. A 14-year-old male patient with accompanying vitiligo had a plaque in the left inguinal region, with histopathological findings consistent with both morphea and lichen scleroatrophicus (LSA). Two female patients (one with mixed JLS; one with plaque JLS) had accompanying genital LSA. Four patients had positive Borrelia antibody test results(2 patients were positive for both IgM and IgG antibodies, other 2 patients were seropositive for IgM antibody only). Half of the patients (n=19) were treated with topical agents (topical steroids, pimecrolimus, tacrolimus, and calcipotriol), whereas another half received systemic therapies, including methotrexate, systemic steroids, mycophenolate mofetil, intravenous immunoglobulin (IVIG), and tocilizumab [2 patients (1: pansclerotic type; 1: linear type with severe joint involvement)]. In most children with aggressive disease, systemic therapies stabilized and/or improved the disease.

CONCLUSIONS: Early diagnosis of morphea is essential, especially in pediatric patients, to control and minimize possible future functional impairments. Close monitoring is required for patients with severe cutaneous involvement and arthralgia.

Keywords: childhood morphea, localized scleroderma, morphea, pediatric patients

Characteristics of pediatric patients with morphea

	Plaque	Linear	PHA	Mixed	Generali-zed	Pansclе-rotic	Total
Number of patients	18	13	1	2	3	1	38
Female	12	10	1	2	2	0	27
Male	6	3	0	0	1	1	11
Site of lesions							
Face/sculp	0	6	1	0	0	0	7
Trunk	4	5	0	0	0	0	9
Extremities	11	1	0	0	0	0	12
Two or more sites	3	1	0	2	3	1	10
Distribution							
Unilateral	11	1	1	0	0	0	13
Bilateral	7	12	0	2	3	1	25
Age (mean/range)	9,83 (4-16)	10,15 (3-16)	16	8,5 (3-14)	12 (6-15)	9	10,18 (3-16)
Age at onset (mean/range)	8 (2-14)	7,23 (2-14)	4	6 (2-10)	9 (3-13)	3	7,47 (2-14)
Complications							
CNS	0	0	0	0	0	0	0
GIS	0	0	0	0	0	0	0
Musculosceletal*	1	1	0	1	1	1	5
Alopecia	0	2	0	0	0	1	3
ANA							
Positive	6	4	0	1	1	0	12
Negative	2	2	1	1	2	0	8
N/A	10	7	0	0	0	1	18
Borrelia antibodies							
Positive	2	1	0	0	1	0	4
Negative	5	1	1	2	2	0	11
N/A	11	11	0	0	0	1	23
Treatment							
Topical treatment only	13	6	0	0	0	0	19
Topical and systemic therapy	5	7	1	2	3	1	19

*PHA: progessive hemifacial atrophy. N/A: not available. CNS: central nervous system. GIS: gastrointestinal system *Three patients had arthralgia and/or muscle cramps. Two patients (generalized/ pansclerotic types) had severe musculosceletal involvement.*

Concomitant Diseases of pediatric patients with morphea

Plaque	Linear	PHA	Mixed	Generalized	Pansclerotic	Total
1- Genital LSA 1-Vitiligo 1-PFAPA 1- History of bone marrow transplantation (ALL)	1- asthma 1-asthma +IgA deficiency	none	1- Genital LSA	none	Severe connective tissue disorder	2- Genital LSA 1- Vitiligo 1- Severe connective tissue disorder 1- PFAPA 1- History of bone marrow transplantation (ALL) 1- asthma 1- asthma+ IgA deficiency

ALL: acute lypmphocytic leukemia, LSA: lichen sclerosus et atrophicus PHA: progressive hemifacial atrophy, PFAPA: periodic fever, aphthous stomatitis, pharyngitis, adenitis

OP-18 [Infectious Diseases, Parasitic Diseases, Infestations]

Efficiency Of Squaric Acid Dibutyl Ester Therapy In Treatment Resistant Cases Of Verruca Vulgaris And Verruca Plantaris

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Introduction & OBJECTIVES: Verrucae are skin and mucous membrane infections caused by human papillomaviruses (HPV) with a prevalence of 10% in the population. The infections are more common in younger people and in immunocompromised individuals, and are latent in nature with a manifestation time of 2-9 months. HPV is transmitted through direct contact and no specific antiviral agent has been developed yet. The treatment of verrucae is a long process with challenges such as non-compliance, multiple sessions and high frequency of recurrence. The aim of topical sensitization with SADBE is to create a late-type hypersensitivity reaction in areas with treatment-resistant verrucas. The study compares the results of using SADBE in the treatment of verrucae with those of other studies, and discusses the advantages and disadvantages of SADBE over other methods.

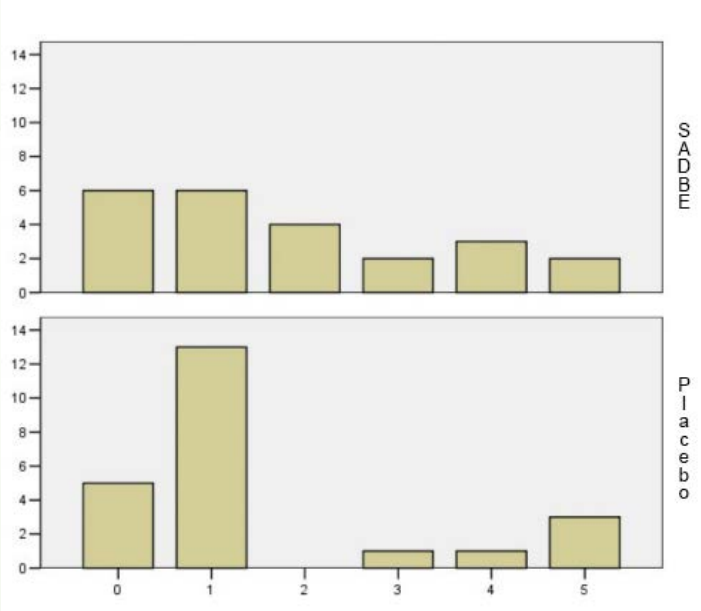
Materials & METHODS: A study was conducted between November 2003 and March 2005 at Haydarpaşa Numune Hospital on patients with verruca vulgaris and plantaris who were resistant to previous treatments or couldn't tolerate invasive procedures. 46 patients, 29 female and 17 male, between 9 and 49 years of age were included. Blood tests and immune system evaluations were done and normal results were considered for inclusion. Participants were divided into 2 groups of 23, one receiving 3% SADBE and the other placebo. Treatment efficacy was evaluated based on changes in lesion areas after 7 weeks of treatment followed by a 3-month follow-up for recurrence. Verruca lesions were photographed and evaluated using software to measure response to treatment. 5 categories were used to evaluate efficacy, from complete response to intensification.

RESULTS: The study evaluated the efficacy of SADBE treatment in 46 patients, who were given SADBE or placebo treatment. At the end of 8 weeks of treatment, the SADBE group showed a 27% reduction in verruca lesion area, compared to 20% in the placebo group. 20 out of 23 patients in the SADBE group experienced sensitization. Side effects caused 4 out of 23 patients in the SADBE group to discontinue treatment. Limited angioedema and allergic dermatitis occurred in 3 patients. The response to treatment was 8% complete, 13% good, 8% moderate, 17% minimal, 26% no response, and 26% increase in lesions in the SADBE group. In the placebo group, the response was 13% complete, 4% good, 4% moderate, 56% no response, and 26% increase in lesions.

CONCLUSIONS: The study found that SADBE was not more effective than placebo in treating treatment-resistant verruca vulgaris and verruca plantaris. The results may have been impacted because only topical SADBE treatment was used and not combined with other methods. Further research is needed to determine the potential efficacy of SADBE with longer and more frequent treatment or in combination with other exfoliating agents. SADBE may still be a viable option for verruca treatment as it is non-mutagenic and can be self-administered at home.

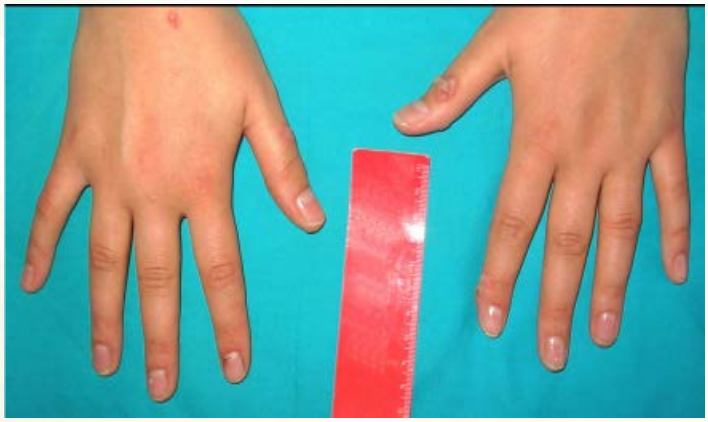
Keywords: SADBE,HPV,Verruca Vulgaris,Verruca Plantaris

Graphic 1



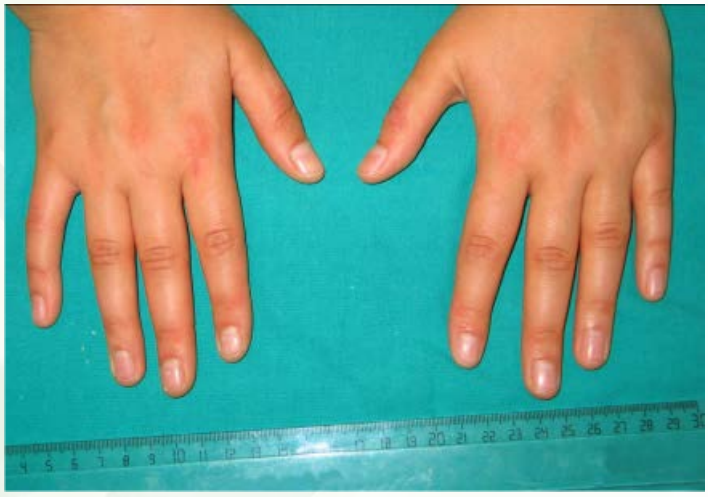
Response to treatment

Photo 1



Verruca vulgaris lesions before SADBE application

Photo 2



Verruca vulgaris lesions resolved after SADBE treatment sessions

OP-19 [Autoimmune Bullous Diseases]

Peristomal localized pemphigoid: Is it a relatively common presentation of bullous pemphigoid with good prognosis?

Can Baykal[1], Elizaveta Ayas[1], Tugba Atci[1], Sule Ozturk Sari[2], Nesimi Buyukbabani[3], Rifkiye Kucukoglu[1]
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[2]Istanbul University, Istanbul Medical Faculty, Department of Pathology
[3]Koc University, Medical Faculty, Department of Pathology

INTRODUCTION & OBJECTIVES: Localized bullous pemphigoid (LBP) is among rare clinical subtypes of bullous pemphigoid (BP) showing favorable prognosis which is most commonly associated with a triggering factor such as operation or burn scars, amputation stumps and radiotherapy sites. LBP occurring on peristomal area has rarely been reported without a well-known incidence and the pathogenesis of lesions in this special presentation of BP is not well understood. MATERIALS & METHODS: This is a retrospective study of BP patients diagnosed between 1990 and 2023 investigating the rate of peristomal involvement and the features of these patients in a tertiary dermatology center. The data including sex, age at diagnosis, diagnosis leading to stoma placement, stoma type and stoma duration, clinical, histological and immunofluorescence findings (direct and indirect immunofluorescence), levels of anti-BP180 and/or anti-BP230 (ELISA), treatment and follow-up were recorded. In addition, our data was compared with literature. RESULTS: We observed peristomal involvement in four (1.5%) (M/F:1) cases among 270 BP patients (Table 1). All patients presented with bullae, vesicles and/or erosions around colostomy site. They were diagnosed as BP with histopathological and direct immunofluorescence examination and anti-BP180 and/or anti- BP230 positivitiy. The mean age at BP diagnosis was 69.5±6.8 (63-78) years. Peristomal lesions occurred 4.7±3.8 (1-10) years after stoma placement. While three patients' BP lesions were on peristomal localization (colostomy limited),

one patient developed only peristomal BP lesions for three years shortly after the initial diagnosis of generalized pemphigoid. One patient was lost to follow-up after peristomal BP diagnosis and topical corticosteroid (n=3), systemic corticosteroid (n=2) and dapsone (n=2) were the treatment of choice in three patients in a mean follow-up period of 4.7±4 years. CONCLUSIONS: The high rate of peristomal BP patients in our series raised the possibility of misdiagnosis of this specific condition as irritant dermatoses. Both in our series and in the literature, the most common diagnosis leading to stoma placement was malignancy operations and in addition to patients showing a disease course limited to peristomal area, there are some patients associated with generalized skin and mucosal lesions. Recognition and prompt appropriate treatment of this specific condition showing a favorable prognosis in comparison with classical BP is important in order to improve the quality of life of patients.

Keywords: Bullous pemphigoid, stoma, colostomy, urostomy

Table 1. The clinical, immunofluorescence and laboratory findings and treatment data of our patients

Age (years) /Sex	Diagnosis leading to stoma placement	Stoma type/ Stoma duration (years)	DIF	IIF	BP180 (ELISA)	BP230 (ELISA)	Localization of BP lesions during disease course	Treatment	Duration of follow-up (years)
63-78†/F (n=2), M (n=2)	Rectal carcinoma (n=3), IBD (n=1)	Colostomy /1-10	IgG, C3 (n=3), C3 (n=1)	+ (n=1) - (n=2) NA (n=1)	+ (n=3) NA (n=1)	+ (n=1) - (n=2) NA (n=1)	Colostomy limited (n=3), generalized pemphigoid lesions followed by only peristomal involvement (n=1)	TC (n=3), SC (n=2), dapson (n=2)/CR (n=3), lost to follow-up (n=1)	4.7±4

†age range, M: Male, F: Female, IgG:Immunoglobulin G, C3: Complement 3, NA: Non-available, DIF: Direct immunofluorescence, IIF: Indirect immunofluorescence, TC: Topical corticosteroid, SC: Systemic corticosteroid, CR: Complete response, IBD: Inflammatory bowel disease, ELISA: Enzyme-linked immunosorbent assay

OP-20 [Hair Disorders/Diseases]

Complete healing of alopecia areata in an eleven year old girl with diphencyprone treatment

Zuhal Erçin
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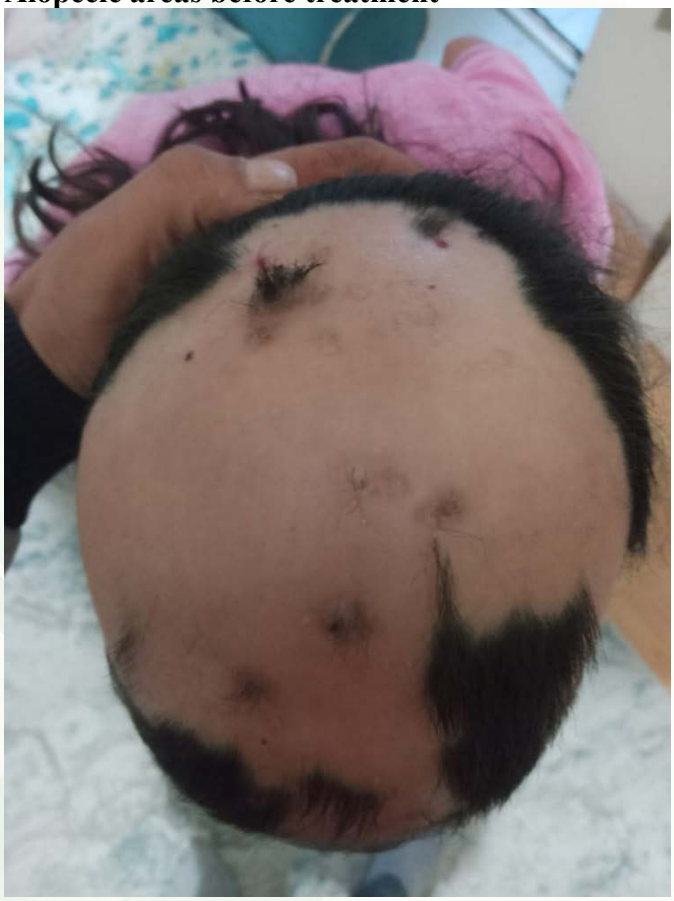
Diphenylcyclopropenone (DPCP), also known as diphencyprone, is a sensitizing agent used by some dermatology centers to treat skin conditions by contact immunotherapy. Diphencyprone is most often used to treat alopecia areata. Application of diphencyprone to the skin results in allergic contact dermatitis. In alopecia areata, it is believed to work by redirecting the autoimmune attacks on the hair follicles, allowing for regrowth. Initial sensitization to diphencyprone is required for the treatment to work. The clinician applies a small test patch of high concentration diphencyprone (2%) and it will be left in place for 2-3 days to induce contact allergy. After initial sensitization, a very low diphencyprone concentration is often chosen to reduce the severity of dermatitis, for example, 0.001%. The strength is gradually increased over time. The solution should remain on the skin for 6-24 hours or as directed and is then washed off. The area of application should be physically covered, as diphencyprone is degraded by sunlight. As diphencyprone causes contact allergy, local dermatitis is an expected part of treatment and sometimes swollen lymph nodes may be noticeable behind the ears. These side effects generally clear up promptly when treatment is stopped. It is recommended that treatment should be continued for 6 months before declaring treatment failure. Diphencyprone treatment is usually continued weekly until the hair is regrown, which may take up 12 months. Treatment is stopped upon hair regrowth and patients are monitored for relapse. Our patient is an eleven year old girl. She applied to our dermatology outpatient clinic with her family in March 2022. She came with the complaint of alopecia. On examination she has been found to have a new onset alopecia areata with a SALT score of 51. Her laboratory findings showed no abnormality except an elevated anti-TPO level. The pediatrician didn't seek any further examination or treatment because

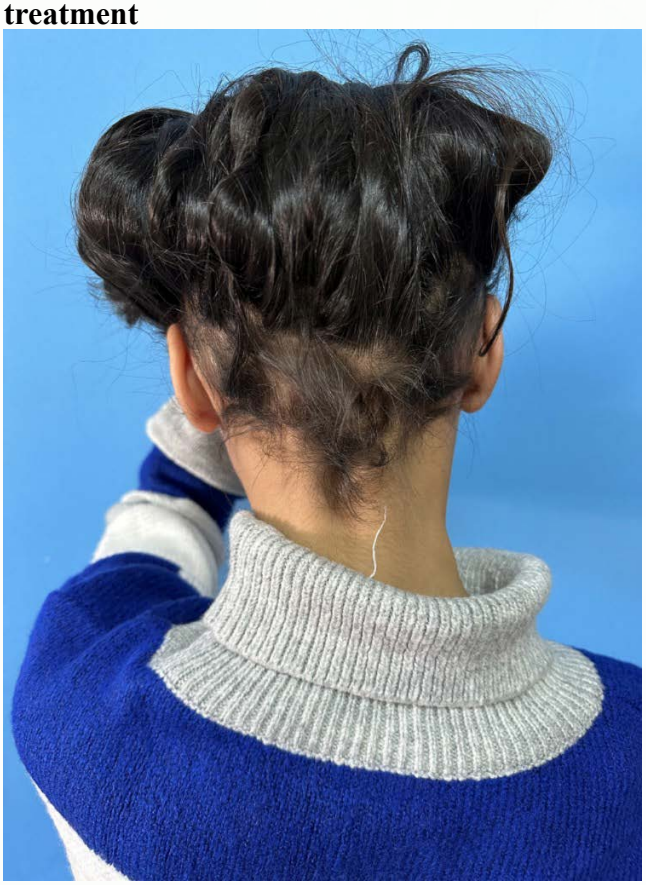
her TSH level was normal. At the beginning she has been prescribed topical anthralin. Her anthralin contact therapy has been started with 10 minutes and has been gradually increased until 30 minutes. After anthralin has been found unsuccesful, topical steroid and 5% minoxidil therapy has been tried with no success. We decided to start topical diphencyprone therapy in our clinic. First we sensitized the patient with 2% DPCP. Then we began weekly treatments starting with 0.001% DPCP. We applied the same dose when an eryhtema developed after the application and otherwise we increased the dose to 0.01%, 0.1%, 0.2%, 0.5%, 1% and 2% respectively. After 16 weeks of treatment she showed full regrowth of hair on her alopecic areas. Diphencyprone contact immunotherapy is a promising treatment for alopecia areata and perhaps should be in the first line of its treatment.

Keywords: Alopecia areata, diphencyprone, diphenylcyclopropenone, contact immunotherapy

Alopecic areas before treatment

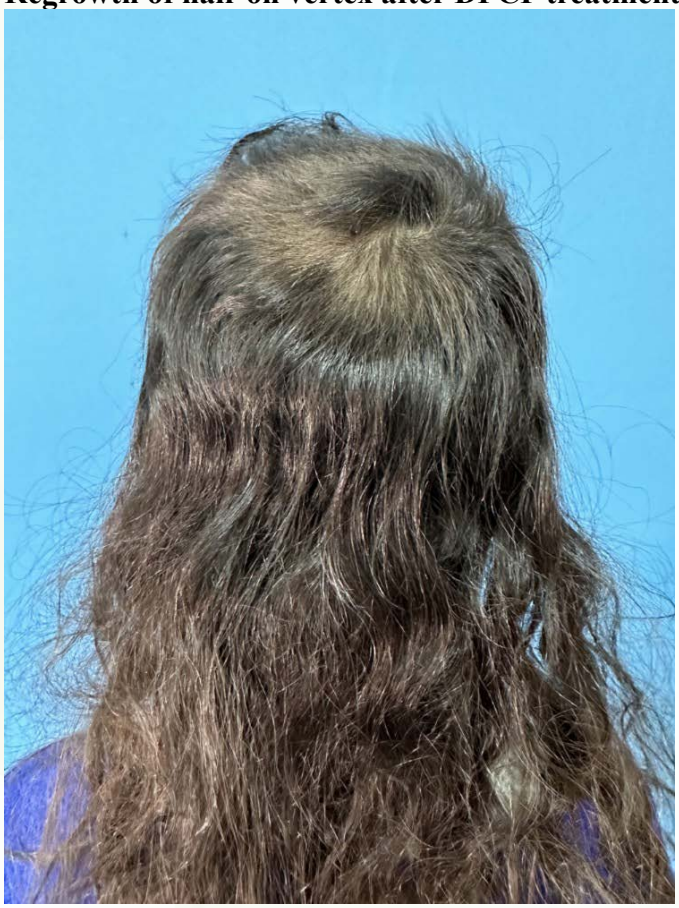


Regrowth of hair on occipital area after DPCP treatment



Regrowth of hair on the temporal area after DPCP treatment

Regrowth of hair on vertex after DPCP treatment



OP-21 [Dermatopathology]

Demographic, clinical, and histopathological features of Merkel cell carcinoma: A single-center retrospective study

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Introduction & OBJECTIVES: Merkel cell carcinoma (MCC) is an extremely rare neuroendocrine carcinoma of the skin with an aggressive clinical course. MCC is more common in Caucasians and data from Asian countries are limited to a small number of case reports. In our study, we aimed to define the demographic, clinicand histopathological features of patients diagnosed with MCC.

Materials & METHODS: Patients diagnosed with MCC in our institute between 2003 and 2022 were evaluated retrospectively. We reviewed the records of 6 patients and re-evaluated the histologic slides of the cases. RESULTS: All patients were over 50 years at diagnosis (mean age 77.5 years). Most patients were female (M:F = 1/2). The most common tumor site was the head and neck region (n=3), followed by the upper extremities (n=2), and the lower extremities (n=1).Tumor diameters ranged between 1.1 and 8 cm. 2 patients had lymph node metastasis and 3 had distant metastasis. 2 patients had previous malignancy,1 prostate cancer and 1 chronic lymphocytic leukemia (Table 1).

CONCLUSIONS: MCC clinically appears as a small, red-purple colored, painless, firm, solitary dermal nodule with a shiny surface and telangiectasias. The most common anatomical site of the primary lesion is the head and neck region, followed by the arms and legs. Advanced age, immunosuppression, hematological malignancies, and presence of other cutaneous tumors are risk factors. Immunosuppression and hematological malignancies are also associated with a worse prognosis. Histopathological examination is essential for diagnosis. MCC typically exhibits sheets and nests of uniform small round blue undifferentiated cells with scant cytoplasm,large lobulated nucleoli, high mitotic rate and occasional necrotic cells. Immunohistochemical markers, especially cytokeratin-20, which are positive in approximately 95% of cases and are useful in differentiating from other neuroendocrine tumors, are required for diagnosis. First-line therapy for primary or regional MCC is wide local ecsion supported by adjuvant radiotherapy. Advanced MCC requires chemotherapy and emerging immunotherapeutic agents. The incidence of MCC is increasing gradually. Large-scale epidemiological studies are needed to determine the demographic, clinical, and histopathological features of the tumor especially for non-Caucasian countries

Keywords: merkel cell carcinoma,dermatopathology,skin tumors

Demographic, clinical, and histopathological features of patients

Case	Age/Sex	Tumor Site	Tumor diameter (cm)	TNM stage	Distant metastasis	Lymph node metastasis	Tumor multifocality	Previous Malignancies	Mitotic rate (mm2)	Necrosis	Ulceration	Perineural invasion
1	70/M	Temporal	1.4	T1NxMx	-	-	Solitary	N/A	8	-	-	-
2	72/F	Lip	1.5	T1NxMx	-	-	Solitary	-	15	-	+	-
3	53/F	Antecubital	8	T4N3M1c	Skin and bone marrow	Jugular and axillary lymph nodes	Multiple	Chronic lymphocytic lymphoma	43	+	-	+
4	95/F	Lower extremity	8	T3N2M1c	Skin and pelvic area	-	Multiple	-	10	+	+	+
5	93/F	Forehead	4.2	T4N1bM1c	Intra-abdominal	Cervical lymph nodes	Solitary	-	35	-	-	+
6	82/M	Finger	1.1	T1NxMx	-	-	Solitary	Prostate adenocarcinoma	15	-	+	+

OP-22 [Dermatology and Internal Medicine, including Skin Manifestations of Systemic Diseases]

A case of skin manifestation of richter's transformation in a patient with chronic lymphocytic leukemia

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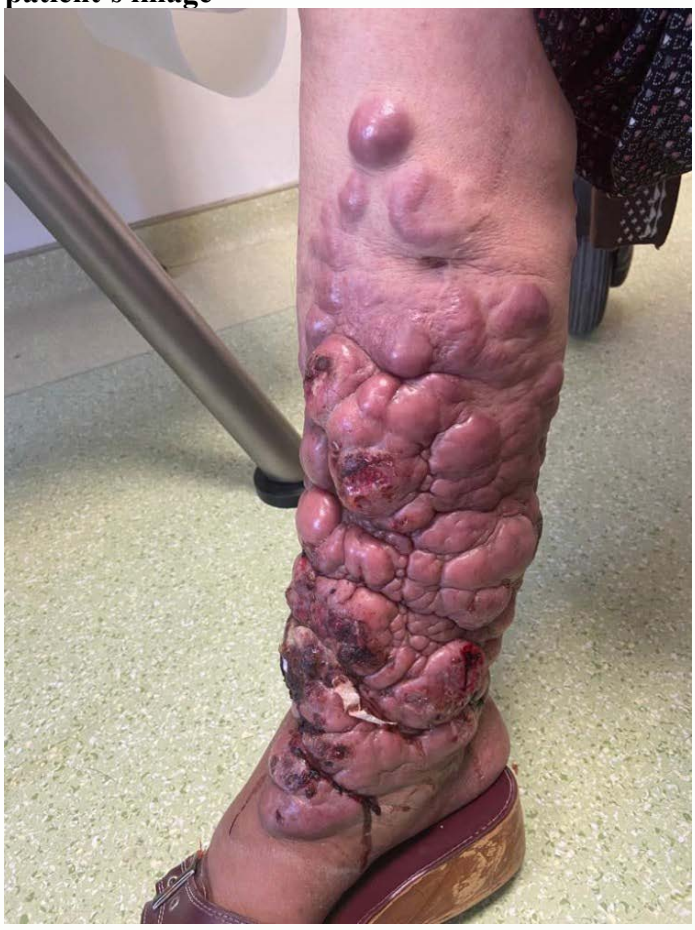
Keywords: cutenous lymphoma, chronic lymphocytic leukemia, richter's syndrome

Cutaneous lesions are seen in about 30%-50% of patients with chronic lymphocytic leukemia. specific skin lesions are seen less frequently in patients with CLL, which can cause a wide spectrum of skin lesions. specific skin lesions are in the form of skin involvement of leukemia cutis and richter syndrome. In our case, an 80-year-old woman with CLL for 2 years was evaluated as cutaneous involvement of richter syndrome and referred to the hematology-oncology department after the biopsy taken from the diffuse lobular lesion on the right leg of an 80-year-old woman with CLL for 2 years was found to be diffuse large b-cell lymphoma. as dermatologists, evaluation of these lesions for primary infiltration or secondary malignancies will provide early diagnosis and treatment of the disease and may have a positive effect on the patient's survival.

patient's image



Patient's right leg

OP-23 [Urticaria, Angioedema]

Efficacy of omalizumab in elderly patients with chronic spontaneous urticaria: a multicenter observational study

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Introduction & OBJECTIVES: Treatment with omalizumab is used effectively and safely in patients with chronic spontaneous urticaria (CSU) who do not respond to non-sedating antihistamines. Chronic spontaneous urticaria can affect elderly patients and impair their quality of life. However, comorbidities in elderly patients and the use of multiple drugs limit treatment options. Our study evaluated the efficacy of omalizumab treatment in patients with CSU over the age of 60 years.

Materials & METHODS: A total of 163 CSU patients treated with omalizumab at a dose of 300 mg every 4 weeks for 12 weeks were enrolled in our study. Patients were divided into two groups: ≥60 years and < 60 years. Patients' sociodemographic characteristics, duration of diagnosis, presence of concomitant angioedema, hemogram parameters, serum immunoglobulin E (Ig E) level, and concomitant comorbidities were examined. The Urticaria Activity Score 7 (UAS7) was used to evaluate the efficacy of omalizumab treatment. Patients with a UAS7 score of "0" on the seventh day of omalizumab treatment were classified as early complete responders (ECR); patients who achieved a UAS7 score of "0" during the first three months of treatment were classified as late complete responders (LCR); patients whose UAS7 score decreased by 50% after three months were classified as partial responders (PR); whose UAS7 score is not decreased by %50 after three months were classified as non responders (NR).

RESULTS: Twenty-eight (17.2%) of the patients were 60 years or older. UAS7 scores were similar in both groups at baseline and at the fourth and twelfth weeks of treatment (Table 1). There was a statistically significant decrease in UAS7 scores in both age groups at the fourth and twelfth weeks compared to baseline (p=0.000, p=0.001) (Table 2). Hypertension was the most common comorbidity in the age group ≥60 years; autoimmune and psychiatric diseases were the most common comorbidities in the age group <60 years. It was observed that 20.7% of patients <60 years and 32.1% of patients ≥60 years achieved an ECR (Table 3).

CONCLUSIONS: Our study demonstrated that the response to omalizumab in patients ≥60 years of age was similar to that in patients <60 years of age. It was concluded that omalizumab is also an effective treatment in the elderly population.

Keywords: chronic spontaneous urticaria, elderly, omalizumab

Table 1. Distribution of mean of UAS7 scores in both age groups

	<60 years	≥60 years	p
UAS7 scores at baseline	19.79±12.13	15.46±9.55	0.072
UAS7 scores at week 4	7.27±6.87	5.54±6.04	0.179
UAS7 scores at week 12	3.41±6.08	4.89±9.47	0.826

Mann-Whitney U analysis, Abbreviation: UAS, urticaria activity score

Table 2. Change from baseline in UAS7 scores at weeks 4 and 12 in two patient age groups

	Change in UAS7 from baseline to week 4	p	Change in UAS7 from baseline to week 12	p
<60 years Mean (SD) Median (Min-Max)	12.23±10.31 10 (-7-42)	0.000	16.08±12.01 14 (-28-42)	0.000
≥60 years Mean (SD) Median (Min-Max)	9.93±8.42 10.5 (-7-24)	0.000	10.57±14.42 12 (-28-42)	0.001

Wilcoxon Signed Ranks Test. Abbreviation: UAS, urticaria activity score; SD, standard deviation; Min, minimum; Max, maximum.

Table 3. Comparison of omalizumab treatment responses in two patient age groups

	<60 years	≥60 years	p
ECR	28 (20.7)	9 (32.1)	0.190
LCR	39 (28.9)	7 (25)	0.677
PR	55 (40.7)	8 (28.6)	0.229
NR	13 (9.6)	4 (14.3)	0.497

Pearson Chi-Square test, Fisher's Exact test.
Abbreviations: ECR, early complete responders; LCR, late complete responders; PR, partial responders; NR, non-responders.

OP-24 [Corrective, Aesthetic and Cosmetic Dermatology]

Botulinum Toxin Induced Prolonged Blepharoptosis Lasting 6 Months: A Case Report

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INTRODUCTION & OBJECTIVES: Botulinum toxin injection is the most common minimally invasive cosmetic procedure performed in all over the world. It is considered as a safe therapy with typically self-limited side effects such as bruising, erythema, and pain. Blepharoptosis is the most significant side effect of botulinum toxin injection presenting as drooping of the upper eyelid. It typically resolves spontaneously within 3–4 weeks, maximum in 12 weeks.

MATERIALS & METHODS: It is a case report. Herein, we report a 53-year-old woman who had a drooping right upper eyelid lasting 6 months after receiving botulinum toxin injection for facial rejuvenation.

RESULTS: A 53-year-old-woman presented with a demand to get botulinum toxin injection for the treatment of facial lines of expression. After detailed consultation and evaluation, she underwent botulinum toxin injection for glabellar frown lines, horizontal forehead wrinkles and crow's feet area. After a couple of days, the patient contacted us and said that her right eyelid drooped. The patient was relieved, and it was explained that this was a complication of botulinum toxin and was temporary lasting 1 to 3 months. Brimonidine tartrate 0.15% (1.5 mg/ml) eye drops was recommended to ease the ptosis period. After 1.5 months, the patient was checked, the ptosis did not resolve although it improved when the patient used the eye drops. After 2 weeks, 5-minute vibration massage to right eyelid and 10-minute radiofrequency massage to right eyelid and forehead once a week for 4 sessions were initiated with the intention of shortening the effect of botulinum toxin. After 4.5 months, the ptosis still persisted so the patient was consulted to a neurologist to investigate other causes of ptosis. Her eye movements, including rapid alternating saccades, were normal, and her pupils were equal and reacted briskly to light and nearness. Right upper lid did not fatigue with sustained upgaze. An ice-pack test was negative. General physical examination was normal. Acetylcholine receptor antibody titer was within the normal limits. No thymus pathology was detected in thorax CT. Based on clinical findings and laboratory tests, it was concluded that ptosis was induced by botulinum toxin excluding Horner's syndrome and myasthenia gravis. Intradermal and intramuscular injection of dimethylethanolamine to upper eyelid and forehead was performed once a week, 4 sessions. Ptosis finally resolved after 6 months.

CONCLUSIONS: Although it is usually expected for botulinum toxin induced ptosis to last approximately 3 months, practitioners should keep in mind that it may take up to 6 months for ptosis to resolve. Practitioners should consider other causes especially for the ptosis lasting longer than 3 months. Based on clinical findings and by the help of diagnostic tests, the accurate cause of ptosis should be revealed and treated accordingly.

Keywords: botulinum toxin, complication, eyelid, ptosis

OP-25 [Dermatopathology]

Clinical polymorphism and treatment of patients with lichen planus

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Lichen planus (LP) is a fairly rare dermatoses and is characterized by a variety of clinical manifestations not only on the skin, but also on the oral mucosa.

The aim of this study was to study the features of the course of lichen planus and develop adequate therapy for this dermatosis. Under observation were 42 patients (men-18, women-24) with various forms of lichen planus, who were in the age group of 20-55 years. The following forms of lichen planus were established: classical - in 27 (64.3%), atypical - in 15 (35.7%), and among the latter, 4 patients were identified with pigmentary, 6 with verrucous, 2 with pemphigoid, 3 - with ring-shaped forms of dermatosis. The manifestations of LP on the oral mucosa were found in 12 of 27 (44.4%) patients with the classical form and in 14 of 15 (93.3%) with atypical forms of dermatosis. All patients, by fluorescent immunoassay, were subjected to quantitative determination of CRP and hs-CRP in blood serum, and the intensity of the fluorescence signal of CRP and hs-CRP antibodies, detected using the Wondfo Finecare FIA Meter, is reflected quantitatively. CRP and hs-CRP results are expressed in mg/l. In patients with LP, the most conclusive inflammatory marker is the hs-CRP index rather than the CRP index. In addition, in patients with atypical forms of LP, these indicators of inflammation were significantly increased ($p<0.001$) compared with those in patients with the classical form of LP. In the treatment of patients with LP, injections of placenta extract were used, which was administered intravenously in 4 ml of the drug diluted in 200.0 ml of saline. Infusions were carried out every other day and the patient received 10 injections of the specified drug for the course of treatment. Thus, in patients with LP, especially with atypical forms, an inflammatory reaction is noted, assessed using CRP and hs-CRP, for the correction of which it is proposed to use placental extract injections, which in most cases allows achieving positive dynamics of LP.

Keywords: Clinical polymorphism, treatment, derma

OP-26 [Autoimmune Bullous Diseases]

Is relapse prediction in pemphigus vulgaris patients possible? Preliminary results of a retrospective study

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Is relapse prediction in pemphigus vulgaris patients possible? Preliminary results of a retrospective study. Object: Pemphigus is a severe autoimmune-blistering disease of the skin and mucous membranes caused by autoantibodies targeting epithelial cell-cell adhesion molecules. Pemphigus vulgaris typically exhibits a chronic relapsing course Clinical and immunological factors that are associated with clinical relapse is not clarified. In this study we aim to identify demographic and clinical factors at diagnosis and during follow□up that could be predictors of relapse. MATERIALS-METHODS: This is a retrospective study including 53 randomly selected and for at least 36 months followed up patients from 480 patients, who are diagnosed between 1988-2022 in our Dermatology Department. Clinic, laboratory and demographic findings were obtained from a review of medical records, histopathological examination of all patients diagnosed with PV. Disease severity is evaluated with modified pemphigus severity scale and patients are divided into three groups as mild, moderate and severe. During their follow-up, the patients were divided into two main groups as at least one or more relapsed and no relapses. Demographic and clinical characteristics of these two groups were compared with appropriate statistical methods.

RESULTS: 53 patients diagnosed as PV with a mean age of 45.9±11.1 were included in this study. %70 (37/53) were female and %30 (16/53) were male with a mean follow up duration of 87 months (36-128). Mucosal involvement detected in %30.2 (16/53) patients, mucosal and cutaneous involvement in %67.9 (36/53) and only cutaneous involvement detected in %1.9 (1/53) of patients. In %24.5 (13/53) of patients there was no relapse and in %75.5 (40/53)

of patients at least one relapse was detected. When a total of 123 relapses observed in 40 patients were examined, rapid discontinuation of corticosteroids was the most common cause of relapse (n=9) and rapid discontinuation of immunosuppressives and dose reduction (n=5), infectious diseases (n=9). Relapse rate is significantly higher in male patients (%93.8 vs %67.6, p=0.026). When the relapsed and non-relapsed groups were compared, the disease severity score (p=0.041), scalp (p=0.02), head-neck (p<0.01) and lower body (p=0.031) involvement rates were significantly higher in the relapsed group. CONCLUSIONS: In pemphigus vulgaris patients, disease severity and some specific localizations such as scalp, head and neck region, lower body involvement may be predictive factors for disease relapse. Misuse and/or discontinuation of systemic corticosteroids and immunosuppressives by both physicians and patients and systemic infections are the most common causes of relapse.

Keywords: pemphigus vulgaris, relapse, corticosteroid

OP-27 [Diagnostic Procedures]

Basic Principles of Ultrasound

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Medical ultrasound is a diagnostic tool that uses high-frequency sound waves to produce images of internal organs, tissues, and vessels. Understanding the basic technical principles of medical ultrasound is essential for optimizing its use and ensuring the best possible patient outcomes. The basic technical principles of medical ultrasound are: transmission, reflection, wavelength, Doppler effect, absorption and scatter. Medical ultrasound has applications in both dermatology and aesthetics, although the ways in which it is used can differ depending on the specific context. In dermatology, medical ultrasound can be used to produce images of subcutaneous structures, including skin, fat, and underlying vessels. This information can be used to diagnose and monitor various skin conditions, such as skin tumors, dermatitis, and cellulitis, as well as to evaluate the effectiveness of treatments. Additionally, medical ultrasound can be used to guide biopsy procedures and to evaluate the thickness of the skin and underlying tissues. In aesthetics, medical ultrasound can be used to produce images of subcutaneous structures, including fat and underlying vessels, which can then be used to evaluate the effectiveness of treatments such as fat reduction and skin tightening. For example, ultrasound can be used to monitor the progression of non-invasive fat reduction treatments, such as ultrasound-assisted lipolysis, and to evaluate the success of skin tightening treatments, such as ultrasound-assisted skin rejuvenation. In conclusion, medical ultrasound has applications in both dermatology and aesthetics, and it can be used to produce images of subcutaneous structures and to evaluate the effectiveness of various treatments. Understanding the relationship between medical ultrasound and dermatology and aesthetics is important for optimizing its use and ensuring the best possible patient outcomes.

Keywords: ultrasound, skin ultrasound, dermatology ultrasound

OP-28 [Urticaria, Angioedema]

The Frequency of Sexual Dysfunction and Its Effect on the Quality of Life In CSU Patients Treated with Omalizumab

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Background: Chronic Spontaneous Urticaria (CSU) is a common, chronic, and debilitating disease. In addition, it seriously affects the quality of life, mental health, and sexual life. The study presented in this abstract investigated the impact of CSU on female sexual functioning, which is largely unknown.

Objective: We planned a retrospective study to investigate the effects of omalizumab on sexual function in CSU patients. We also aimed to evaluate the quality of life (QoL), depression, anxiety, and stigma states of patients.

Methods: The records of female patients with CSU who applied to the dermatology outpatient clinic from January 2022 to January 2023 were reviewed. The patients who use omalizumab treatment due to the unresponsive of the fourfold increased H1 antihistamine treatment were included in the study. Urticaria activation score (UAS7), Beck depression inventory (BDI), Beck anxiety inventory (BAI), Dermatology life quality index (DLQI), female sexual function index (FSFI), Rosenberg self-esteem scale and internalized stigma in chronic urticaria to female participants were performed at the start of omalizumab treatment and the sixth month of treatment. The obtained data were analyzed by using SPSS software.

Results: Sexual functioning, that is, total Female Sexual Function Index scores and all subscores, was markedly reduced at six months of Omalizumab treatment in female patients with CSU. Impaired sexual functioning was linked to high disease activity and poor disease control. Reduced sexual functioning was associated with anxiety and depression and significantly correlated to impaired quality of life.

Conclusions: Our study shows that CSU is related to sexual functioning in female patients with CSU. Sexual dysfunction is widespread in female patients with CSU. It should prompt physicians who treat patients with CSU to talk about sexual health and functioning with their patients and to take sexual dysfunction into account when making treatment decisions. Effective treatment of CSU may improve sexual functioning together with anxiety.

Keywords: chronic urticaria, omalizumab, psychological, quality of life, sexual dysfunction

OP-29 [Dermatological Practice Management]

The study of cytokine status and immunological changes in patients with non-segmental form of vitiligo

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We observed 37 patients with non-segmental vitiligo to study cytokine status and immunological changes. Of the cytokines, FNO-α and IL-21 were of interest to us. The immunogram was studied by flow cytometry. All patients were aged 18-68 years, men and women were equally divided. Cytokine levels in patients with vitiligo

Table 1.

Index Reference interval Control group (n=22) Main group (n=37) Patients carrying mutant alleles (n=10)
ФНО-альфа, пг/мл 0-5,9 0,99± 0,1 8,63± 1,03* 12,1± 0,3*
ИЛ-21, пг/мл 0,7 ±0,1 0,33± 0,01 1,82± 0,91* 1,62± 0,02*
*- statistically significant relative to the control group at $p<0,05$.

The study of the immunogram in patients with vitiligo revealed that the average values were within the reference interval; there were no differences between the experimental and control groups for the following parameters: for CD45, CD3, CD20, CD4, CD4CD8 (cortical thymocytes), Natural killer T-lymphocytes (TNK-lymphocytes), Natural killer cells (NK), T-activated lymphocytes (IL-2), B-activated lymphocytes (IL-4, IgE), while Cytotoxic T-lymphocytes CD8+, IRI, T-activated lymphocytes (IL-2), B-activated lymphocytes (IL-4, IgE), Fas-apoptosis receptor, Marker of activated IL-2 apoptosis were significantly higher, than in control. Even though the mean values for the experimental group did not differ from the control group, the number of persons with deviations in the experimental group was significantly higher than in the control

group - 80% versus 15% ($p<0.05$). Signs of an autoimmune lesion according to the immunogram were detected in 24 (8.4%) patients with vitiligo, they were expressed in an increase in CD8+, CD95+, as well as activated lymphocytes CD3+ CD25+. The study of the immunogram in patients with vitiligo revealed that the average values were within the reference interval; there were no differences between the experimental and control groups for the following parameters: for CD45, CD3, CD20, CD4, CD4CD8 (cortical thymocytes), Natural killer T-lymphocytes (TNK-lymphocytes), Natural killer (NK), T-activated lymphocytes (IL- 2), B-activated lymphocytes (IL-4, IgE), while Cytotoxic T-lymphocytes CD8+, IRI, T-activated lymphocytes (IL-2), B-activated lymphocytes (IL-4, IgE), Fas-receptor apoptosis, the marker of activated IL-2 apoptosis were significantly higher than in the control. Even though the mean values for the experimental group did not differ from the control group, the number of persons with deviations in the experimental group was significantly higher than in the control group - 80% versus 15% ($p<0.05$). Signs of an autoimmune lesion according to the immunogram were detected in 24 (8.4%) patients with vitiligo, they were expressed in an increase in CD8+, CD95+, as well as activated lymphocytes CD3+ CD25+.

Keywords: cytokine, immunological, vitiligo

Immunogram parameters in patients with vitiligo

Subpopulations of lymphocytes	Differentiation markers	Reference values, %	Control group	Result
Lymphocytes	CD45+	17-47	28,1±1,4	32,4± 2,0
T-lymphocytes	CD3+	61-85	70,0±6,0	68,1 ±1,31
B-lymphocytes	CD20+	0.7-17	15,4±0,7	15,9±1,57
T-helpers	CD3+CD4+	35-55	43,2±4,1	48,2±2,2
Cytotoxic T-lymphocytes	CD3+CD8+	19-35	24,6±4,0	28,2±1,62*
Immunoregulatory index	CD4/CD8	1,5-2,6	1,75±0,15	2,8±0,9*
Cortical thymocytes	CD4+CD8+	0,1-1,5	1,2±0,25	1,1±0,3
Natural killer T cells (TNK lymphocytes)	CD3+CD16+	0,5-6	2,54±2,41	3,16±1,02
Natural killers (NK)	CD3-CD16+	8-17	15,6±1,3	16,3±1,27
T-activated lymphocytes (IL-2)	CD3+CD25+	3-9	3,2±0,22	7,05±1,05*
B-activated lymphocytes (IL-4, IgE)	CD23+CD20+	42-58	45,8±5,1	56,6±5,5*
Fas apoptosis receptor	CD95+	10-25	15,1±4,0	20,5±1,98*
Marker of activated IL-2 apoptosis	CD25+CD95+	0,5-2,0	1,7±0,35	1,89±0,9*

OP-30 [Urticaria, Angioedema]

Low IgE Levels And High Systemic Inflammation Response Index Predict Omalizumab Response

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INTRODUCTİON & OBJECTIVES: Chronic spontaneous urticaria (CSU) is a common inflammatory disease characterized by wheals and/or angioedema for ≥ 6 weeks. Omalizumab, a monoclonal anti-immunoglobulin E (IgE) antibody, is highly effective in the treatment of CSU. However, there are also patients with poor or no response to treatment. In this study, we aimed to investigate the laboratory and clinical effects of omalizumab in CSU patients, and to identify biomarkers that can guide treatment response.

MATERIALS & METHODS: In this study, the data of 440 patients who were started on 300mg omalizumab every 4 weeks for CSU between March 2015 and May 2022 were analyzed retrospectively. Of these patients, those with missing complete blood count and total IgE values before and at the 6th month of treatment were not included in the study, and as a result, 91 patients were included in the study.Disease activity was assessed by the use of the urticaria control test (UCT), and patients with UCT <12 were considered unresponsive to treatment. Demographic features, accompanying autoimmune and allergic comorbidities, laboratory findings of the patients were evaluated. Before the start of omalizumab treatment and after the 6th dose; total IgE, eosinophil count, lymphocyte count, monocyte count, basophil count, platelet count, platelet distribution width (PDW), neutrophil-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI) levels recorded.

RESULTS: 70 patients responded to omalizumab treatment, 21 patients did not. The response rate to treatment of patients with IgE value below 30 IU/L (n=4, 44.44%) was significantly lower than

patients with IgE>30 (n=66, 80.49%, p=0.015). The SIRI value was significantly higher in patients who did not respond to treatment (1536.67+-1037.73 vs 1154.79+- 776.98, p=0.026). When the pre-treatment and post-treatment values were compared, omalizumab did not cause any change in lymphocyte and monocyte counts, while it caused a significant increase in eosinophil count, basophil count and total IgE levels (p=0.005, p=0.009, p<0.001, respectively). Significant decreases were observed in platelet count, PDW, NLR, SII and SIRI levels (p<0.001, P=0.006, p<0.001, p<0.001, p=0.003, respectively).

CONCLUSIONS: Our study confirms the association of low IgE levels with poor response to omalizumab. In addition, we found that high systemic inflammation response index was also associated with poor response. CSU treatment is a journey that requires time and patience, and reliable biomarkers are needed to guide the patient and physician in this process.

Keywords: Chronic spontaneous urticaria, omalizumab, biomarkers

POSTER PRESENTATIONS

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PP-01	Halogenoderma: A Case Report and Review of the Literature	*Mohammed Ghazi Alqurashi*
PP-02	Fixed Drug Eruption After Covid-19 Sinovac Vaccine	*Selami Aykut Temiz*
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PP-21	Pink, Purple Nodular Lesion in the Gluteal Region: Primary Cutaneus B Cell Lymphoma	*Şule Ulualan*
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PP-25	Carcinoma Erysipeloides: A Case Report	*Ahmet Soyugür*
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PP-30	A case of kyrle disease in a patient with multiple sistemik disease	*Sheyda Gharehdaghi*
PP-31	A Case of Exrtanodal B-cell Marjinal Zone Lymphoma	*Sheyda Gharehdaghi*
PP-32	3 cases of morhpea like atrophic lesions developed after Abobotulinumtoxin A treatment: A new theory for a rare complication	*Sertaç Sever*
PP-33	Idiopathic Granulomatous Mastitis and Erythema Nodosum	*Firdevs Turan*
PP-34	CD30-positive anaplastic lymphoma kinase-negative systemic anaplastic large cell lymphoma presenting with cutaneous lesions	*Fatih Mehmet Topdağ*

PP-01 [Miscellaneous]

Halogenoderma: A Case Report and Review of the Literature

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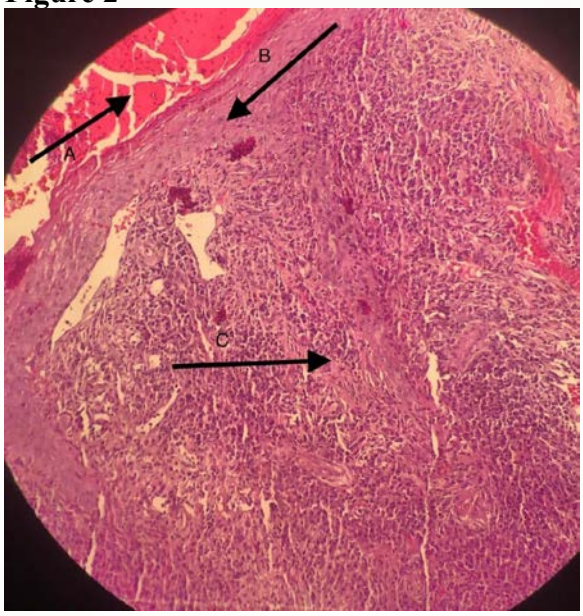
Halogenoderma (HD) is an uncommon dermatosis that develops following exposure to halogens such as iodide and bromide, referred to as iododerma and bromoderma, respectively. Here, we report the case of a 40-year-old male who presented with a three-week history of slightly itchy progressive skin lesions associated with low-grade fever and malaise. The patient had a history of using food supplements containing iodide and bromide for four months prior to the appearance of skin rashes. Skin examination revealed multiple crusted papules and nodules scattered on his face, neck, and trunk. A skin biopsy was taken from the lesions. The epidermis showed crustation, exocytosis of neutrophils, and multiple intraepidermal abscesses. The dermis showed heavy cellular infiltrates composed mainly of neutrophils. The skin lesions disappeared completely after the cessation of food supplements, along with the use of topical corticosteroids for a few weeks.

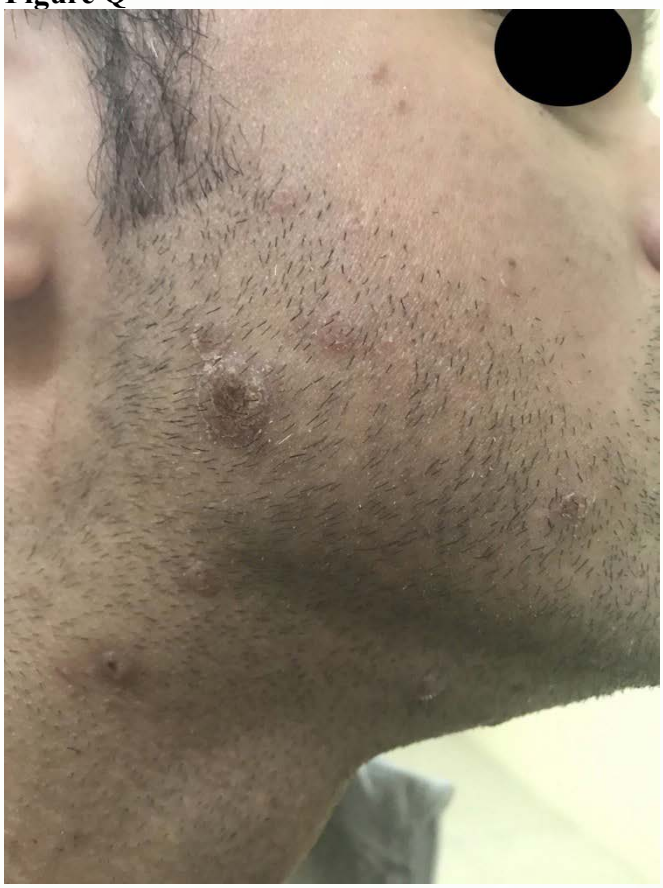
Keywords: Halogenoderma, iododerma, bromoderma

Figure 2



A skin biopsy showing epidermal crustation (A) and exocytosis of neutrophils (B). The dermis showed heavy cellular infiltrates composed mainly of neutrophils (C) (hematoxylin and eosin stain; original magnification, ×20).

Figure Q



Multiple crusted papules and nodules scattered on the patient's face and neck

PP-02 [Adverse Drug Reactions, TEN]

Fixed Drug Eruption After Covid-19 Sinovac Vaccine

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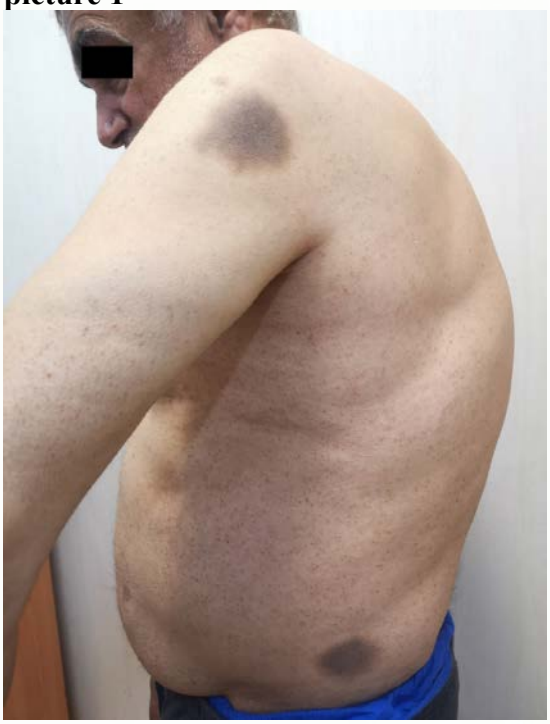
After the 2019 coronavirus disease (COVID-19) spread worldwide, various vaccines have been developed to control the pandemic, with varying efficacy and potency and based on different platforms. As with all other vaccines, side effects are observed with these vaccines. Reported side effects occur mostly after mRNA-derived vaccines. However, cutaneous adverse reactions are rarely seen after inactivated vaccines. The most common side effects are local injection site skin reactions. We present this case because it is very rare among cases where fixed drug eruption (FDE), which is one of the cutaneous reactions other than local injection site reactions, is reported.

A 57-year-old male patient applied to our dermatology outpatient clinic 10 days after the first dose of the Sinovac vaccine because of brown spots on his body. It was learned in his history that he had not made any medication changes or started a new medication in the last 1 year. The lesions did not have itching or pain and were cosmetically disturbing to the patient. In his dermatological examination, there were hyperpigmented plaques with a diameter of 2-3 cm on the dorsum of both hands and feet, 6 cm in diameter in the deltoid region of the left upper arm, 5 cm in diameter in the lower part of the left trunk, 2 cm in diameter in the left frontal region, and 4 cm in diameter on the right side of the neck (picture 1). A punch biopsy was taken from the patient with the preliminary diagnosis of fixed drug eruption, actinic lichen, and postinflammatory hyperpigmentation. Findings consistent with postinflammatory hyperpigmentation were observed in the histopathology result (picture 2). The patient was diagnosed with postinflammatory hyperpigmentation due to fixed drug eruption. 4% hydroquinone, topical tacrolimus, and moisturizer were used in the treatment.

FDE is characterized by annular, erythematous, or hyperpigmented patchy lesions of the skin and mucosa. There are several main variants of FDE, including pigmented, non-pigmented, bullous and mucosal types. FDE can be triggered by certain foods (seafood, nuts, berries, kiwis, and others) and drugs (non-steroidal anti-inflammatory drugs, antiepileptics such as phenytoin, antibiotics such as cotrimoxazole, and others) and can occur at any age and in both sexes. In the pigmented variant, the FDE disappears over time and post-inflammatory hyperpigmentation remains. Typically, FDE lesions reappear at the same sites after re-exposure to the causative drug. The disease is usually mild and self-limited, and primary treatment is the identification and discontinuation of causative stimuli and conservative care. FDE can occur after using the Sinovac vaccine. We consider it important for a dermatologist to recognize and report these complications, as many real-world side effects may not be seen in clinical trials.

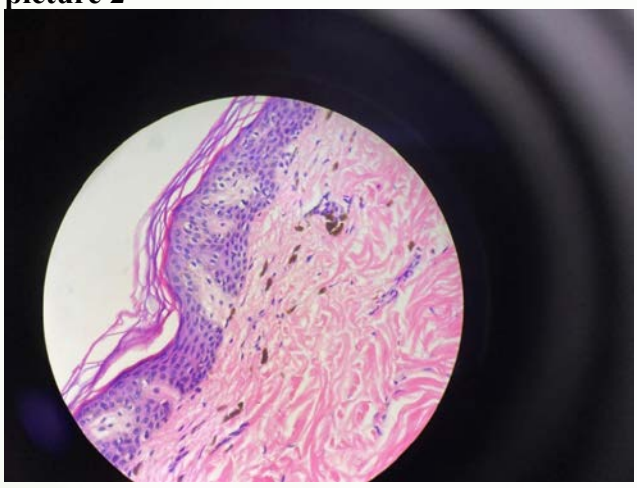
Keywords: Covid-19 Vaccine, Fixed Drug Eruption, Adverse Reaction

picture 1



6 cm in diameter in the deltoid region of the left upper arm, 5 cm in diameter in the lower side of the left trunk

picture 2



increase in melanin pigment in the dermis

PP-03 [Adverse Drug Reactions, TEN]

Flagellate Erythema And Nail Pigmentation After Bleomycın

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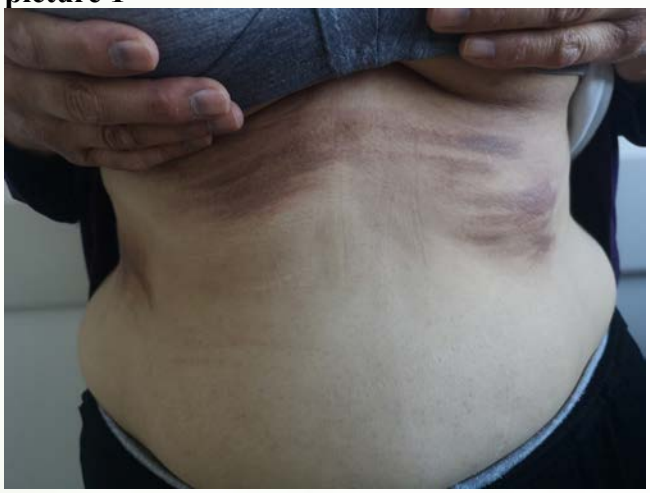
Bleomycin is a cytotoxic glycopeptide derived from Streptomyces verticillus. It is used in the treatment of many human cancers, especially lymphomas, testicular and ovarian germ cell tumors, and squamous cell carcinoma. Various dermatological side effects of bleomycin include flagellate dermatitis, erythema, hyperpigmentation, hyperkeratosis, palmoplantar desquamation, Raynaud's phenomenon, various nail changes, gangrene, fibrosis, neutrophilic eccrine hidradenitis (NEH), alopecia, edema, and skin side effects including various other reactions. We present a case who developed flagellate erythema on the trunk and pigmentation on the nail bed after receiving a chemotherapy regimen containing bleomycin.

A 53-year-old female patient was consulted to our polyclinic with complaints of brown spots on her trunk and discoloration of her nails about one month after she started taking ABVD (adriamycin, bleomycin, vinblastine, dacarbazine) regimen for Hodgkin lymphoma. In the dermatological examination, linear horizontal hyperpigmented plaques under both breasts in the upper abdomen (Picture 1), and hyperpigmentation in the fingernails and toenails (Picture 2-3). The case was diagnosed with flagellate dermatitis and nail hyperpigmentation due to bleomycin based on clinical findings and anamnesis. Liver and kidney function tests were normal in the investigations performed in the case. Since it was not severe enough to interrupt the bleomycin treatment, the case was followed up. Topical antihistamine, moderately potent topical corticosteroid, and moisturizer were recommended for treatment.

Bleomycin is an antineoplastic drug that acts by disrupting DNA in the G2 S phase of the cell cycle. It is metabolized by bleomycin hydrolase, toxication is more common in tissues where this enzyme is relatively low, such as lungs and skin. Although the exact mechanism of flagellate erythema is still unknown, several hypotheses exist, localized increase in melanogenesis, change in normal pigmentation patterns secondary to inflammation; or accumulation of bleomycin in the skin may result in a fixed drug eruption due to the direct effects of bleomycin on keratinocytes. In a study, it was concluded that the histopathological findings of flagellate erythema and fixed drug eruption were similar and the relatively low level of bleomycin hydrolase led to the accumulation of this drug. Bleomycin has been associated with nail pigmentation. Most drug-induced nail pigmentation results from increased melanin production by nail matrix melanocytes. Most drug-induced nail pigmentation results from increased melanin production by nail matrix melanocytes. In conclusion, early recognition of these rare specific skin reactions occurring in patients treated with bleomycin by dermatologists is of great importance in preventing the toxication of the drug. We share this case in order to raise awareness.

Keywords: Flagellate erythema, bleomycin, nail pigmentation

picture 1

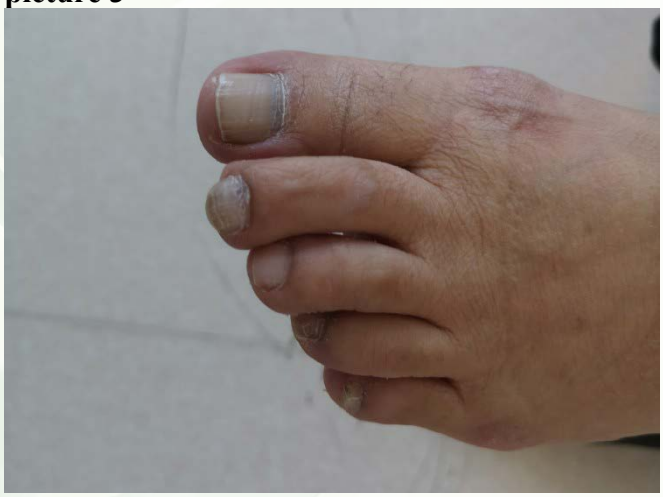


linear horizontal hyperpigmented plaques under both breasts in the upper abdomen hyperpigmentation

picture 2

hyperpigmentation in the fingernails

picture 3



hyperpigmentation in the toenails

PP-04 [Photobiology and Photoallergy]

A rare presentation of actinic damage: Actinic comedonal plaque of the eyelids

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INTRODUCTION: Favre-Racouchot syndrome (FRS), also known as senile comedones, solar comedones and nodular elastosis with cysts and comedones, is a condition that arises in a background of actinically damaged and atrophic skin as a result of solar degeneration of the skin. It is characterized by diffuse a yellowish hue, open comedones, cysts, nodules. Actinic comedonal plaque is a rare and localized variant of FRS, presenting with a plaque consisting of grouped comedones. Although it was mostly described on upper extremities, it can be found on the face and helix of the ear. Here, we describe an unusual case of bilateral actinic comedonal plaques of upper eyelids.

CASE: A 58-year-old man was referred to dermatology outpatient clinic from ophthalmology clinic with a 2-year history of purplish black discoloration of the eyelids. The patient was a taxi driver and had been working without any sun protective measures for more than 30 years. He was also a heavy smoker and has been consuming 20 cigarettes per day for 40 years. On dermatologic examination, multiple closely-spaced open comedones forming two well-defined hyperpigmented plaques were located on medial part of both upper eyelids (Figure 1 a,b). Several small fibroepithelial polyps were also present on the upper eyelids and small number of scattered open comedones was seen on the malar areas. Examination of other skin and mucosal sites were normal. Dermatoscopic examination of the lesion revealed multiple black clods with peripheral bluish color, thus, confirming the presence of open comedones (Figure 1c). The patient was diagnosed with actinic comedonal plaque. Photoprotection was recommended. The patient did not demand treatment.

CONCLUSION: Although actinic comedonal plaque is mostly reported in fair skinned individuals, patients with higher Fitzpatrick skin types can also be affected as in our case. Sun exposure, smoking and therapeutic radiation are thought to contribute to development of actinic comedonal plaque. Actinic comedonal plaque should be considered in differential diagnosis of comedonal lesions in elderly men with significant sun damage. The lesion must be distinguished from comedonal nevus. However, the latter is typically present at birth or appears during childhood. Treatment options include cryotherapy, CO2 laser treatment, comedone extraction, dermabrasion and curettage, as well as surgical excision.

Keywords: comedone, Favre-Racouchot syndrome, skin of color, smoker, sun exposure

Figure 1 (a-c)

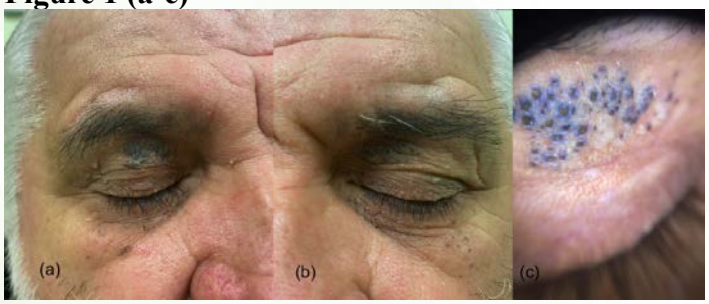

Figure 1 (a-c): Right and left upper eyelids display hyperpigmented plaques composed of grouped comedones while malar region shows several scattered comedones (a,b). Polarized dermatoscopy reveals black clods with peripheral bluish color (c).

PP-05 [Infectious Diseases, Parasitic Diseases, Infestations]

Ophthalmic Herpes Zoster in a Healthy Child

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Herpes zoster(HZ) is a disease characterized with vesicular rash developing due to the reactivation of Varicella zoster virus (VZV) staying as latent in the dorsal root ganglion, involving one or more dermatoma.(1) HZ might ne encountered more frequently due to the usage of immunosuppressive medications and malignities during childhood, however, it can also be seen in healthy children rarely.(2) Here, a case of a health child diagnosed with ophthalmic HZ diagnosis will be presented.

Five years old male child brought to our clinic by his family with complaints of redness and blister on the scalp and on one side of the face. Complaints of the patient was stated to be present for 5 days. According to the history of the patient, he did not have a known previous disease, immunosupression or drug usage. The patient was reported to had chickenpox infection when he was 2 years old. In the dermatological examination, grouped vesicubullous lesions on an erythematous background were observed in the region compatible with right V2 dermatoma area.(Figure1) The patient was diagnosed with HZ with history and dermatological examination findings. As a result of ophthalmologic consultation, herpetic conjunctivitis was detected. Treatment with acyclovir 20 mg/kg as 4 doses per day was started. All lesions were seen to regress in his control performed 10 days later. While HZ is frequently seen adults, it can rarely be seen in children, especially under the age of 10.(2) While HZ infection seen in is observed in cervical and thoracic dermatoma, involvement of the ophthalmologic region is rare(2,3). Ophthalmologic HZ arises due to the reactivation of VZV and involvement of the ophthalmologic branch of the trigeminal nerve. Ophthalmologic HZ, consists of 10-15% of HZ cases.(1,4) Vesicular rash, covering the periorbital area in one side of the face that can extend to the scalp vertex along with significant edema especially in the eyelids are observed. Antiviral treatment initiated at an early stage is reported to be effective in shortening the duration of the disease and preventing or reducing pain following zoster. (4,5) As a result, trigeminal involvement due to HZ in childhood is quiet rare and systemic antiviral treatment should be started without delay in respect to complications

Keywords: Child, herpes zoster, ophthalmic

Figure1

PP-06 [Cutaneous Oncology]

Dermatofibrosarcoma protuberance: A case report

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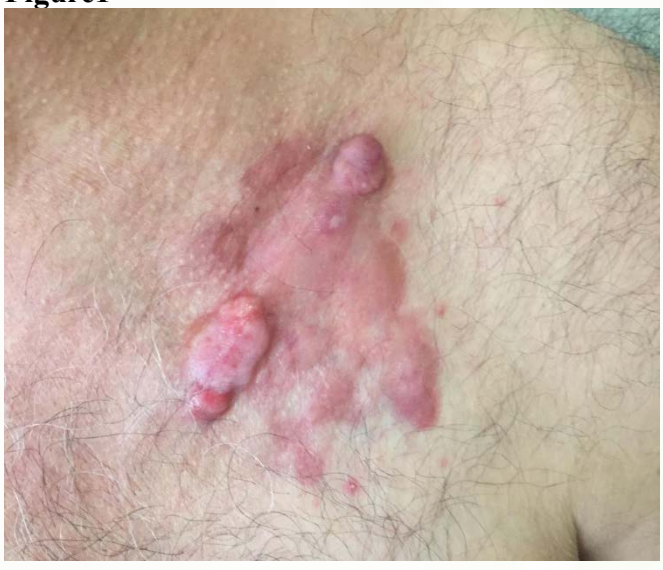
Dermatofibrosarcoma protuberance(DFSP) is a rarely seen local and aggressive tumor.(1) It is generally characterized with slow growing indurate plaques localized on the trunk, having hard, protruding skin colored or reddish-brown nodules.(1,2) It might start with a small size and can infiltrate the skin, subcutaneous tissue, muscle and bones.(2) Here, we present a DFSP case rarely seen in the clavicular region.

Forty four years old male patient applied with the complaint of an asymptomatic mass found in the left clavicular region and gradually growing for eight years. In his examination, hard and fixed plaque lesion on the left clavicular region with approximate size of 6x5x4 cm and having two nodular lesions were seen (Figure 1). The patient did not have an accompanying systemic and dermatological disease. In the histopathological examination of the case, diffuse proliferation of thick fusiform cells showing dermis localized subcutaneous lipid tissue were detected. In the immunohistochemical examination, positive staining with CD34 was seen in tumor cells. DFSP diagnosis was made with current histopathological and immunohistochemical findings. Metastatic findings were not observed with performed chest radiography, all body bone scintigraphy, head and lung tomographies. Tumoral lesion was totally excised by the department of plastic surgery. DFSP is rarely seen primary, well-differentiated mesenchenymal tumor of the skin showing localization in dermal and subcutaneous tissues. The tumor is locally aggressive, recurrence ratio following excision is high, however distant metastasis is rare. (3) In histopathological examination, diffuse proliferation of thick fusiform cells in the dermis and appearance similar to vortex arising from crossing of these with each other attracts attention. Staining with CD34 is positive in immunohistochemical examination. (3,4) Dermatofibroma, morphea, malign melanoma and cheloid are included in the diagnosis of DFSP. (1,5) Surgical resection including with extensive safety margins is performed in the treatment.(2,4)In the presence of slow growing, hard and fixed lesions in the skin, DFSP diagnosis should be considered and histopathological examination should be performed.

Keywords: Dermatofibrosarcoma protuberance, chest, oncology

Figure1



PP-07 [Hair Disorders/Diseases]

A Case Report of Uncombable Hair Syndrome Treated with Zinc

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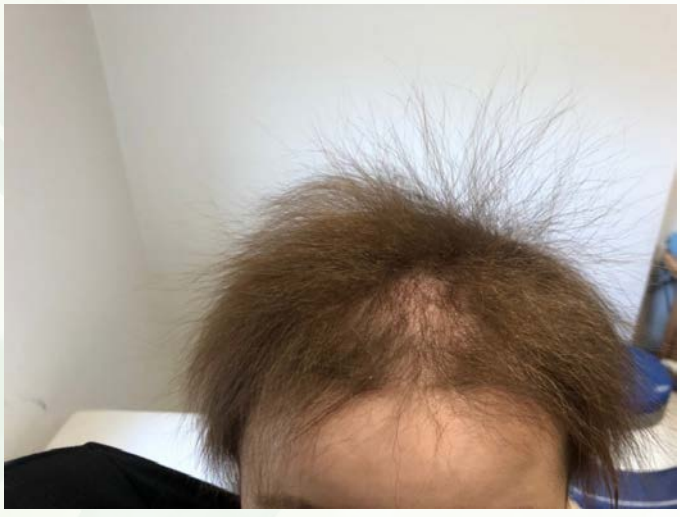
[3]Professor Dr. Ümit Türsen, Deparment of Dermatology, Mersin University, Mersin, Turkiye

Uncombable hair syndrome is a rare anomaly of the hair shaft, that results in a disorganized, unruly hair that is impossible to comb flat. Hair grows unevenly and in different directions. When viewed under the light microscope, the body of the hair should be cylindrical, but rather triangular. The small grooves that go up and down in the triangular shape cause the hair to be uncombable and the hair is irregular, silvery yellow or straw-colored. This syndrome develops between infancy and 3 years of age and begins to appear around the age of 12. There is no definitive treatment, and most cases improve with the onset of puberty. In this poster presentation, we present a 13-month-old baby patient with uncombable hair syndrome who had hair growth and improvement with oral zinc treatment.

Keywords: uncombable, hair disease, zinc

hair



Uncombable hair syndrome

PP-08 [Autoimmune Bullous Diseases]

Bullous Lupus Erythematosus: Rare Variant of Systemic Lupus Erythematosus

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[2]Department of Dermatology, Mersin University, Mersin, Türkiye

Introduction: A 37-year-old female patient presented with the complaint of watery sores on the body and oral mucosa for 1 month. The patient who was diagnosed with bullous pemphigoid in another center applied to our center. She has no known disease. She's on prednol therapy for her lesions. In his dermatological examination, excoriated eroded areas on the shoulders, axilla, breast and legs, and eroded areas on the oral mucosa were observed.

Diagnosis: In the microscopic examination; In the epidermis, compact hyperkeratosis, subepidermal separation, dense fibrin material with band-like distribution on the base of the bulla, as well as mixed type inflammatory cell infiltration, rich in neutrophil leukocytes and accompanied by clasia findings, were observed. In immunofluorescence examination; granular staining of the basement membrane was observed with IgG and fibrinogen.

In the serological examination of the patient, ANA +++, Antidsdna ++, antiRNP +++ were detected. With these clinical, serological and histopathological findings, the patient was diagnosed with Bullous Lupus Erythematosus. The patient was diagnosed with lupus nephritis class 3 in the kidney biopsy performed afterwards.

Discussion: Bullous lupus erythematosus is a rare variant of systemic lupus erythematosus. It most commonly affects African-American women. It most commonly affects the trunk, proximal arms, face and neck. Patients must fulfill the American College of Rheumatology criteria for the diagnosis of systemic lupus erythematosus. It is characterized by pruritic tense vesicles and bullae. Mucosal involvement may be seen. Lesions respond dramatically to

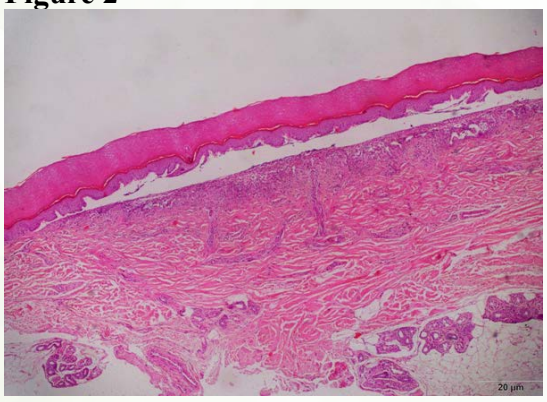
dapsone. There are autoantibodies against type VII collagen. Dermatitis herpetiformis, linear IgG A bullous dermatosis and acquired inflammatory epidermolysis bullosa can be considered in the differential diagnosis.

Keywords: Bullous, Lupus, band-like distribution

Figure 1

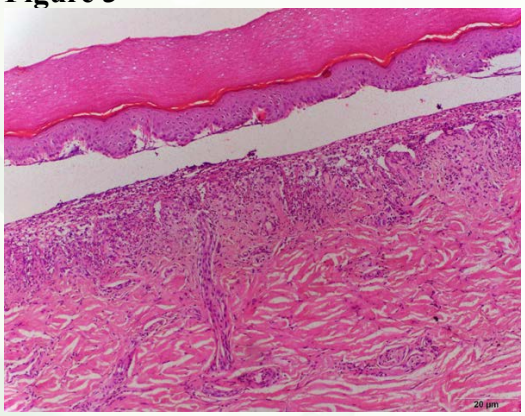
Excoriated eroded areas on the axilla and oral mucosa

Figure 2



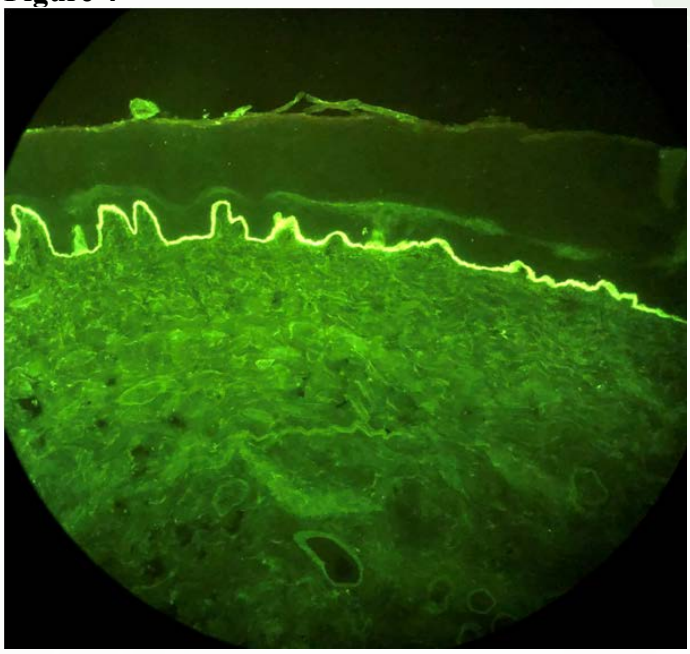
In the epidermis, compact hyperkeratosis, subepidermal separation, HE;x40

Figure 3



Dense fibrin material with band-like distribution on the base of the bulla, as well as mixed type inflammatory cell infiltration, rich in neutrophil leukocytes and accompanied by clasia findings HE; x100

Figure 4



Granular staining of the basement membrane was observed with IgG, x40

PP-09 [Dermatological Practice Management]

Diagnostic and therapeutic approach in a case of leishmania

Fatih Ay, Abdullah Fatih Açık, Ümit Türsen
Mersin Üniversitesi, Dermatoloji Ana Bilim Dalı,

A patient with an erythematous lesion on the face and forearm with a crusty surface for about 2 months. She had received various treatments before and did not benefit. Leishmania was considered in the patient and blood smear and PCR was sent. After tzanck staining of the sample, amastigotes were seen at a microscopic magnification of one hundred using immersion oil. Weekly intralesional meglumine antimonate treatment was started.

Keywords: Leismania, smear, amastigote

PP-10 [Dermatopathology]

Ectopic Hidradenoma Papilliferum of Neck: A Rare Localization

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[2]Department of Dermatology, Mersin University, Mersin, Türkiye

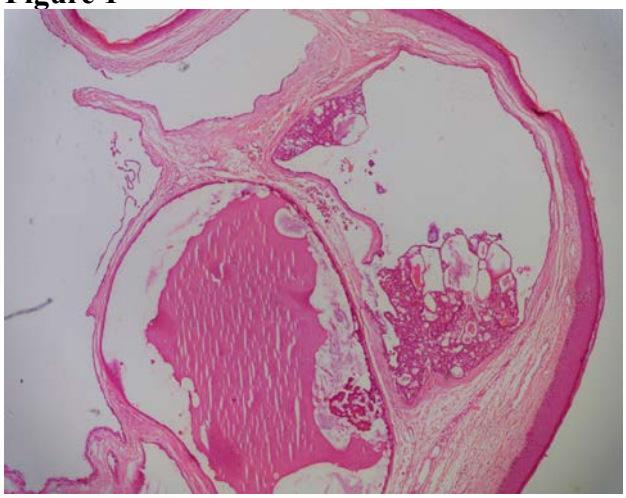
Introduction: A 63-year-old male patient was admitted to the dermatology clinic with the complaint of nodular pigment resolution in the right side of the neck, behind the ear. The patient's lesion was excised with preliminary diagnoses of dermal nevus, fibroma, skin tag and nodular basal cell carcinoma.

Diagnosis: On histological sections, there were papillary structures lined with cuboidal cells within the well-circumscribed cystic structures without any connection with the epidermis (Figures 1 and 2). Focal areas of apocrine differentiation and decapitation secretion were seen in the lesion (Figure 3). Diffuse, moderate-to-strong cytoplasmic staining with CK7, EMA and GCDFP-15 was observed in the cuboidal cells lining the lesion without atypia and significant mitotic activity. No staining was observed with CK20, mCEA, CK5/6, Amacr, Pax8, TTF-1 and p63 (Figure 4). The lesion which was not associated to the epidermis was reported as Hidradenoma papilliferum.

Discussion: Hidradenoma papilliferum (HP) is a benign adnexal tumor that can show apocrine differentiation. Since the apocrine sweat glands are predominantly located in the anogenital region and axilla, most cases of HP have been reported in these regions. Rare ectopic forms of HP have been described in various locations, including the head and neck, chest, and extremities. In contrast to anogenital HP, approximately half of the patients with ectopic HP are male and the lesions are located mainly on the head and neck. Although malignant transformation is rare, it can be confused with a malignant tumor due to its complex papillary pattern. The overall prognosis of this neoplasm is good with total excision, regardless of location. Syringocystadenoma papilliferum (SP) should be considered in the differential diagnosis, but SP is associated with the epidermis and shows cystic invaginations extending downwards. Other histopathological differential diagnoses include tubular apocrine adenoma, clear cell (apocrine) adenoma, and intraductal carcinoma.

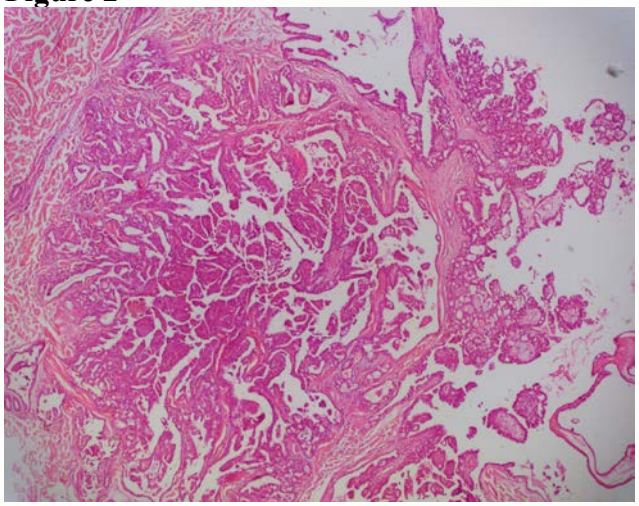
Keywords: adnexal tumors, skin, hidradenoma papilliferum, ectopic

Figure 1



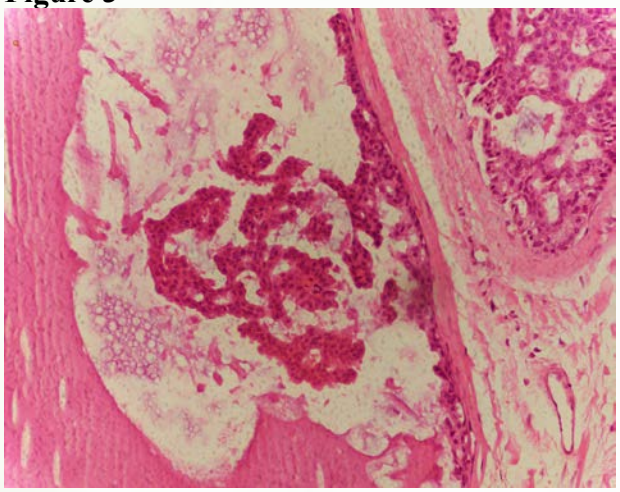
Cystic papillary structures located in the dermis, not connected with the epidermis (H&E, x40)

Figure 2



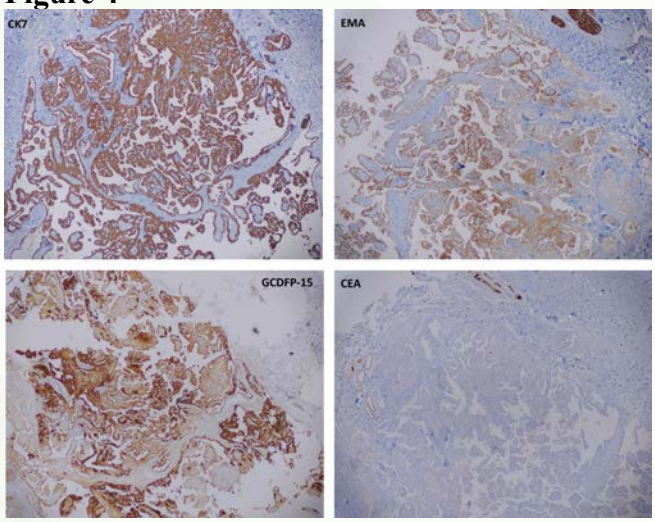
Papillary structures containing central fibrovasculary cores (H&E, x40)

Figure 3



Focal area of apocrine differentiation and decapitation secretion on the left (H&E, x200)

Figure 4



Cytoplasmic staining was observed with CK7, EMA and GCDFP-15. No staining was observed with CEA (x40).

PP-11 [Dermatopathology]

A rare acantholytic genodermatosis: Hailey Hailey Disease

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[2]Department of Dermatology, Mersin University, Mersin, Turkey

Introduction: A 48-year-old female patient was admitted to the dermatology clinic with itchy lesions that started 30 years ago, were aggravated by heat and friction and predominantly localized flexural areas. In dermatological examination, there are erythematous, eczematized, eroded, bullous lesions located in the neck, axilla and inguinal region.

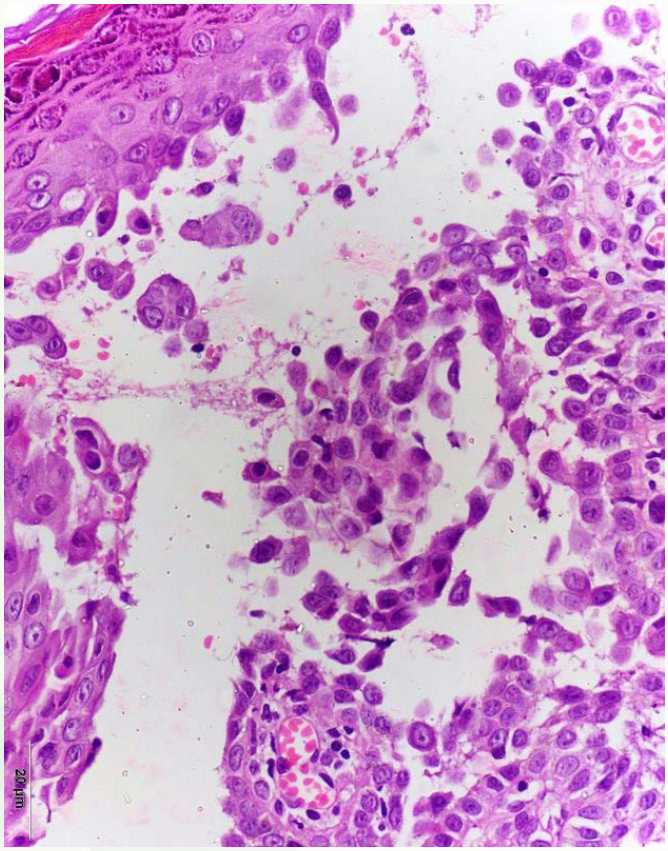
Case: Biopsies were taken from the patient, which would allow direct immunofluorescent examination with localization of the neck and inguinal region. Similar histomorphological findings were observed in samples from both localizations in hematoxylin-eosin examination. In biopsy specimens with mild orthokeratosis and parakeratosis in the epidermis, large areas of intraepidermal suprabasal acantholytic dehiscence were noted(Photograph 1). Villi or elongated dermal papillae lined with a single layer of basal cells protruded into the bulla. Dyskeratotic keratinocytes were seen in the corneal layer, more prominently in the inguinal region localized sample(Photograph 2). Mild lymphohistiocytic inflammatory cell infiltration accompanied by sparse neutrophil leukocytes, eosinophil leukocytes and melanophages was observed around partially congested vascular structures in the superficial dermis. No specific accumulation was observed in the direct immunofluorescence examination. When the case was evaluated together with clinical and pathological findings, Hailey-Hailey Disease was considered primarily, considering the early onset and family history.

Discussion: Hailey-Hailey disease (HHD), also known as benign familial pemphigus, is a rare autosomal dominant genodermatosis caused by mutations in the ATP2C1 gene that encodes a calcium pump of the

Golgi apparatus firstly described in 1939 by the Hailey brothers. HHD is a chronic disease with a relapsing-remitting clinical course. Exacerbations are mainly triggered by sweating, minor trauma, and secondary infections. HHD is characterized by ruptured vesicles and blisters that tend to form eroded, erythematous plaques with painful "rhagades" in flexural areas. Histologically, well-developed lesions are characterized by incomplete acantholysis, resulting in a "dilapidated brick wall" appearance. Chronic lesions present epidermal hyperplasia with ortho- and parakeratosis. The parakeratotic crust sometimes contains neutrophils and bacteria. The superficial dermis can contain focal perivascular lymphohistiocytic infiltrate. Direct immunofluorescence is negative. Hailey–Hailey disease can be recognized clinically based on the distinctive distribution pattern and the usual presence of a positive family history. There is no curative treatment. Mild cases can be controlled successfully with intermittent courses of topical corticosteroids and antibiotics.

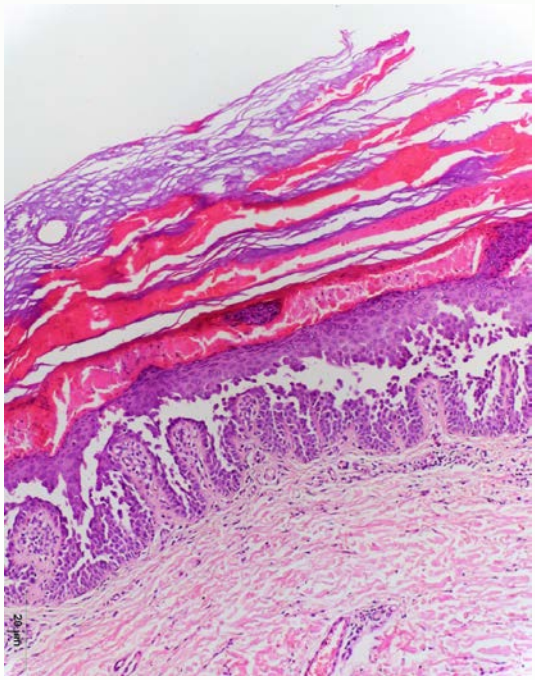
Keywords: Hailey Hailey, genodermatosis, acantholytic

1



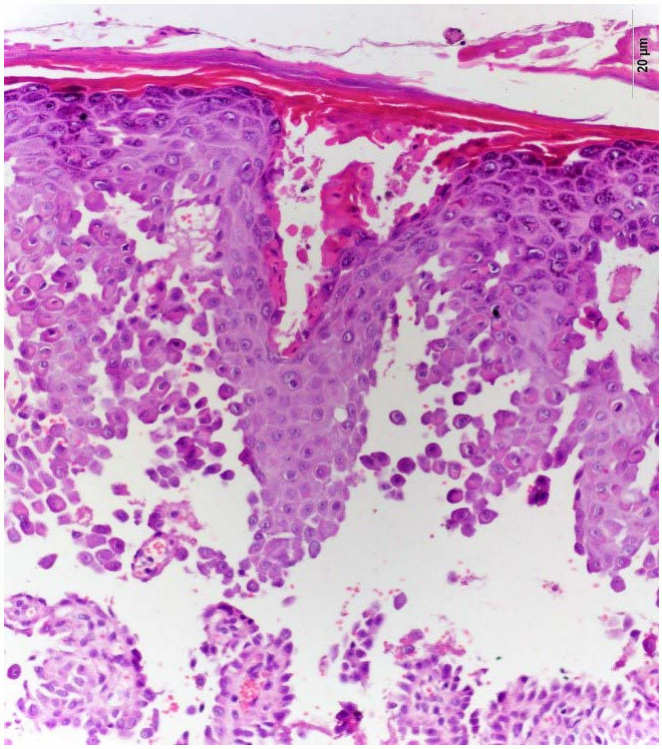
Intraepidermal suprabasal acantholytic dehiscence, H&E, x200

1



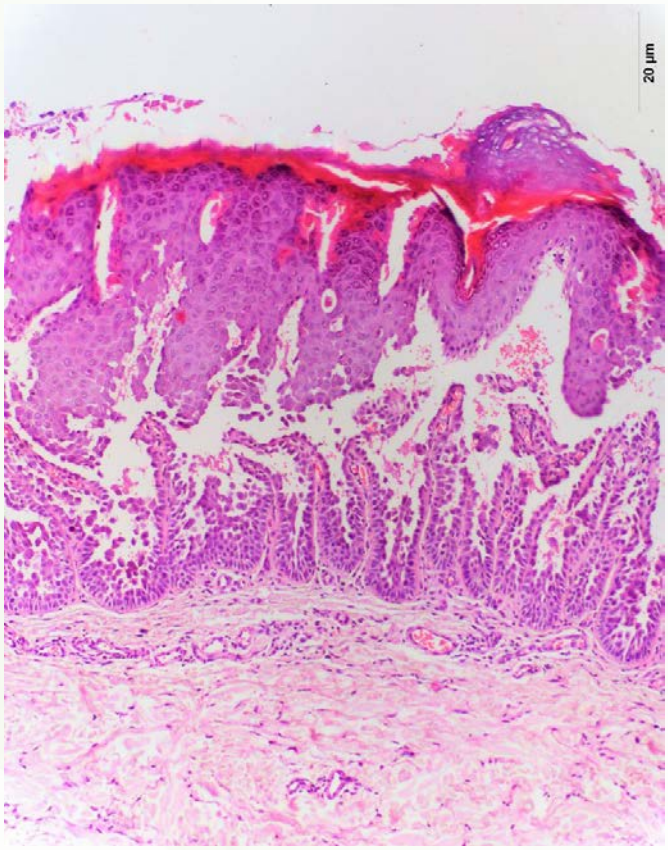
Orthokeratosis and parakeratosis in the epidermis, H&E, x100

2



Subcorneal dyskeratotic keratinocytes, H&E, x200

2



Elongated dermal papillae lined with a single layer of basal cells protruded into the bulla, H&E, x100

PP-12 [Dermatopathology]

Acrodermatitis Enteropathica

Damla Melemezoglu[1], Yasemin Yuyucu Karabulut[1], Guliz Ikizoglu[2], Umit Tursen[2]
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A 21-year-old female patient with a diagnosis of celiac disease presenting with cachexia, diarrhea, vomiting, diffuse brownish erythematous hyperpigmented papules and plaques on the dorsum of the feet and hands, arms, knees and legs, desquamation and erythematous plaques in the nasolabial, medial eyebrows and perioral area, and hair loss.

In the microscopic examination, hyperkeratosis, parakeratosis, mild irregular acanthosis were observed in the epidermis, cytoplasmic paleness and keratinocyte dismaturation were noted in the upper half of the epidermis. In the biopsy sample, in which the papillary dermis was observed in an edematous appearance, mild lymphohistiocytic inflammatory cell infiltration was observed around the vascular structures with endothelial prominence in the superficial dermis.

With these histomorphological findings, a diagnosis of Acrodermatitis Enteropathica was considered. Acrodermatitis Enteropathica is an autosomal recessive metabolic disorder affecting the uptake of zinc through the inner lining of the bowel, the mucous membrane. It is characterized by inflammation of the skin (dermatitis) around bodily openings (periorificial) and the tips of fingers and toes (acral), hair loss (alopecia), and diarrhea. It can also be related to deficiency of zinc due to other, i.e. congenital causes.

Keywords: diarrhea, dermatitis, hair loss

PP-13 [Cutaneous Oncology]

Association of Mycosis fungoides and Kaposi Sarcoma: Is only a coincidence ?

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INTRODUCTION: Mycosis fungoides (MF) is the most common form of cutaneous T cell lymphoma that arise from skin-tropic memory T lymphocytes[1]. Kaposi Sarcoma (KS) is a multifocal angioproliferative neoplasm that develops due to Human-Herpes virus 8 (HHV-8), which often occurs on the skin. Patients with KS are at risk of lymphoma, such as Hodgkin's lymphoma, Castleman's disease and plasmablastic lymphoma[2]. However, the coexistence of MF and KS in the same patient is a rare phenomenon especially in HIV negative patients. Herein we report a patient with concurrent diagnosis MF and Classic KS in an elderly man.

CASE REPORT: An 68 year old man applied to our hospital because of infective scar tissue that was not healing on his right foot. Histopathological examination of excisional biopsy of the lesion taken by Department of Plastic Surgery revealed CD30 positive T cell lymphoproliferative disease. Then he was consulted to our department. Physical examination found both brown atrophic macules (Fig. 1) and purple macular lesions (Fig. 2) on his thighs. Histopathological examination of these lesions were compatible with MF and KS (patch stage) respectively. He was consulted to Department of Oncology and Hematology. Positron emission tomography was taken and reactive lymph nodes 2 cm diameter were observed in inguinal region. Histopathological examination of reactive lymph nodes were Grade 1 according to Dutch system. Peripheral blood smear and flow cytometric analysis were compatible with B0 according to EORTC classification. The patient was considered as stage 2a MF with large cell transformation in one lesion. Oral acitretin (25 mg/day) and pegylated interferon alfa 2a was started. Clinical and histopathological improvement was achieved in six months.

DISCUSSION: In the literature, mostly cases of KS developing with MF includes patients who received therapy such as phototherapy and nitrogen mustard for MF or who had previous chemotherapy exposure for another lymphoma[3-6]. Immunosupression induced by either MF itself or treatment modalities including photoherapy or chemotherapy for another cancer are proposed mechanisms in these reports. In our case, MF and KS diagnosis was made concurrently with no history of immunosupression or phototherapy. In the literature only one 88 year old patient was reported with concurrent MF and KS with no previous immunosupression. In this case they proposed that the development of MF, induced an immunosuppressive state and in combination with immunosenescence due to advanced age of that patient along with HHV-8 positivity contributed to the development of KS [7]. In conclusion coexistence of MF and KS in a patient is a rare condition. However it should be kept in mind that this association may be present especially in elderly patients.

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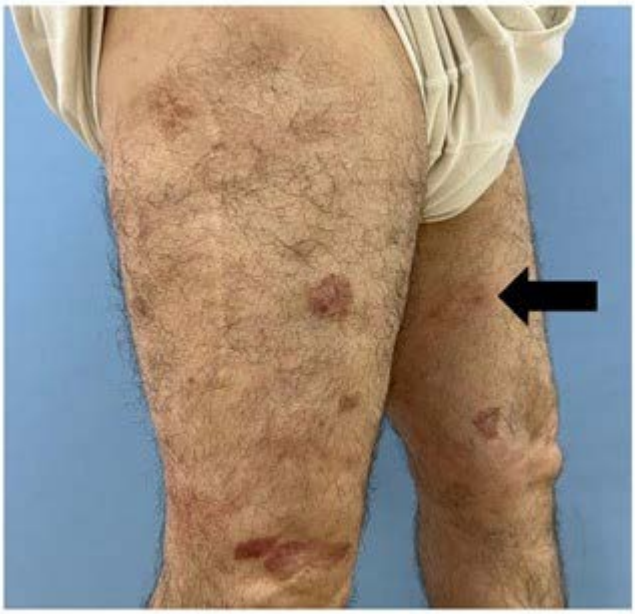
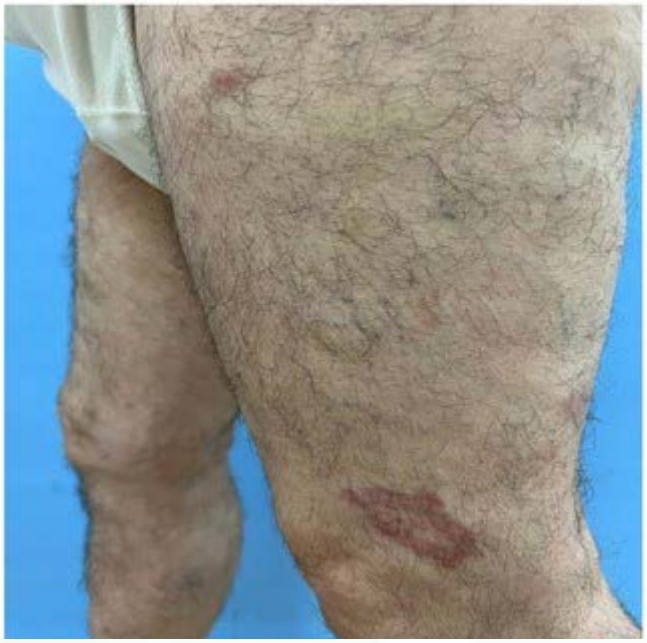
Keywords: mycosis fungoides, kaposi sarcoma, coexistence of mycosis fungoides and kaposi sarcoma

Figure 1



Atrophic macular lesion (arrow)

Figure 2



Purple macular lesions on his thighs

PP-14 [Pigmentary Diseases]

An unexpected cause of hyperpigmentation: A case of Berloque dermatitis

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[2]Department of Dermatology, Mersin University, Mersin, Turkey

INTRODUCTION: Berloque dermatitis is a phototoxic reaction due to using bergamot oil. Phototoxic effect of bergamot arise as a result of bergapten (5-methoxypsoralens). Bergapten and UVA contact results melanogenesis and hyperpygmentation. Bergamot are used for perfumes, colognes, fragrances. Using of these products may cause hyperpygmented lesions.

CASE: A 15-year-old patient was admitted to the dermatology outpatient clinic with hyperpygmented skin lesions. Dermatological examination revealed irregulated border, hyperpygmented patchy skin lesions on the neck and chest areas(Figure 1). İncisional biopsies performed from the neck. Actinic Lichen Keratosis, Acanthosis Nigrikans and Berloque dermatitis were considered as preliminary diagnosis. Histopathological examination revealed basal vacuolar degeneration and necrotic keratinocytes on the dermoepidermal junction (Figure 2). Melanophages accompanying lymphohistiocytic infiltrate were detected in the papillary dermis (Figure 3). Considering localization and anamnesis finally diagnosis were determined Berloque Dermatitis.

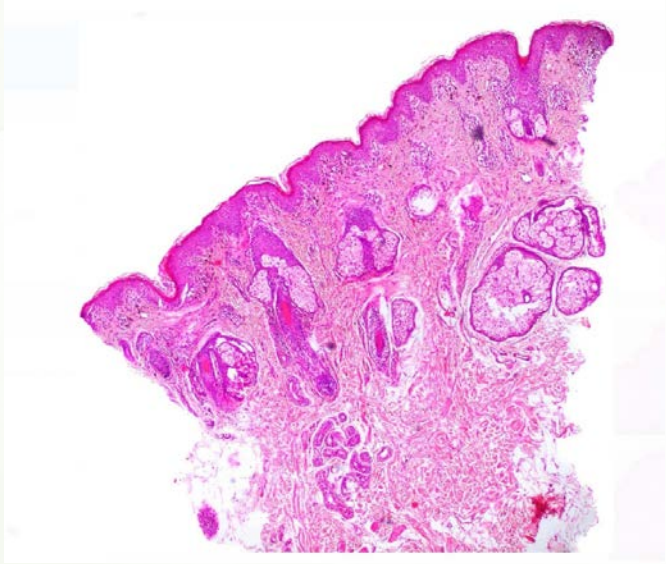
DİSCUSSİONS AND CONCLUSİONS: Berloque dermatitis occurs after cosmetic products containing bergamot are applied to the skin followed by exposure to UVA. After that detection, using for cosmetic purpose of bergamot was decreased. However bergamot is stil using in colognes, aromatherapy oils. Nowadays aromatherapy very popular as a consequence of several cases were reported related bergamot aromatherapy oil in the literature. Additionaly there is a case report of berloque dermatitis mimicking child abuse in the literature. Berloque dermatitis was caused by perfume in the our case. The aim of the present this case was attrack attention phototoxic effects of bergamot and hyperpigmented lesions.

Keywords: Pigmentation, Berloque Dermatitis, Berg

FIGURE 1

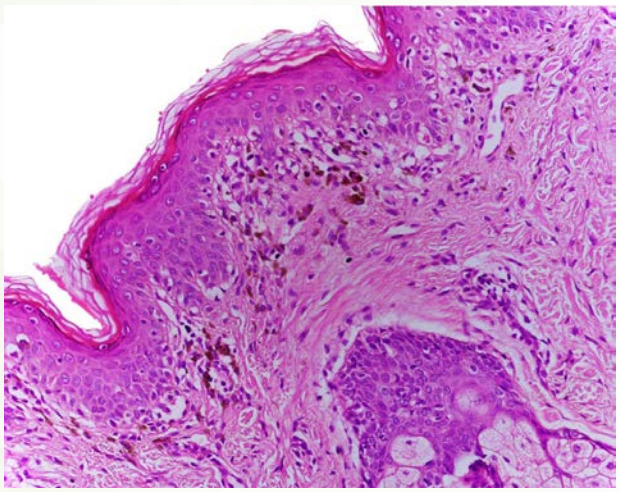
Hyperpigmented patchy skin lesions on the face and neck in the dermatologic examination

FIGURE 2



Basal vacuolar degeneration, necrotic keratinocytes, and an increasing number of melanocytes on the dermoepidermal junction (H&E, x40).

FIGURE 3



Prominent basal vacuolar degeneration in the dermoepidermal junction. Lymphohistiocytic infiltrate and melanophages in the papillary dermis (H&E, x400).

PP-15 [Genetics]

Punctate Palmoplantar Keratoderma: A Case Report

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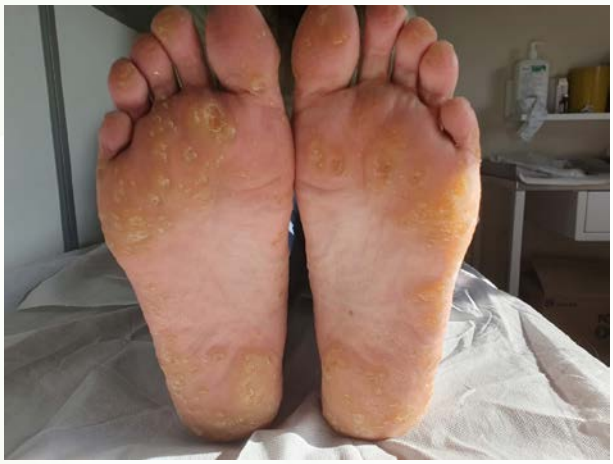
INTRODUCTION: Palmoplantarkeratodermas (PPK) are heterogeneous disorders characterized by abnormal keratinization. Especially, punctate PPK (PPPK), one of the rare subtypes of hereditary PPK. It is characterized by tiny “raindrop” keratoses having a tendency to coalesce on the edge of soles, which are exposed to sustained pressure.The condition is identified underseveral names such as “musicbox spine keratosis” and “palmoplantarfiliformhyperkeratosis”.Keratosis is usually beginning in thefirst to third decades of life. Discomfort can be causedby a tendencytocatch on clothing and other objects.The exactetiology of PPPK has not been fully understood.

CASE: A 37 years-old female, otherwise healthy, presented with asymptomatic persistent slowly progressing skin lesions on her palms and soles.There were many tiny punctate keratotic lesions on her palms and soles. The lesions started when she was 15. And they have been progressing slowly.Past medical history and review of systems were unremarkable. Also her two sister and her father have same problem on their palmes and soles.

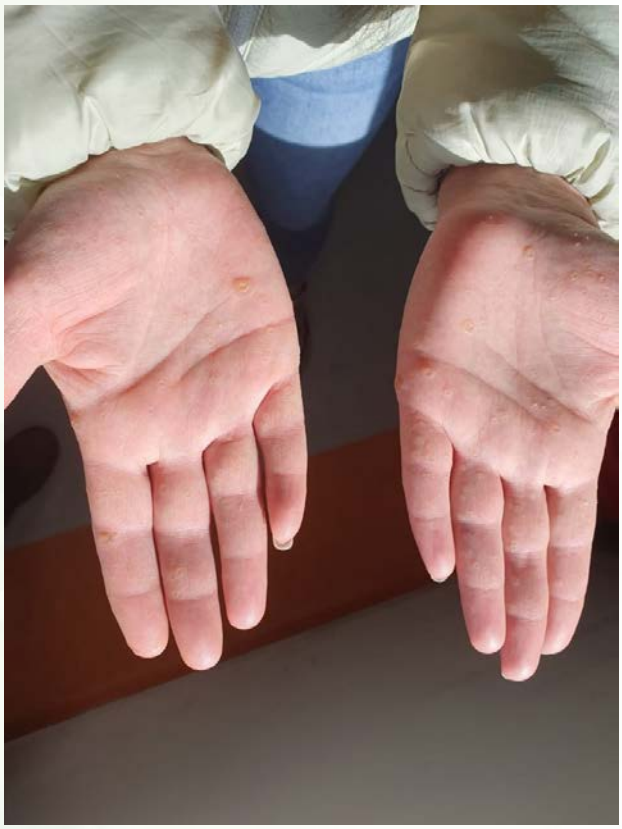
CONCLUSION: PPK have been classified by a clinically based descriptive system. In recent years, many causative genes of PPK have been identified, which has confirmed and/or rearranged the traditional classifications. It is now important to diagnose PPK by a combination of the traditional morphological classification and genetic testing. Because of not having genetic testing,we diagnosed by using morfological classification. We found this case worth presenting, since PPPK is a rare disease.

Keywords: hereditary palmoplantar keratoderma, keratinization disorders, punctate

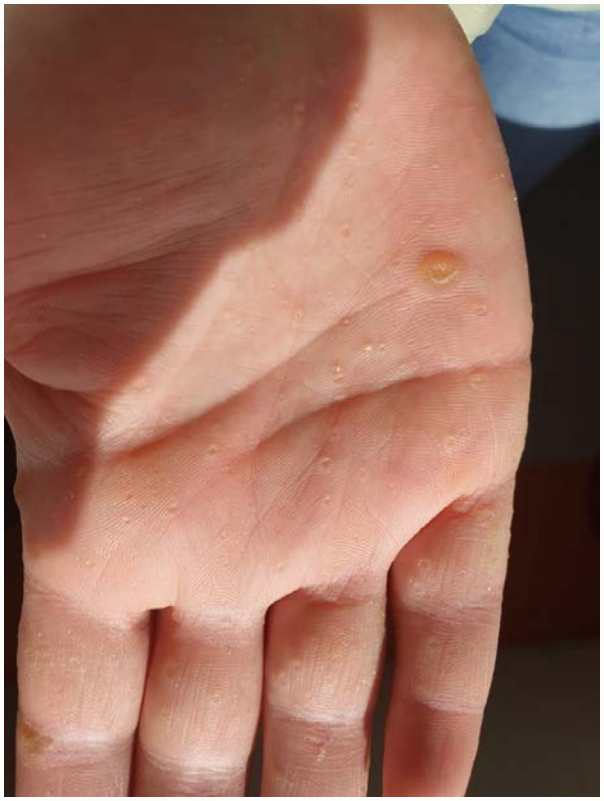
Plantar areas



Soles



Soles 2



PP-16 [Corrective, Aesthetic and Cosmetic Dermatology]

Nasolabial area correction with multi level filler placement

Tokzhan K Clay
Medstella Skin Care Clinic

We used 2 types of fillers for the nasolabial areas correction with placement of each filler to a different planes.

1. Teoxane Teosyal RHA3 filler was placed into subdermal plane of the nasolabial areas followed by

2. Teoxane RHA Redensity filler placed superficially in the same areas

Standard precautions were used with aspiration prior to injections.

There was no complications after procedure and patient expressed high level of appreciation due

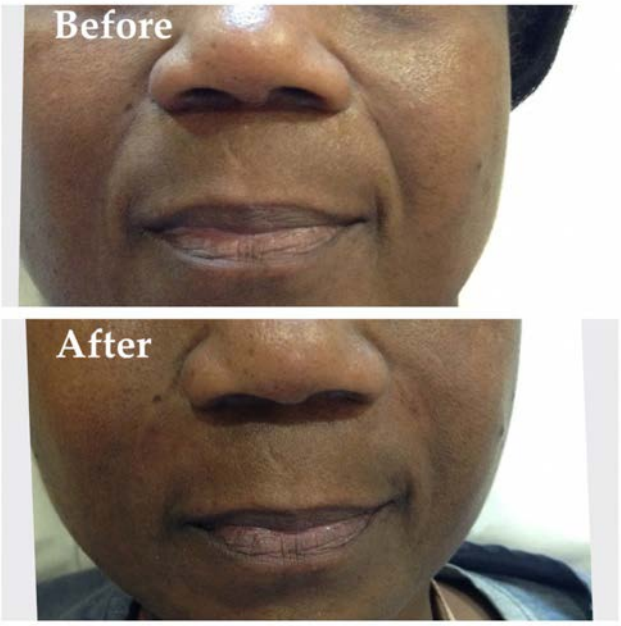
to instant correction of the nasolabial creases.

Explanation: Nasolabial creases have dermal and epidermal defects which make this area difficult to correct. Acceptable techniques recommend subdermal plane for the filler placement. But because nasolabial area also has sub epidermal volume loss, filler that is placed in the deep plane may not provide adequate correction. Hence using thicker filler for the subdermal placement and thinner filler for the superficial plane would improve overall appearance with a higher level of patient satisfaction.

Keywords: fillers, subdermal plane, superficial placement, nasolabial creases

Before and after

Before and after



PP-17 [Cutaneous Oncology]

A case of breast lobular cancer diagnosed with cutaneous metastases

EKİN KAPLAN, Yasemin Yuyucu Karabulut, Semanur Çakır, Ümit Türsen
Mersin Üniversitesi Tıp Fakültesi

İntroduction: In women, breast cancer is the leading cancer diagnosis and the second leading cause of cancer-related death(1), as well as the most common malignancy to metastasize to the skin(2). Cutaneous breast carcinoma may present as cutaneous metastasis or can occur secondary to direct tumor extension. Five percent to 10% of women with breast cancer will present clinically with metastatic cutaneous disease, most commonly as a recurrence of early stage breast carcinoma(2).

Case Report: A 49-year-old female patient with no known disease was admitted to our clinic with conglomerate nodular lesions lasting 1.5 months, forming diffuse sclerodermoid indurations on the chest wall and abdomen and neck.The lesions were not itchy or painful. There were no symptoms suggestive

of malignancy such as weight loss or night sweats. The mother had a history of breast cancer. This was the patient's first admission to the hospital due to skin lesions and the patient had not received any treatment before. Atypical cells and lymphocytes were seen in the tzanck test. Cutaneous lymphoma and cutaneous metastasis, leukemia cutis, sarcoidosis are included in differential diagnosis. Biopsie was performed. Hematoxylin and eosin staining revealed a relatively monomorphic epithelioid cell infiltrate extending from the superficial reticular dermis into the deep dermis and displaying an open chromatin pattern and pink cytoplasm was observed, as well as dermal collagen thickening. Linear, single-filing cells along with focal irregular nests and scattered cells were observed. Immunohistochemical staining was positive for cytokeratin 7, estrogen receptor, progesterone receptor; focal gross cystic disease fluid protein 15 positivity also was present. Cytokeratin 20, LCA, CD3, CD20, e-cadherin, mammoglobulin stains were negative. Findings identified were consistent with metastatic cutaneous lobular breast carcinoma.

Conclusion: Invasive lobular breast carcinoma represents approximately 10% of invasive breast cancer cases. Compared to invasive ductal carcinoma, there tends to be a delay in diagnosis often leading to larger tumor sizes relative to the former upon detection and with lymph node invasion. These findings may be explained by the greater difficulty of detecting invasive lobular carcinomas by mammography and clinical breast examination compared to invasive ductal carcinomas (3-5). Cutaneous metastases of breast cancer most commonly are found on the anterior chest wall and can present as a wide spectrum of lesions, with nodules as the most common primary dermatologic manifestation (6). Providers should be aware of the varying clinical presentations that may arise in the setting of cutaneous metastasis. When faced with lesions suspicious for cutaneous metastasis, biopsy is warranted to determine the correct diagnosis and ensure appropriate management.

Keywords: Cutaneus metastasis, Lobular breast carcinoma, Tumor extension

PP-18 [Dermatopathology]

A rare case of cutaneous leiomyosarcoma

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A 77 year old male patient presented to the dermatology outpatient clinic with a lesion located at his left gluteal region. Physical examination revealed a verrucous looking plaque lesion which was hard with palpation. Preliminary diagnoses from the clinician were calcified pilomatrixoma, verrucous carcinoma and dermatofibrosarcoma protuberans (DFSP). The patient underwent an incisional biopsy. Histopathologic examination showed a cellular lesion that consisted of relatively uniform, spindle shaped cells that had eosinophilic cytoplasm, forming fascicules located in the dermis. The cells had nuclear enlargement and cigar shaped nuclei. Brisk mitotic activity and atypical mitoses were observed. The lesion infiltrated into the neighboring dermis and focally involved the subcutaneous adipose tissue. On a detailed immunohistochemical analysis, the tumor cells showed diffuse strong positivity with h-caldesmon and desmin. There was no staining with CD34. Ki67 proliferative index was approximately 30%. With these histomorphologic and immunohistochemical findings, the final diagnoses was Cutaneous leiomyosarcoma. Cutaneous leiomyosarcoma is a rare malignant neoplasm with a muscular origin, representing around 2%-3% of all cutaneous soft tissue sarcomas and 0.04% of all skin tumors. Cutaneous Leiomyosarcoma can occur at any age, but it mostly affects older adults, with a peak incidence between 50 and 70 years. It is more common in males and appears to be more common in whites. Histologically, Cutaneous Leiomyosarcoma is characterized by a dermal proliferation of elongated spindle-shaped cells arranged in interweaving fascicles with blunt-ended, cigar-shaped nuclei and eosinophilic cytoplasm. Mitotic figures are usually easily identifiable.

Keywords: leiomyosarcoma, cutaneous, sarcoma, skin, caldesmon, desmin

PP-19 [Inflammatory Skin Diseases]

A Case of Lichen Planus Pemphigoides in a Patient

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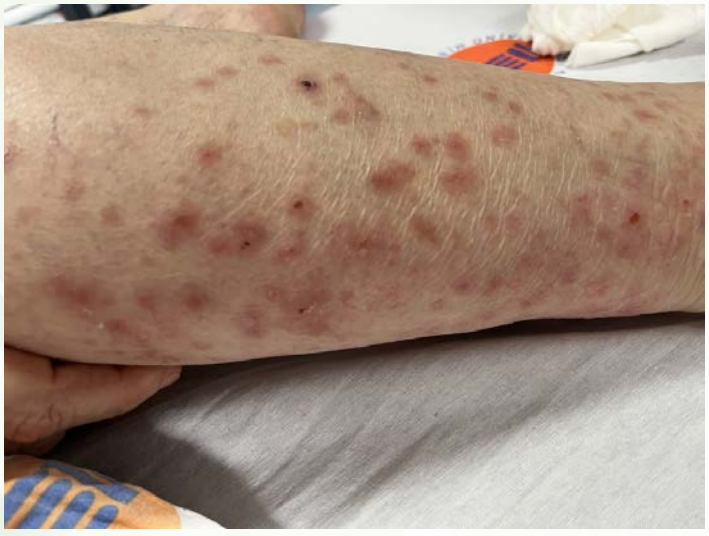
Lichen planus pemphigoides is a rare acquired autoimmune disease. It is a dermatosis in which lichen planus and bullous pemphigoid-like lesions coexist. It is characterized by bullae located on the classic lesions of lichen planus or on normal skin. It is thought that the basement membrane damage seen in lichen planus triggers autoimmune bullous diseases by causing some antigens to be exposed. Histopathology shows subepidermal bulla formation and direct immunofluorescence examination reveals band-shaped Igg and c3 deposition in the basement membrane of lesioned and normal skin. This picture is the same as for bullous pemphigoid. In this case, we present a 69-year-old patient with recurrent lichenoid papules and bullous lesions in the tibial area for six years.

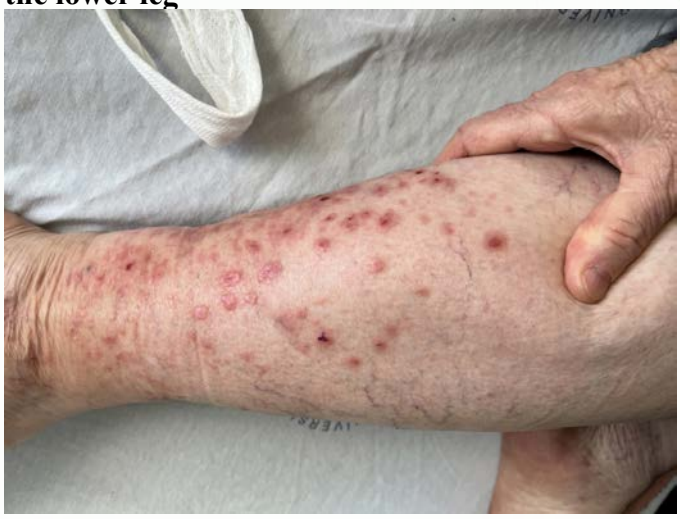
Keywords: lichen planus,bullous pemphigoid,lichen planus pemphigoides

bullous lesions and eroded areas around the left ankle



bullous lesions and eroded areas around the left ankle

erythematous, bright papules and eroded areas on the lower leg



erythematous, bright papules and eroded areas on the lower leg

PP-20 [Corrective, Aesthetic and Cosmetic Dermatology]

Nanotherapy devices for topical treatment of Rosacea

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Polyclinic of Specialties No 2 Tirana- Velvet Clinic

Introduction: Rosacea is a common chronic skin condition affecting the face, characterised by flushing, redness, pimples, pustules and dilated blood vessels. The eyes are often involved and thickening of the skin with enlargement (phymas), especially of the nose, can occur in some people. A range of treatment options are available but it is unclear which are most effective. The current treatments include oral and topical antibiotics and antimicrobials.We will report a case of a Rosacea patient treated effectively topically with nanotech therapy.

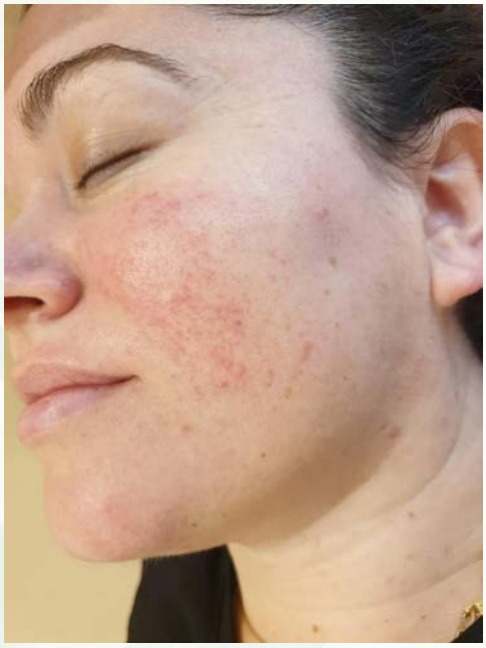
Material and methods: CASE: A forty -two year old woman presented in our clinic, with papules and pustules, erythema and teleangiectasia spread in the middle face. The lesions have a lifetime of at least three months and we found them at different stages of evolution. The patient refers that has been through many visits with dermatologists and has tried some

protocols of treatment with oral and topical antibiotics. Laboratory tests were done and the results were normal. The data from skin biopsy were specific for Rosacea. The diagnosis of Rosacea was done. The patient was treated with nanoparticles of hyaluronic acid and dead sea salts inserted topically in the site of lesions by a device of nano therapy. Nano therapy was performed every week for 12 consecutive weeks and then 1 in a month for 3 months. The most of lesions were disappeared after 4 weeks of treatment and persist only erythema After 6 months the result was impressive and the patient was very happy.

DISCUSSION: A chronic skin disorder called Rosacea is primarily characterized by inflammation associated with abnormal innate immune response. One of the main goals of innovative topical treatment options for inflammatory skin diseases such as rosacea is to selectively deliver the drug at the inflammation site. Recent studies have highlighted the beneficial use of nanoparticles for anti-inflammatory therapy due to their ability to form a drug reservoir retaining the drug locally at the site of action. Although, our nano therapy is specific to the treatment of Rosacea, this approach can be applied to other inflammatory skin disorders.

Keywords: nanoparticles, Rosacea, devices, inflammatory skin diseases

rosacea 1



rosacea 2

rosacea3

PP-21 [Cutaneous Oncology]

Pink, Purple Nodular Lesion in the Gluteal Region: Primary Cutaneus B Cell Lymphoma

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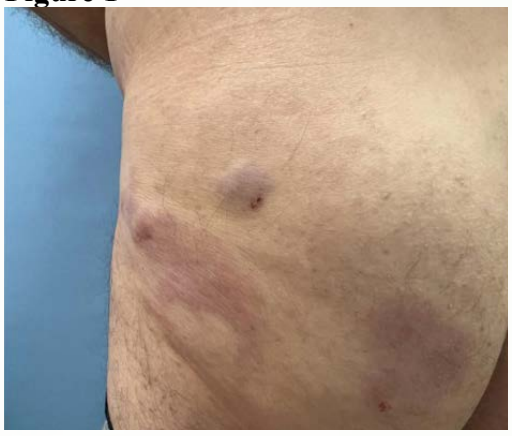
Introduction: Primary cutaneous lymphomas are unique, heterogeneous group of lymphoproliferative disorders which have primary cutaneous manifestation in the absence of systemic involvement of lymph nodes, bone marrow, or visceral organs at the time of diagnosis. Among the primary cutaneous lymphomas, B-cell lymphoma is much less common and accounts for 20%–25% of cases. Primary cutaneous diffuse large B-cell lymphomas (PCDLBCLs) are rare but aggressive neoplasms with poor prognosis, most commonly affecting elderly women and manifesting with rapidly enlarging nodule(s) on one or both legs. In this article, we present a case of PCDLBCL diagnosed on the basis of clinical features, histomorphology, and characteristic immunohistochemical expression.

Case Report: An 80-year-old male patient was admitted to our clinic with the complaint of a rapidly growing purple-colored swelling on the left hip for one year. On clinical examination, there were firm purple nodular lesions and pink plaques in the left gluteal region (Fig. 1). A biopsy was taken and histopathological and immunohistochemical analysis revealed diffuse large B cell lymphoma. The patient was referred to the Department of Hematology. Positron emission tomography, complete blood cell count, peripheral smear examination were made and no systemic involvement was observed. He had no weight loss, fever, night sweats, and additional complaints. R-CHOP (rituximab, doxorubicin, vincristine sulfate, cyclophosphamide) chemotherapy was started for the patient. Clinical and radiological response was achieved and he was decided to be followed-up.

Discussion: Primary cutaneous B-cell lymphomas (PCBCL) were previously classified into three distinct subtypes; primary cutaneous marginal zone lymphoma, primary cutaneous follicle center lymphoma and primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL, LT). In an update in 2018, a new entity of Epstein–Barr virus positive mucocutaneous ulcer was included in PCBCL. Among all the PCBCLs, PCDLBCL, LT has the worst prognosis, with a 5-year disease-specific survival ranged between 40 and 60%. Recurrences and extracutaneous progression are common. In our patient, after chemotherapy, the lesion regressed and no recurrence was observed in 6 months follow-up period. The term PCLBCL, LT is preferred for both lesions on the legs and similar lesions at the other sites. Lesions outside of the lower extremities develop in 10% to 15% of cases. Our case is PCLBCL, LT with gluteal region involvement. In conclusion, primary cutaneus B-cell lymphoma should be considered in the differential diagnosis of pink-purple nodular lesions in the elderly. Collaboration with the Department of Hematology and screening for systemic involvement should be considered.

Keywords: primary cutaneous B-cell lymphoma, primary cutaneous diffuse large B-cell lymphoma, pink-purple nodular lesions

Figure 1



Purple nodular lesions and pink plaques in the left gluteal region

PP-22 [Urticaria, Angioedema]

Importance of differentiating subcutaneous emphysema from angioedema

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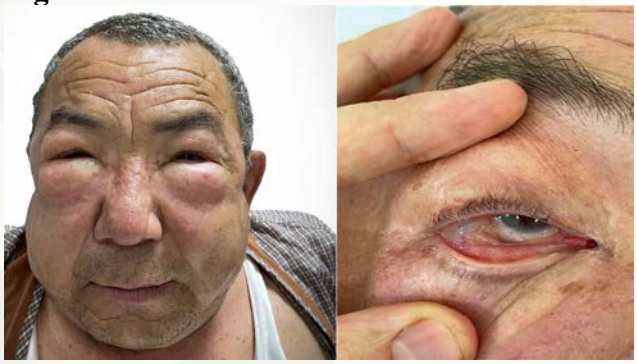
While subcutaneous emphysema is easily recognized when it is secondary to many surgical operations, it is confused with angioedema in very few cases. Although we have not yet come across a publication on this subject, we observe that clinicians neglect the physical examination most of the time in the Covid 19 pandemic. In our case, we described a patient with extensive subcutaneous emphysema mimicking angioedema. Since the patient's lesions were not palpated by the emergency physicians, subcutaneous emphysema was not noticed and systemic steroids and adrenaline were given. Cases of spontaneous pneumothorax and pneumomediastinum are increasingly being reported, even in asymptomatic Covid 19 patients. We encountered subcutaneous emphysema patients in Covid 19 patients. In our patient, the polymerase chain reaction for Covid 19 was negative, but based on this case, we wanted to remind subcutaneous emphysema as a rare differential diagnosis of angioedema, to emphasize the importance of the physical examination, and to warn clinicians that subcutaneous emphysema may be a sign of asymptomatic covid infection.

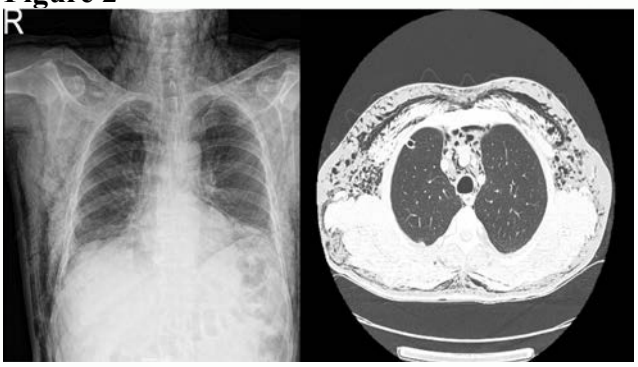
Keywords: subcutaneous emphysema,angioedema, covid 19, pneumothorax

Figure 1



Diffuse facial swelling involving the periorbital region, bilateral cheeks, and neck region with sparing the lips (left), air bubble in the lateral cantus of the right eye (right)

Figure 2



Widespread opaque lines/shadows of gas density suggesting emphysema in the subcutaneous region of the neck and trunk (left), subcutaneous air accumulation in the anterior chest wall and bilateral axilla, and air leak in the superior anterior mediastinum compatible with pneumomediastinum (right)

PP-23 [Adverse Drug Reactions, TEN]

Pembrolizumab Related Lichenoid Drug Eruption

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Introduction: Pembrolizumab is humanized monoclonal antibody that inhibit the interaction between the programmed death-ligand 1(PD-L1) and PD-L2 ligands on tumor cells and PDL-1 receptor on T-cells. Pembrolizumab is used in the treatment of many cancers such as advanced melanoma, non-small cell lung cancer, Hodgkin lymphoma, Primary Mediastinal B-cell lymphoma and urethral carcinoma. Pembrolizumab triggers T-cell reaction and it is causing T cells to attack healthy cells. This leads to appear of various autoimmune diseases. Among the cutaneous immune mediated side effects, maculopapular rash, pruritus, psoriariform and lichenoid eruption are the most reported types. Here we report a case of patient with non small cell lung cancer undergoing pembrolizumab therapy who developed a lichenoid drug eruption.

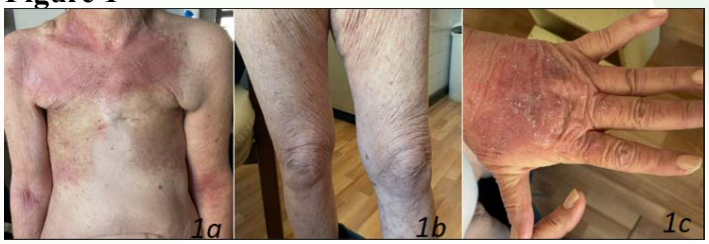
Case Report: A 65-year-old female patient presented with pruritic erythematous scaly papules and plaques. These lesions started 1.5 months ago on the trunk, bilateral arm flexor regions, dorsum of the hand, and bilateral legs. Her medical history include breast carcinoma, psoriasis and non-small cell lung

cancer diagnoses in remission. She had a history of using 16 courses of pembrolizumab every 3 weeks for 1 year for the treatment of non-small cell lung cancer. She had not received any treatment for these rashes. Histopathology study of performed biopsy was reported as "interphase dermatitis compatible with drug eruption". Treatment was started by single dose of ıntramuscular betamethasone dipropionate and betamethasone sodium phosphate and topical methylprednisolone aceponate. Significant regression was observed in the lesions of the patient at the follow-up 3 weeks later under these treatments.

Discussion: Pembrolizumab, an immune checkpoint inhibitor, is a revolutionary immunotherapeutic agent in cancer treatment. Anti PD1 treatments are generally well tolerated, but cutaneous side effects are observed in 18-42% of patients. Among the cutaneous immune mediated side effects, maculopapular rash, pruritus, psoriariform and lichenoid eruption are the most reported types. The risk of autoimmune diseases due to PD1 inhibitors also increases. In this case we report lichenoid drug eruption that started at the 16th cycle of pembrolizumab treatment. In the literature, it has been recommended to use topical steroids in mild cases, systemic steroid therapy in advanced stages, and to interrupt immunotherapy in advanced stages where life-threatening results may occur. In this case, similar to the literature, the patient responded to systemic and topical steroid combination and the rashes regressed significantly. Early recognition and treatment of immunotherapy associated adverse drug eruption are critical to provide patient safety. In this case report, it is aimed to draw attention to pembrolizumab-related cutaneous side effects and to provide early diagnosis and management.

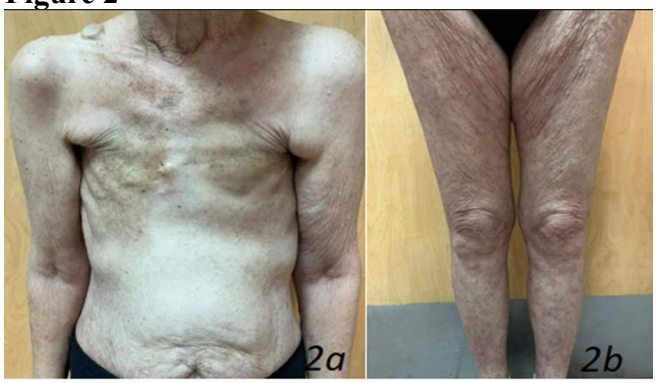
Keywords: pembrolizumab, drug eruption, lichenoid

Figure 1



1a/1b/1c: Erythematous scaly papules and plaques on the trunk, bilateral arm flexor regions, dorsum of the hand, and bilateral legs

Figure 2



2a/2b: Significant regression was observed in the lesions 3 weeks after topical and systemic corticosteroid treatment.

PP-24 [Dermatology and Internal Medicine, including Skin Manifestations of Systemic Diseases]

A Treatment Option in the Acute GVHD: Mesenchymal Stem Cell Therapy

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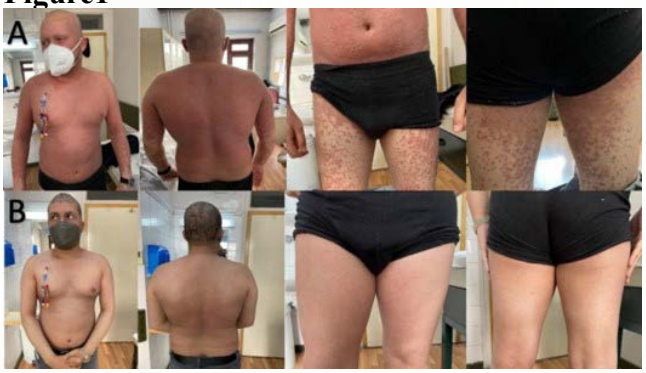
Allogenic Hematopoietic Stem Cell Transplantation (allo-HSCT) is an effective treatment option for many malignant and non-malignant hematological diseases. However, as a result of this treatment, Graft Versus Host Disease (GVHD), may occur when the donor T cells recognize the recipient's tissue as foreign. GVHD is a multisystemic disease that can involve many organs;

including the hepatobiliary system, gastrointestinal tract, and skin. The first and most common manifestation of GVHD is a maculopapular eruption. Mild skin involvement tends to regress spontaneously; additionally bulla formation, desquamation or erythroderma may be observed. Topical and systemic corticosteroids are the first-line treatments, while various immunosuppressive and immunomodulatory treatments are used in resistant cases. Here we report a case of patient with acute GVHD that was resistant to systemic steroid therapy and benefited from mesenchymal stem cell (MSC) treatment. A 21-year-old patient who had allo-HSCT 20 days ago due to the diagnosis of AML; admitted to our outpatient clinic with diffuse maculopapular eruption which was more prominent on the trunk. The patient had itching and fever. The histopathologic finding of skin showed "minimal perivascular dermatitis characterized by sparse neutrophil leukocytes". Since GVHD was considered clinically, the patient was administered cyclosporine, mycophenolate mofetil and methylprednisolone treatments by hematology for a month. In addition to all, ruxolitinib was used for control skin rashes. However, the skin rashes were resistant to all of these treatments. Therefore, we performed rebiopsy and it was reported as compatible with GVHD Grade 2. The patient had no other system involvement, except skin involvement. Extracorporeal photopheresis (ECP) treatment was started for the patient 2 days in a week. 4 weeks later, once a week MSC treatment was added to the treatment. Significant regression was observed in the lesions at the follow-up 2 weeks later. GVHD is an important immune-mediated complication. According to the European consensus recommendations, skin biopsy is recommended for diagnosis. Treatment should not be delayed because early treatment affects the prognosis. In this case, the first biopsy was inconsistent with the clinical presentation. However, treatment was started due to clinical suspicion. Topical corticosteroids and calcineurin inhibitors are used in grade 1 cases in the treatment of acute GVHD. Systemic corticosteroids are the first-line treatment in cases with grades 2-4. ECP, mycophenolate mofetil, rapamycin inhibitors, ruxolitinib, methotrexate, pentostatin, alemtuzumab and MSC treatments can be used in patients who resistant to corticosteroid therapy. Since early and effective treatment of GVHD positively affects the prognosis, new treatment options should be evaluated in corticosteroid-resistant cases. MSC treatment can be considered as an effective and safe option in resistant cases.

Keywords: GVHD, Mesenchymal Stem Cell Therapy, corticosteroid resistance

Figure1



A: Before Treatment B: 2 weeks after Mesenchymal Stem Cell Therapy

Table 1

Histopathological Grading	Histopathological Grading	Clinical Staging	Clinical Staging	Clinical Grading	Clinical Grading
0	Normal skin	0	No GVHD rash	1	Skin Stage 1-2
1	Mild vacuolization of epidermal cells	1	Maculopapular rash less than 25% of body surface area (BSA)	2	Skin stage 3 or liver/intestinal stage 1
2	Diffuse vacuolization and dyskeratotic bodies in basal cells	2	Maculopapular rash in 25-50% of BSA	3	Skin stage 3 or liver stage 2-3/ intestinal stage 2-4
3	Subepidermal separation	3	>50% of BSA maculopapular rash	4	Skin stage 4 or Liver stage 4
4	Complete epidermal separation	4	Generalized erythroderma + bullous formation		

PP-25 [Cutaneous Oncology]

Carcinoma Erysipeloides: A Case Report

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Cutaneous metastases are observed in 5.3% of cancers and usually occur within 3 years of diagnosis. Cutaneous metastases from breast cancer tend to be located in the thoracic region. The dermatological pattern of cutaneous metastases of breast cancer is papulonodular lesions, but erysipeloid infiltration is also possible. Carcinoma erysipeloides is a rare condition observed in 3% of all cutaneous metastases. It presents as a fixed, well-circumscribed erythematous patch or plaque resembling cellulitis or erysipelas. Differential diagnoses include cellulitis, eczema, inflammatory breast cancer, radiation dermatitis, and breast Paget's disease. Here we will present a case of carcinoma erysipeloides, which appeared as the first sign of metastasis in a patient diagnosed with breast cancer that was in remission.A 49-year-old female patient was admitted to our clinic with an erythematous patch observed on the anterior trunk for 1 month. Systemic and local symptoms were absent. During dermatological examination of the patient, there was a 25 cm surgical scar on the anterior side of the trunk and a widespread erythematous patch around the scar that faded with pressure. After diagnosis of breast cancer, she underwent left total mastectomy in 2012 and right total mastectomy in 2020. She had been treated by letrazole for 18 months. No recurrence or metastasis was observed 3 months ago. Considering the cellulite/ erysipel diagnoses in another center, she was started on amoxicillin/clavulanic acid, topical isoconazole and fusidic acid+betamethasone valerate cream treatments. Despite this treatment for a week no improvement was detected. According to current clinical data, 5 mm punch biopsy was performed considering Carcinoma Erysipeloides. In histopathological examination and immunohistochemical studies, Proliferative activity was observed with Ki-67 at a rate of 10-15% in invasive tumor cells. Since the patient had a clinical history of breast carcinoma, breast carcinoma metastasis was considered first.In this case, too, the patient developed a well-defined cutaneous lesion resembling an acute infectious process such as erysipel and/or cellulitis. It was misdiagnosed as cellulite and given the wrong treatment. The diagnosis of carcinoma erysipeloides requires rapid diagnosis and treatment in order to increase patient survival. Response to induction chemotherapy is the most important prognostic factor. The prognosis varies according to the underlying cancer type, but generally low survival is observed.While patients with breast cancer have a better prognosis than other cancers, the estimated survival after diagnosis of cutaneous metastases is 50% at 6 months.The median survival for all forms of cutaneous metastasis in breast cancer is 13.8 months, with a 10-year survival rate of 3.1%. This case report highlights the need for accurate differential diagnosis of carcinoma erysipeloides and prompt initiation of treatment.

Keywords: Carcinoma Erysipeloides, cellulite, erysipel

PP-26 [Inflammatory Skin Diseases]

Mondor Disease: A Case Report

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INTRODUCTION & OBJECTIVES: Mondor disease is a benign clinical condition characterized by thrombophlebitis of the superficial veins of the anterolateral thoracoabdominal wall. Primary Mondor disease is idiopathic while secondary Mondor disease may be traumatic or iatrogenic. Cases of Mondor disease have been reported after breast surgeries such as cosmetic mammoplasty, mastectomy, and breast-conserving surgery for breast cancer. Herein, we present a 73-year-old male patient who had superficial thrombophlebitis after excision of a breast tumor.

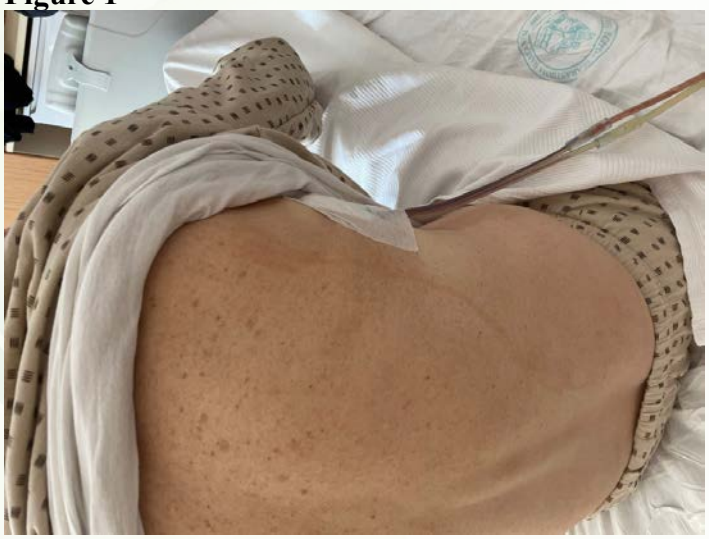
MATERIALS & METHODS: It is a case report.

CASE: A 73-year-old male patient was admitted to general surgery clinic for diagnosis and treatment of a breast tumor and consulted to dermatology department because they noticed a new asymptomatic lesion that appeared on lateral side of the trunk after excision of a mass from right breast. Medical history and family history were not remarkable. General physical examination was normal. Dermatological examination revealed linear, erythematous, indurated, subcutaneous cord-like lesion running diagonally on the right lateral thoracoabdominal wall (figure 1-2). There was no pain or itching associated with the lesion. Based on the history and clinical findings, a diagnosis of secondary Mondor disease due to breast surgery was made and the patient was prescribed a non-steroidal anti-inflammatory drug perorally two times a day and topical mometasone furoate cream for 10 days.

CONCLUSIONS: Mondor disease is a rare and usually self-limiting condition, with spontaneous resolution. It is important for the clinician to be aware of this condition in order to make an accurate diagnosis and avoid unnecessary investigation.

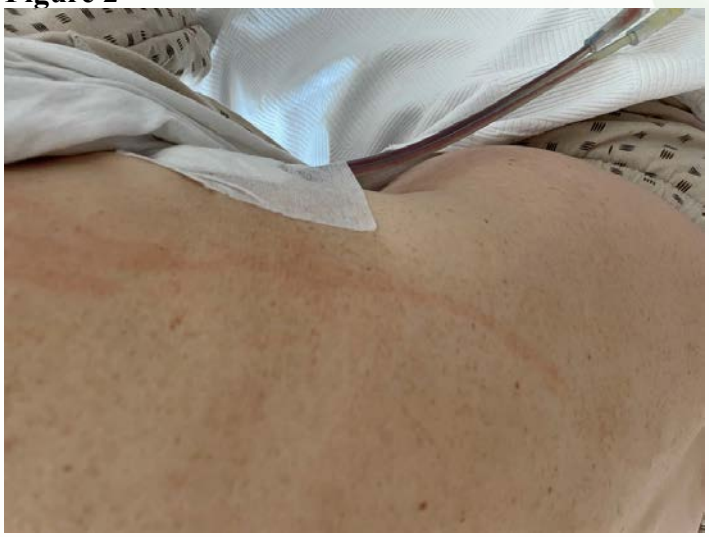
Keywords: breast, mondor, thrombophlebitis

Figure 1



A linear, erythematous, indurated, subcutaneous cord-like plaque

Figure 2



The lesion ran diagonally on the right lateral thoracoabdominal wall

PP-27 [Dermatology and Internal Medicine, including Skin Manifestations of Systemic Diseases]

X-Linked Ichthyosis

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INTRODUCTION: Ichthyoses are a group of in herited keratinization disorders of the skin that are clinically and etiologically heterogeneous. It is characterized by diffuse skin dryness, peeling and scaling of the skin, sometimes erythroderma and histopathologically by hyperkeratosis. X-linked ichthyosis is a genetic disease caused by a mutation in the steroid sulfatase (STS) enzyme. X-linkedichthyosis (XLI) is seen at birthor in theimmediate neonatal period. Most typically, X-linked ichthyosis appears in infancy with scaling on the posterior neck, upper trunk, and extensor surfaces of the extremities. The scalp is often in volved. In childhood, the boy who is affected has a “dirty-face” appearance, with an increase in in volve men twith age.

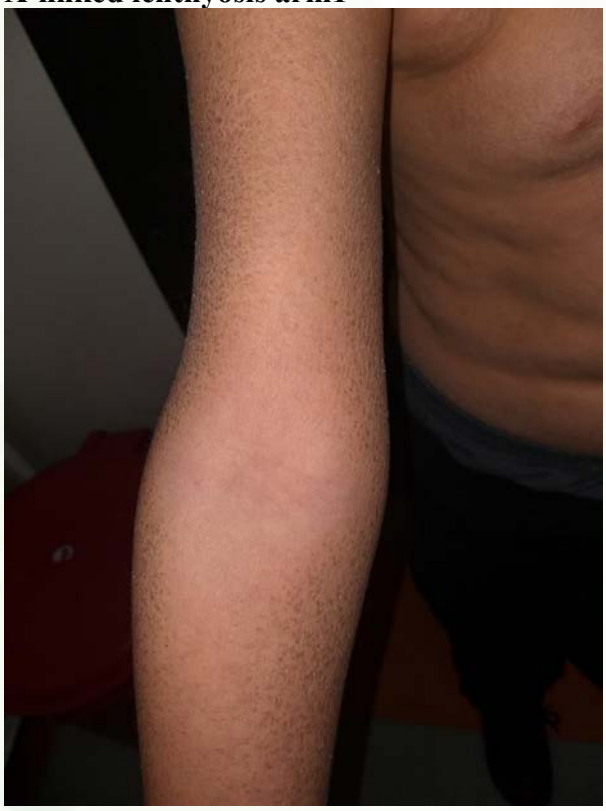
CASE: A 10-year-old boy presented with scaly skin on the extremities and trunk. His scalp, elbow and knee flexures are spared. He had the appearance of an

unwashedlook neck. Lesions started in the neonatal period. Past medical history and review of systems were unremarkable. Family history was unremarkable.

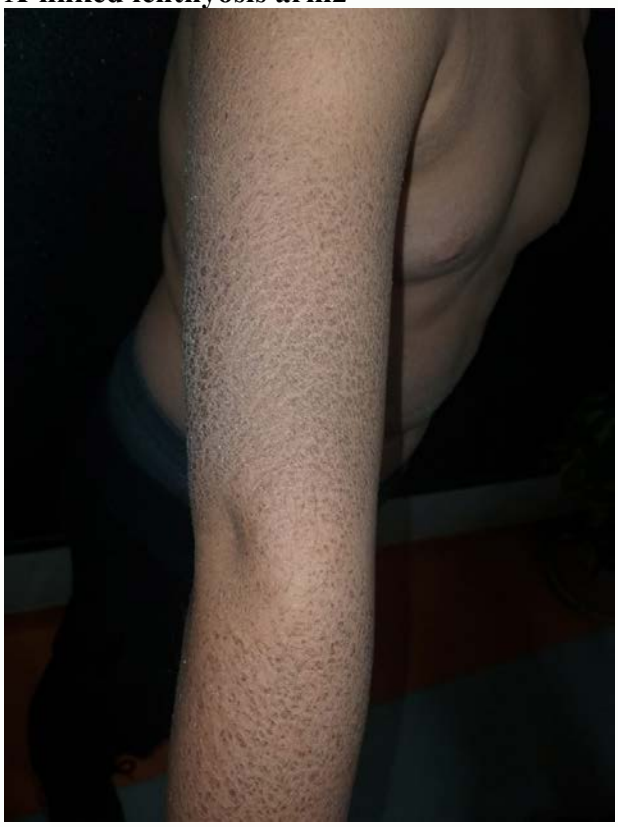
CONCLUSION: We found this case worth presenting, since X-linked ichthyosis (XLI) is a rare disease. The medical management of X-linked ichthyosis is directed at reducing scales, decreasing skin dryness, andimproving skin appearance. This can be accomplished with regular bathing and theuse of emollients and keratolytic agents. Petrolatumor humectant-based moisturizers should be applied to damp skin.

Keywords: Steroid sulfatase, dryness, ichthyosis

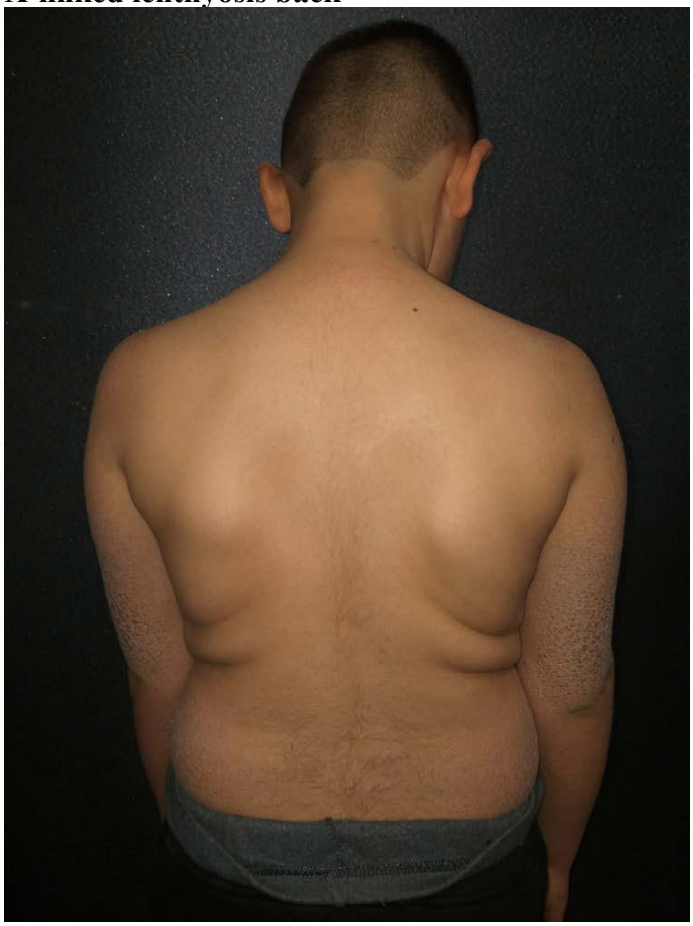
X-linked ichthyosis arm1



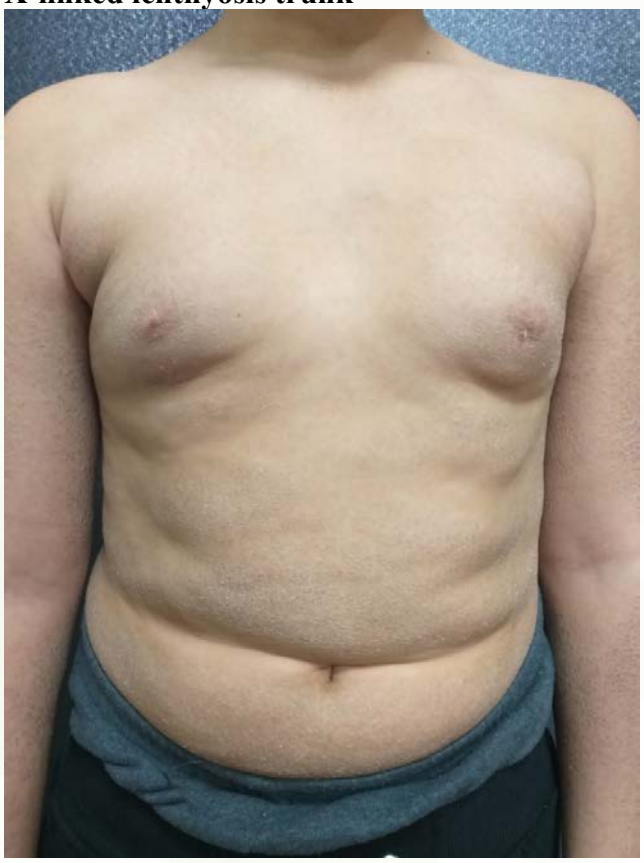
X-linked ichthyosis arm2



X-linked ichthyosis back



X-linked ichthyosis trunk



PP-28 [Dermatology and Internal Medicine, including Skin Manifestations of Systemic Diseases]

Nevus Comedonicus: A Case Report

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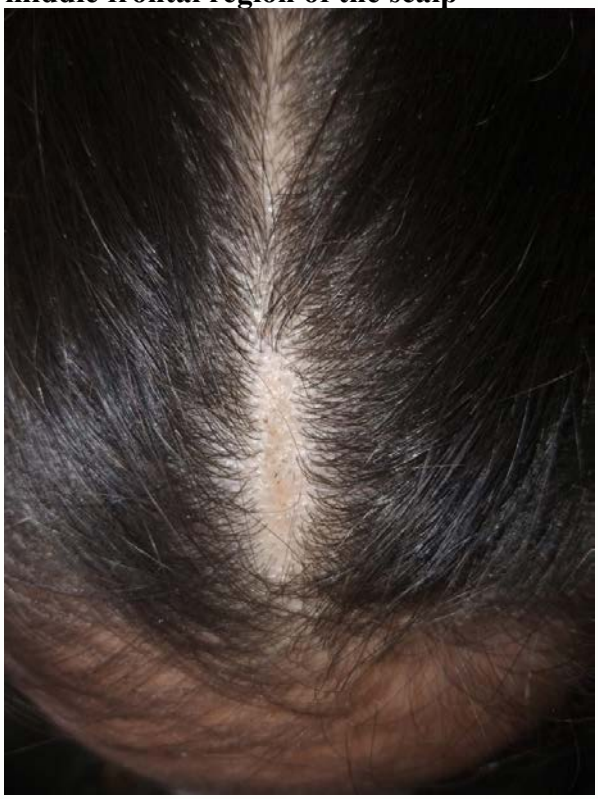
INTRODUCTION: Nevus comedonicus (NC) is a rare development alanomaly of follicular infundibulum plugged with keratinous material that resembles comedo-likelesions. Frequently affected site sare face, neck, trunk, an dupper arm. Few cases have been described on palms, soles, scalp, andgenitalia. Herein, we are reporting a case of NC on the scalp with its review of literature.

CASE: A 9-year-old girl presented with an asymptomatic hairless patch on scalp. It was present since birth. It was not associated with any other congenital anomalies. There was no family history of similar type of lesion. On examination, a patch of alopecia of size 6 cm × 3 cm was present over the middle frontal region of the scalp. The lession was studded with multiple discrete pits filled with keratinous material and comedo-like lesions.

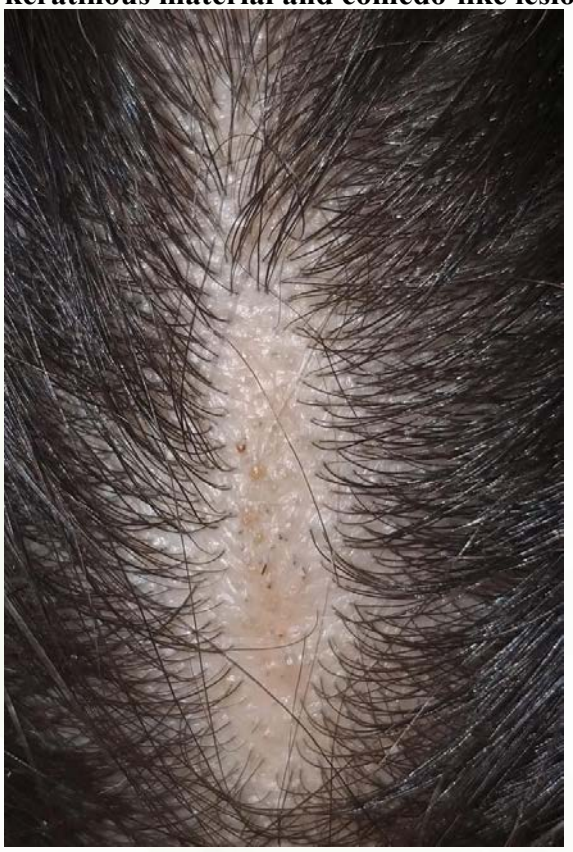
CONCLUSION: Nevus comedonicus is usually treated conservatively, with moisturizers, topical corticosteroids, and keratolytics. Retinoids have also been used. Topical tretinoin treatment has shown limited efficacy in nevus comedonicus.

Keywords: comedo nevus, alopecia,topical tretinoin

a patch of alopecia of size 6 cm × 3 cm over the middle frontal region of the scalp



The lession with multiple discrete pits filled with keratinous material and comedo-like lesions



PP-29 [Oral Mucosa and other Skin-adjacent Mucous Membranes]

A slowly growing mass on the tongue

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A 67-year-old female with known coronary artery disease presented with a slowly growing indurated and well-demarcated ulcerative lesion on her lateral tongue. The lesion was present for 2 months and glowing slowly since then.

The patient was showing no symptoms of pain, itch or burning sensation. She described no history of trauma, dental procedure, consuming irritating foods or any other drug administration.

In the past, the patient was prescribed with topical analgesics, topical antibacterial and antifungal sprays with no improvement.

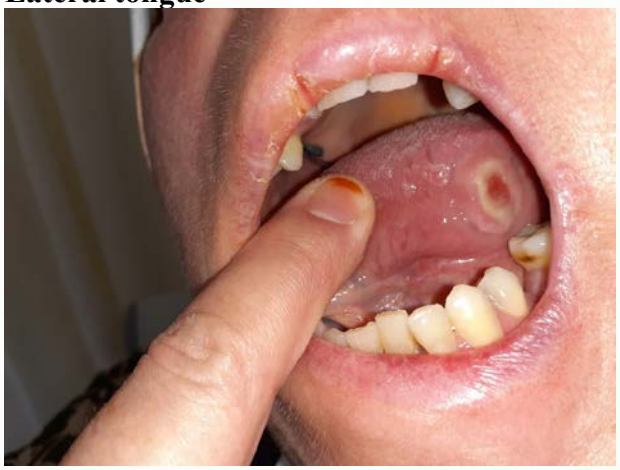
After examination, the patient was consulted to ENT clinic for performing incisional biopsy with preliminary diagnosis of squamous cell carcinoma and trauma-induced ulceration.

The biopsy showed a mixed inflammation containing mainly eosinophils and other inflammatory cells in submucosa and mucosa and some dilated vessels. The histopathology and clinical signs were supportive for the diagnosis of Traumatic ulceration with stromal eosinophilia. After the diagnosis, topical triamcinolone acetonide was prescribed and criyotherapy was applied twice a month. The lesion showed regression on the first follow-up.

Traumatic ulceration with stroma eosinophilia, also called as ulcerative eosinophilic granuloma, Riga-Fede disease is a rare lesion with unknown aetiology and pathogenesis. It is considered to be a benign, reactive and chronic but self-limiting disease. The most suspected trigger is trauma; however, injury is identified in less than 50% of cases. Several therapeutic approaches like topical steroids, mouthwashes, topical antibiotics, curettage and cryotherapy have been reported. The most preferred therapy is surgical excision. In our case the patient did not prefer excision therefore criyotherapy and topical steroid were applied.

Keywords: eosinophilic granuloma, mucosa, ulceration, trauma

Lateral tongue



PP-30 [Dermatology and Internal Medicine, including Skin Manifestations of Systemic Diseases]

A case of kyrle disease in a patient with multiple sistemik disease

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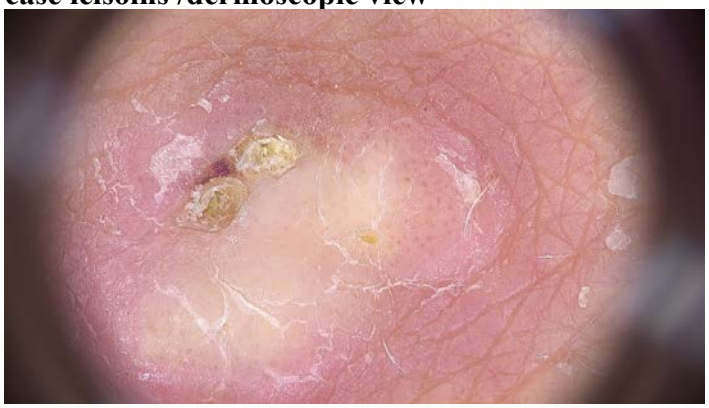
[2]Department of Pathology, Gazi University,Ankara, Turkey

Kyrle disease (KD; or hyperkeratosis follicularis et parafollicularis in cutem penetrans) is a rare skin condition classified as a subtype of acquired perforating dermatosis, along with reactive perforating collagenosis, elastosis perforans serpinginosa, and perforating folliculitis.2 KD has been seen in association with multiple disorders, including diabetes mellitus, renal and liver diseases, congestive heart failure, hyperlipidemia, infective diseases and abnormal metabolism of vitamin A.3 Here we report a case of kyrle disease who used sorafenib because of liver cancer and had known DM, CAD, COPD and asthma. A 70-year-old female patient who was using sorafenib for known lung cancer presented with a 7-month history of widespread pruritic and erythematous lesions on the body. In the dermatological examination there are multiple erythematous and keratotic papules and nodules on the trunk and lower extremities. Histopathological funding showes a transepidermal elimination disorder. Histochemical study showed epidermal elastic fiber with von Gleson elastin stain. Upon to the patient's systemic diseases (CAD, COPD, DM, Lung cancer and asthma) and histopathologic finding the diagnosis was accepted as kyrle's disease. Treatment was started by Narrowband UVB twice a week and topical steroid. After 8 weeks, topical dapsone and bilastine (anti histamine) were added to the treatment and after 12 weeks the patient's pruritus was reduced and the lesions were healed partially. KD is one of the rare variants of primary perforating dermatosis. İt affects more commonly 30–50-year-old females, presents with pruritic hyperkeratotic and ulcerated nodules, and papules with a central keratotic plug mostly located on extensor surface of upper and lower limbs, and on the trunk. While the proper management of underlying systemic disease is fundamental, as no guidelines or evidence-based treatment regimen has been specifically developed for this disease. İt is important that dermatologists be aware of the various treatment options that have been previously employed for KD, particularly since chronic disease rates related to its development are consistently on the rise. This case showed that combinated treatments are more effective. Despite the high incidence of comorbidities in KD patients, treatment of the underlying disease is important for complete remission. Phototherapy and topical steroids may be preferred as the first line with fewer side effects.

Keywords: kyrle disease, acquired perforating dermatosis, liver cancer

case leisoins /dermoscopic view



PP-31 [Cutaneous Oncology]

A Case of Exrtanodal B-cell Marjinal Zone Lymphoma

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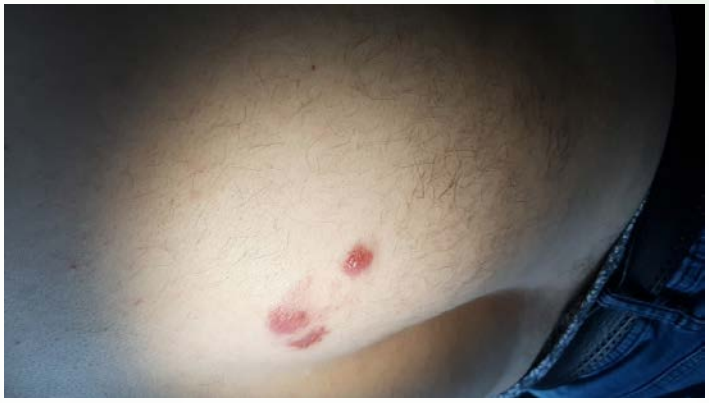
Primary cutaneous lymphomas (PCLs) are the most frequent extra-nodal lymphomas. Primary cutaneous B-cell lymphoma (PCBCL) is a heterogeneous group of mature B-cell neoplasms with tropism for

the skin, with a rate of only 5%–10% in the East. Clinically, PCMZL is an indolent disease and has an excellent prognosis. PCMZL is composed of a polymorphous infiltrate that includes centrocyte-like, monocytoid, and lymphoplasmacytoid lymphocytes and plasma cells. The neoplastic cells express B-cell markers and usually bcl-2 and are negative for CD5, CD10, and bcl-6. Here we report a case of primary cutaneous marginal zone lymphoma with multiple leisions arising at the back of patient. A 40-year-old man presented with 3 erythematous leisions on his back that appeared 6 months ago. The patient, who only had a history of chronic gastritis, During the physical examination of the patient, revealed 3 erythematous hard nodules on the back.(3*2, 2*2 and 2*1 cm diameter). İn the histopathological examination Atypical lymphoid proliferation was observed. İmmunohistochemical studies performed diffuse staining with lymphoid cells CD3, CD4, CD8, CD20 and bcl-2. Follicular dendritic network was observed with CD23, but CD10, bcl-6, CD30, MUM-1, Perforin and Granzyme B were negative. Finally, the patient was diagnosed as having PCMZL by dermatology and hemato-oncology examinations. PCMZL is an indolent lymphoma with a tendency for local recurrence, but extracutaneous dissemination is very rare. The pathology of PCMZL is still poorly understood; however, the origin appears to be multifactorial and its genesis probably involves chronic antigen stimulation. Usually, clinical manifestations consist of solitary lesion or clusters of asymptomatic, reddish brown to violaceous or purpuric papules, nodules, and plaques measuring from 1 to 10 cm in diameter. The trunk and arms are predominantly affected. Considering the clinical features, the diagnosis is established by skin biopsy, Our report illustrates the existence of a peculiar form of PCMZL exhibiting at least two different clones that initially presented with papules and later involved clinically normal and minimally erythematous skin. Therefore, in a patient with PCZML, biopsies of evanescent erythematous patches and even normal skin should be considered during staging and clinical follow-up.

Keywords: Primary cutaneous lymphoma, primary cutaneous marginal zone lymphoma, extra-nodal lymphomas

case leisoins on the back



PP-32 [Corrective, Aesthetic and Cosmetic Dermatology]

3 cases of morhpea like atrophic lesions developed after Abobotulinumtoxin A treatment: A new theory for a rare complication

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Introduction & OBJECTIVES: Botulinum toxin treatments for facial rejuvenation are a popular, non-surgical aesthetic option due to their low complication rate, immediate onset of effect and long-lasting results. The case report presents tree instances of morphea-like skin atrophy after Botulinum toxin treatment that resolved without additional treatment in 3-4 weeks. The report also aims to present a new theory and evaluation method for the etiology of this complication.

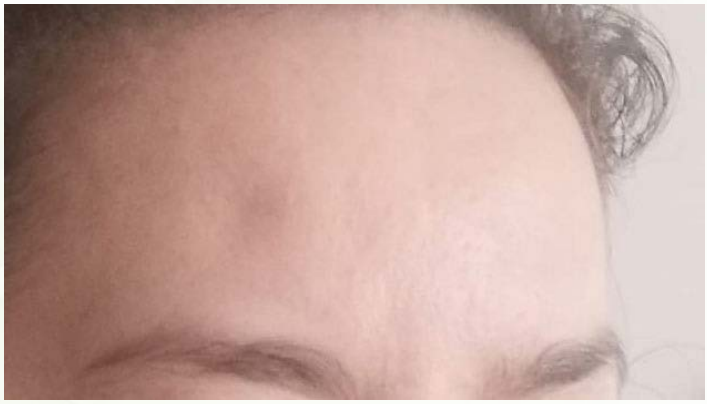
Materials & METHODS: This case report describes three patients who received abobotulinumtoxin A treatment for active wrinkles in the frontal and periorbital region. In each case, the patients developed a morphea-like skin atrophy, which disappeared within 4 weeks without the need for additional treatment or intervention. The report highlights the re-epithelialization effect of Hamamelis virginiana, which was advised as a topical treatment in one of the cases.

RESULTS: Three cases of skin atrophies after Botulinum toxin treatments were reported by Landau M. et al. and Nyckowski T. et al. The cause of the atrophies is not clear, but theories range from local muscular atrophy due to neural stimulus deficiency, silicone oil reaction, and aberrant contraction of the subcutaneous branches of the frontal muscle.

CONCLUSION: The authors suggest that a possible pathology originating from adipose tissue is the cause, as there is no pigment change and a faster recovery course compared to normal botulinum toxin recovering times. The authors recommend using high-frequency ultrasound to distinguish a possible muscular or adipose tissue pathology in future cases. Saline injections applied every 1-2 weeks were reported to be effective in temporarily eliminating the aesthetic problem, which takes approximately 1-6 months to resolve according to the reported cases.

Keywords: Abobotulinumtoxin A, atrophy, botulinum toxin, cutaneous depressions, frontalis, morphea

Case 1

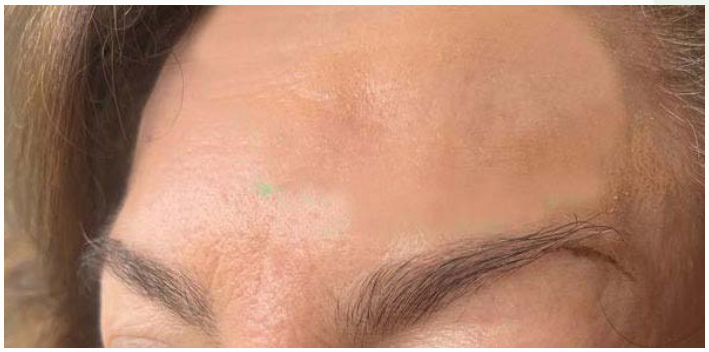


43 year old female patient

Case 2

34 year old female patient

Case 3



72 year old female patient

PP-33 [Dermatopathology]

Idiopathic Granulomatous Mastitis and Erythema Nodosum

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Idiopathic granulomatous mastitis (IGM) is a rare form of inflammatory breast condition associated with breast pain, swelling and mass formation. Although the disease pathogenesis remains unknown, several reports have associated IGM with manifestations such as erythema nodosum and occasionally with arthritis, suggesting that IGM might have an autoimmune disease component. We aim to describe a case of coexistence of IGM and erythema nodosum. In this case, a 39 year-old woman presented with a 3-month history of right breast pain and a 1.5-month history of painful rashes on her legs. A physical examination revealed a reddish, firm and painful lump on her right breast and multiple tenders, reddish nodules on both legs. A skin lesion biopsy showed septal panniculitis, indicating erythema nodosum. Right breast tru-cut biopsy showed granulomatous mastit. Aspiration culture of the breast lump was negative.

All blood test, including serum calcium, angiotensin-converting-enzyme for diagnosis of sarcoidosis were normal. Chest computed tomography showed no bilateral hilar lymphadenopathy or pulmoner findings. A diagnosis of idiopathic GM and EN was made. After 10 days of potassium iodide (90 mg per day) and 2 weeks of prednisolone(60 mg per day) administration, her symptoms resolved promptly.

Keywords: idiopathic granulomatous mastit, erythema nodosum, corticosteroid

PP-34 [Dermatology and Internal Medicine, including Skin Manifestations of Systemic Diseases]

CD30-positive anaplastic lymphoma kinase-negative systemic anaplastic large cell lymphoma presenting with cutaneous lesions

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INTRODUCTION & OBJECTİVES: Anaplastic large-cell lymphoma (ALCL) is a CD30-positive non-Hodgkin lymphoma of T-cell origin.

Cutaneous ALCL presents either as primary cutaneous disease or as secondary skin involvement due to systemic disease. Herein, we present a rare case of ALK (anaplastic lymphoma kinase)-negative S (systemic)-ALCL, was evaluated for rapidly growing nodules and an evolving ulcers on the left leg for about 2 months.

MATERIAL &METHODS: A 60 years of male presented with a two months history of rapidly growing nodules and an evolving ulcers on his left leg. Dermatological examination revealed numerous nodules which have ulcer on top of them on the lateral aspect of the upper leg. There are also two distinct ulcerated tumoral lesions which completely involves the ankle.

The lesion was violaceous in colour and firm on palpation and has necrotic crusts.

Lymphadenopathy was detected on the left inguinal region via physical examination. The patient also complained of fever and weight loss. All laboratory tests were negative, including full blood count, biochemistry, routine urine examination, except C-reactive protein, (CRP: 60 mg/L normal range: 0-5 mg /L) erythrocyte sedimentation rate (ESR: 29 normal range:1-15 mm/h) and lactate dehydrogenase (LDH:297 normal range:135-225 U/L). Serology tests for viruses were negative, except anti-HBC immunoglobulin G positive. A skin biopsy specimen from the tumor showed infiltrate of atypical mononuclear cells with large nucleoli and hyperchromatic nucleus in the dermis. Also a few atypical cells with multinucleation were present. These atypical cells stained positive for CD30 and CD4, but negative for ALK.

Fluorodeoxyglucosepositron emission tomography/ computed tomography (FDG-PET/CT) revealed abnormal FDG uptake in skin tumor at the left lower extremity and also bilateral inguinal region, suggesting the systemic involvement of lymphoma cells. The features were consistent with ALK negative systemic ALCL with skin metastasis and the patient was referred to Department of Hematology.

RESULTS: Skin involvement in systemic ALCL is relatively rare. Our case was evaluated due to initial skin lesions. Dermatologists should be aware that systemic lymphomas may occur as skin lesions such as nodules, ulcers and erythematous plaques. Necessary examinations and biopsy procedures should be made almost immediately for avoid delay diagnosis.

Keywords: lymphoma, anaplastic, nodule, ulcer

FULL TEXT

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UPDATE AND TRANSMISSION FACTORS OF THE HIV/AIDS EPIDEMIC IN UKRAINE

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AIM: On account of the geographic nearness the development is the HIV/AIDS figures in Ukraine also from epidemiological meaning for Europe. The medium-term purpose of Ukraine is the entry in the European Union. The number of newly diagnosed HIV infections in Ukraine ranks second in the WHO European Region after Russia according to the European Centre for Disease Prevention and Control (1). However, because of many unreported cases the actual figures are supposed the official reports considerably.

METHODS: Reported HIV/AIDS cases from the official epidemiological register of the Ukrainian Centre for AIDS Prevention between 1987 and 2021 were reviewed and analysed and this information was supplemented with published HIV prevalence and sexually transmitted disease case reporting information.

RESULTS: The first HIV Infections were registered in 1987. By the end of 1987, six Ukrainina citizens (including five women) were registered as HIV-positive. Until 1994, the number of newly infected Ukrainina citizens fluctuated yearly beween six and 40 pepole. In 1995, there was an explosive increase in the number of new HIV infections, with a tolat of 1,490 regiestered cases. Since then, the number of people teste das HIV-positive has risen rapidly. Between 1987 and 2004, 74,856 Ukrainian were registered with HIV. The number of officially registered HIV-infections increased from 16,078 in 2006 to 17,289 in 2021, Table 1.

Table 1: Newly diagnosed HIV infections, AIDS cases and AIDS deaths in Ukraine, 1987-2021[1]

	1987-2004*	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
New HIV infections																		
New HIV infections in total	74856	13770	16078	17669	18963	19840	20489	21177	20743	21631	19273	15869	17066	18194	18099	18425	17588	17289
AIDS																		
AIDS cases	8918	4217	4723	4573	4386	4446	5861	9189	10073	9362	9844	8468	8867	9325	8852	7518	4145	4155
Deaths among AIDS cases	5367	2188	2420	2507	2714	2594	3096	3736	3870	3514	3426	3032	3253	3298	3448	2977	2114	1928
*Cumulative HIV new infections since 1987	74856	88626	104704	122373	141336	161176	181665	202842	223585	245216	264489	280358	297424	315618	333717	352142	369730	387019

A considerable increase in the number of newly registered AIDS cases in Ukraine can be seen since 1995. The number of newly registered AIDS cases in the Ukraine rose from 45 in 1995 to 4,155 in 2021 (Figure 1). There was a similar increase in the number of registered AIDS deaths, too.

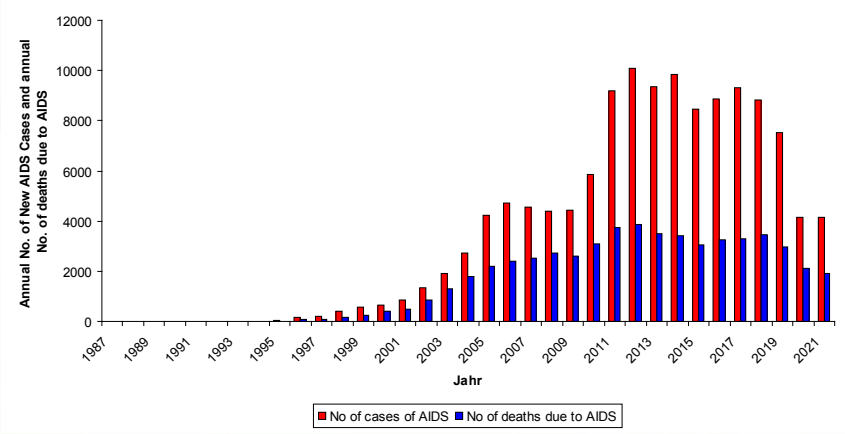

Figure 1. Registered AIDS cases and AIDS deaths in total population of the Ukraine, 1987-2021

5,325 new infections were transmitted by intravenous drug use, 9,534 by heterosexual contacts and 1,977 by vertical transmissions from HIV infected mothers to their children in 2021.

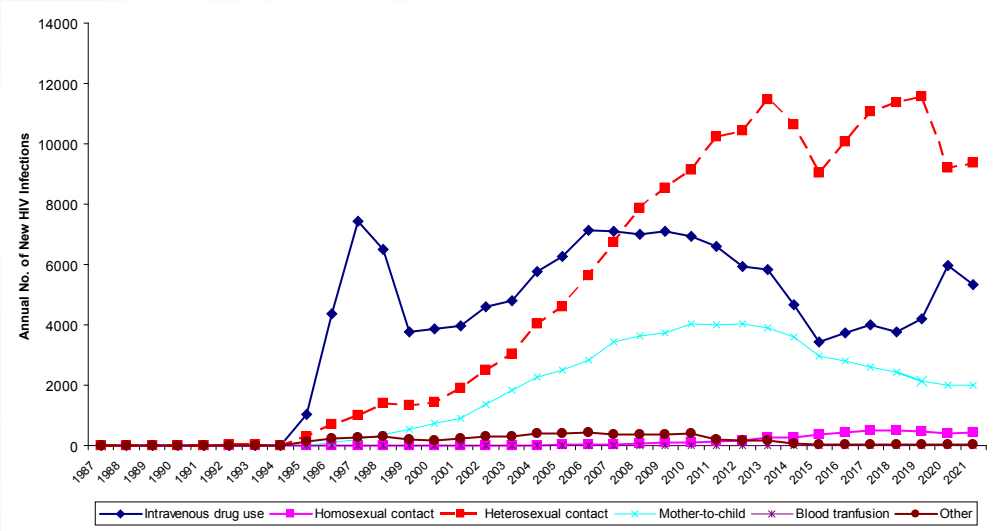

Figure 2. Routes of HIV transmission, Ukraine 1987-2021

DISCUSSION: The spread of HIV and AIDS was not a significant problem in the Ukraine before 1995. Since then, however, there has been a considerable increase in the number of HIV/AIDS registered cases, not only among men, but also among women. Despite efforts by government agencies, local governments, non-governmental organizations and international donors, the number of HIV infection with the most rapidly increasing number of newly diagnosed HIV cases mainly transmitted through heterosexual, but also through contact IDU and mother-to-child-transmission still increases in Ukraine over the past few years (2, 3, 4, 5). Mortality in patients with AIDS is high, but still stable over the last years. However, without effective prevention and intervention measures the HIV epidemic can develop in the Ukraine during the coming years for the European Union to a long-term population-medical problem.

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Keywords: HIV infection, AIDS, Ukraine

HALOGENODERMA:ACASEREPORTANDREVIEWOFTHELITERATURE

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Abstract

Halogenoderma (HD) is an uncommon dermatosis that develops following exposure to halogens such asiodide and bromide, referred to as iododerma and bromoderma, respectively. Here, we report the case of a40-year-old male who presented with a three-week history of slightly itchy progressive skin lesionsassociated with low-grade fever and malaise. The patient had a history of using food supplementscontaining iodide and bromide for four months prior to the appearance of skin rashes. Skin examinationrevealed multiple crusted papules and nodules scattered on his face, neck, and trunk. A skin biopsy wastaken from the lesions. The epidermis showed crustation, exocytosis of neutrophils, and multipleintraepidermalabscesses.Thedermisshowedheavycellularinfiltratescomposedmainlyofneutrophils.Theskin lesions disappeared completely after the cessation of food supplements, along with the use of topicalcorticosteroidsforafewweeks.

Categories: Dermatology

Keywords: bromide,iodide,bromoderma,iododerma,halogenoderma

Introduction

Halogenoderma (HD) is an uncommon dermatosis that develops following exposure to halogens such asiodide and bromide, referred to as iododerma and bromoderma, respectively. Patients with HD presentmainlywithpustulesorpapulopustularlesionsfrequentlylocatedontheface,neck,back,andextremities[1].HDcansometimespresentasextensivevegetatinglesionsratherthanpustulareruptions[2].

The exact pathogenesis of HD remains unknown. It is believed to be caused by a type 2 delayedhypersensitivityreaction[3].ThetreatmentofHDincludestheavoidanceofintakeofiodide-orbromide-containing substances, and lesions usually spontaneously disappear after four to six weeks following thestopping of iodide or bromide intake [3]. Systemic corticosteroids can be used for more rapid healing oftheselesions[4].

Here,wepresentararecaseofHDina40-year-oldmalewhopresentedwithmultiplecrustedpapulesandnodulesscatteredonhisface,neck,andtrunkfollowingtheuseoffoodsupplementscontainingiodideandbromide.

CasePresentation

A 40-year-old male presented with a three-week history of slightly itchy progressive skin lesions associatedwith fever and malaise at the beginning and then disappearing. There were no similar attacks before and nohistory of contact with a similar condition. The patient had a positive history of using iodine and bromidefoodsupplementsforfourmonthspriortotheappearanceofskinrashes.Anallergyhistory,surgicalhistory,medicalhistory,familyhistory,andreviewofsystemswereallunremarkable.Thepatientdidnotexperienceany symptoms of iodism such as mouth burning or increased salivation, metallic taste, tooth and gumsoreness, and headache. Skin examination revealed multiple crusted papules and nodules scattered on hisface,neck,andtrunk(Figure*1*).

Howtocitethisarticle

GhazzawiRA,AlqurashiMG,AlmalkiNA,etal.(November23,2022)Halogenoderma:ACaseReportandReviewoftheLiterature. Cureus14(11): e31846.DOI 10.7759/cureus.31846

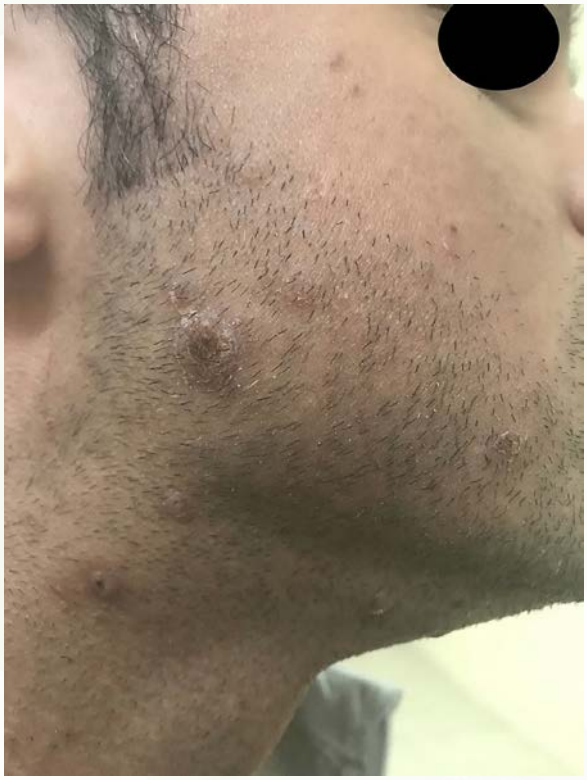

FIGURE 1: Multiple crusted papules and nodules scattered on the patient's face and neck.

Hair, nail, and mucus membrane examinations were all normal. Differential diagnoses included chicken pox, pityriasis lichenoides varioliformis acuta, dermatitis herpetiformis, Sweet syndrome, bacterial folliculitis, and lymphomatoid papulosis. A skin biopsy of the lesion was performed. The epidermis showed crustation, exocytosis of neutrophils, and multiple intraepidermal abscesses. The dermis showed heavy cellular infiltrates composed mainly of neutrophils (Figure 2).

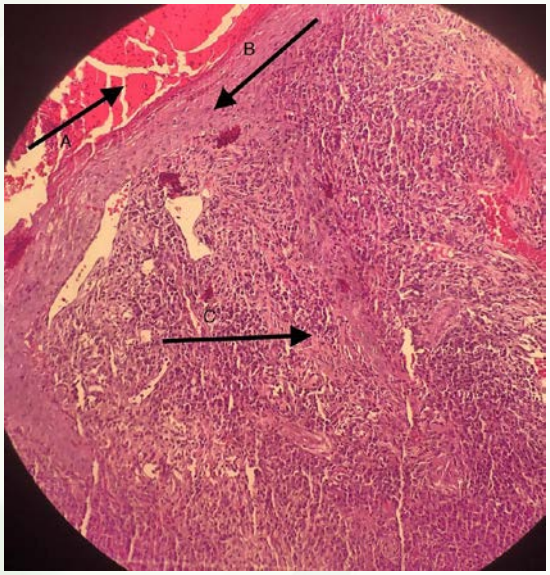

FIGURE 2: A skin biopsy showing epidermal crustation (A) and exocytosis of neutrophils (B). The dermis showed heavy cellular infiltrates composed mainly of neutrophils (C) (hematoxylin and eosin stain; original magnification, ×20).

Based on the above clinicopathological findings, the patient was diagnosed with HD. The patient was reassured and told to stop using the food supplements. A topical corticosteroid was prescribed. One month after using the topical corticosteroid, the lesions disappeared with no recurrence at the time of this report.

Discussion

HD is an uncommon inflammatory dermatosis that develops following exposure to halogens such as iodide- and bromide. Iodide is found in seaweed, salt, amiodarone, radiocontrast media, and potassium iodide, andrarelyastopicaliodideuse[3,5].Iododermausuallyappearsfollowingthesystemicuseofpotassiumiodides,such as in the case of asthma, Graves' disease, and bronchitis [1]. Bromide is found in some drugs such asbromocriptine, analgesics, and hypnotics [6]. Bromide is also found in topical preparations, such as methylbromide, which is used by farmers for feeding animals [7]. Both iodide and bromide are found in foodsupplements [5]. Iododerma commonly presents as acneiform lesions and rarely as vesicular, pustular,hemorrhagic, urticarial, fungating, suppurative, nodular, or ulcerative lesions on the face [3], whereasbromodermacommonlypresentsasverrucous,ulceratingplaquesonthelowerextremities[5,7].

Aliagaoglu et al. reported a case of iododerma following the topical use of a povidone-iodine solution fordisinfection purposes at work [4]. Another study reported iododerma in a pregnant female who was takingiodine-containing multivitamins to decrease the risk of neural tube defects during pregnancy [8]. Young andGrossman reported a case of acute iododerma after receiving 1,942 g of iodine within three days afterundergoing contrast CT [9]. In our study, the patient had been using oral food supplements with iodine andbromideformuscle-buildingpurposesforfourmonthspriortotheonsetofhisskineruptions.HDcanmimicother skin conditions that have similarities in both clinical and histological findings. These include Sweetsyndrome and pyoderma gangrenosum [10,11]. However, our patient showed the classical histopathologicalfeaturesofHD.Ourpatientdidnothaveanymanifestationsofiodismsuchasincreasedsalivation,metallic taste,toothandgumsoreness,andheadache.

The main treatment of HD is the complete cessation of the causative agent and the use of topical or systemic corticosteroids [2,3]. A dramatic response has been observed after using a systemic corticosteroid in a patient with extensive HD [12]. Silver sulfadiazine cream (a topical antibiotic) with topical corticosteroids has been used successfully in a patient with extensive vegetative bromoderma [2]. Our patient stopped using the food supplements and responded well after four weeks of topical corticosteroid use. At follow-up, there was no recurrence at the time of writing this report.

Conclusions

HD is a rare skin eruption that develops following exposure to halogens such as iodide and bromide, referred to as iododerma and bromoderma, respectively. HD should be considered in patients with a history of iodine and bromide use presenting with papulopustular lesions, and it should be carefully distinguished from other skin conditions that mimic the clinical and histological appearance of HD.

Additional Information

Disclosures

Humansubjects: Consent was obtained or waived by all participants in this study.**Conflictsofinterest:**Incompliance with the ICMJE uniform disclosure form, all authors declare the following:**Payment/servicesinfo:** All authors have declared that no financial support was received from any organization for thesubmittedwork. **Financialrelationships:**Allauthorshavedeclaredthattheyhavenofinancialrelationshipsatpresentorwithinthepreviousthreeyearswithanyorganizationsthatmighthaveaninterest in the submitted work. **Other relationships:** All authors have declared that there are no otherrelationshipsoractivitiesthatcouldappeartohaveinfluencedthesubmittedwork.

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ARISING MOLLOSCUM CONTAGIOSUN IN AN ADULT PATIENT TREATED WITH FINGOLIMOD AND REVIEW OF THE LITERATURE

Molluscum contagiosum is a self-limiting viral eruption characterized by umbilical papules on the skin (1). Extensive, chronic, and larger lesions may occur in case of immunodeficiency (2). Fingolimod therapy used for Multiple Sclerosis (MS) treatment can also lead to immunosuppression and promote the occurrence of molluscum contagiosum and other opportunistic infections (3).

Some conditions commonly associated with molluscum contagiosum in adults include acquired immunodeficiency syndrome, solid organ transplantation, systemic lupus erythematosus, sarcoidosis, neoplasms, immunosuppressive and biologic therapies (4). Diffuse and giant molluscum contagiosum lesions may also occur in DOCK8 deficiency, a genetic disorder that affects dendritic and T cell migration (5).

In this presentation, we discuss a case of extensive long-term molluscum contagiosum infection in the face of an adult patient treated for Multiple Sclerosis with fingolimod (after the discontinuation of which Molluscum contagiosum regressed), as well as similar cases from the literature.

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COVID-19 FIX DRUG ERUPTION AFTER SINOVAC VACCINE

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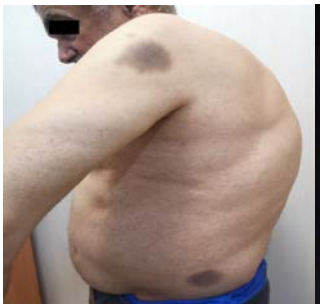
Introduction

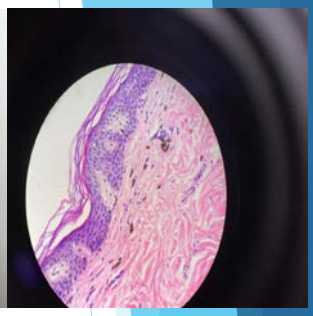
After the 2019 coronavirus disease (COVID-19) spread worldwide, various vaccines have been developed to control the pandemic, with varying efficacy and potency and based on different platforms. As with all other vaccines, side effects are observed with these vaccines. Reported side effects occur mostly after mRNA-derived vaccines. However, cutaneous adverse reactions are rarely seen after inactivated vaccines.(2) The most common side effects are local injection site skin reactions.(1). We present this case because it is very rare among cases where fixed drug eruption (FDE), which is one of the cutaneous reactions other than local injection site reactions, is reported.(3)

Case

A 57-year-old male patient applied to our dermatology outpatient clinic 10 days after the first dose of Sinovac vaccine because of brown spots on his body. It was learned in his history that he had not made any medication changes or started a new medication in the last 1 year. The lesions did not have itching or pain, was cosmetically disturbing to the patient. In his dermatological examination, there were hyperpigmented plaques with a diameter of 2-3 cm on the dorsum of both hands and feet, 6 cm in diameter in the deltoid region of the left upper arm, 5 cm in diameter in the lower part of the left trunk, 2 cm in diameter in the left frontal region, and 4 cm in diameter on the right side of the neck. (picture1) Punch biopsy was taken from the patient with the preliminary diagnosis of fix drug eruption, actinic lichen and postinflammatory hyperpigmentation. Findings consistent with postinflammatory hyperpigmentation were observed in the histopathology result. (Picture 2) The patient was diagnosed with postinflammatory hyperpigmentation due to fix drug eruption. 4% hydroquinone, topical tacrolimus and moisturizer were used in the treatment.



Picture1



Picture 2

Results&Conclusion

The side effects and safety of various vaccines developed due to the Covid-19 pandemic are a concern for many people. In a systematic review of the side effects of different COVID-19 vaccines, 5941 cases were examined, and local injection site reactions were the most common (34.05%). Unspecified skin rashes (32.88%), urticaria (10.89%) and angioedema (5.35%), herpes zoster (2.69%), morbilliform/maculopapular/erythematous macular rash (1.78%), pityriasis rosea and pityriasis rosea-like rashes (1.62%), and other less common dermatological manifestations followed. Fix drug eruption was seen only in 8 cases and was observed at a rate of 0.13%. Two of these cases occurred after the Pfizer vaccine, three after the Moderna vaccine, and the vaccine type was not specified in three cases. Dermatological reactions were more common after Pfizer and Moderna vaccines. (3) FDE is considered a delayed hypersensitivity reaction. Although the exact mechanisms underlying post-vaccine allergic reactions are still unknown, it is the antibody and cell-mediated response that leads to the production of cytokines such as interferon-gamma (IFN-y) and tumor necrosis factor-alpha (TNF-a).(4) FDE is characterized by annular, erythematous or hyperpigmented patchy lesions of the skin and mucosa. There are several main variants of FDE, including pigmented, nonpigmented, bullous and mucosal types. FDE can be triggered by certain foods (seafood, nuts, berries, kiwis, and others) and drugs (non-steroidal anti-inflammatory drugs, antiepileptics such as phenytoin, antibiotics such as cotrimoxazole, and others) and can occur at any age and in both sexes. In the pigment variant, the FDE disappears over time and post-inflammatory hyperpigmentation remains. Typically, FDE lesions reappear at the same sites after re-exposure to the causative drug. The disease is usually mild and self-limited, and primary treatment is identification and discontinuation of causative stimuli and conservative care. FDE can occur after using Sinovac vaccine. We consider it important for a dermatologist to recognize and report these complications, as many real-world side effects may not be seen in clinical trials.

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FLAGELLAT ERYTHEM AND NAIL PIGMENTATION AFTER BLEOMYCİN

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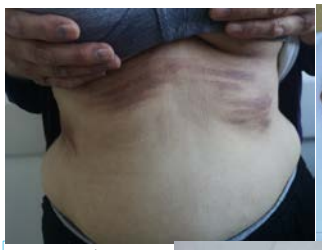
Introduction

Bleomycin is a cytotoxic glycopeptide derived from Streptomyces verticillus. It is used in the treatment of many human cancers, especially lymphomas, testicular and ovarian germ cell tumors, and squamous cell carcinoma.(1) Various dermatological side effects of bleomycin include flagellate dermatitis, erythema, hyperpigmentation, hyperkeratosis, palmoplantar desquamation, Raynaud's phenomenon, various nail changes, gangrene, fibrosis, neutrophilic eccrine hydradenitis (NEH), alopecia, edema, and skin side effects including various other reactions. (2) We present a case who developed flagellate erythema on the trunk and pigmentation on the nail bed after receiving a chemotherapy regimen containing bleomycin.

Case

A 53-year-old female patient was consulted to our polyclinic with complaints of brown spots on her trunk and discoloration of her nails about 1 month after she started taking ABVD (adriamycin, bleomycin, vinblastine, dacarbazine) regimen for Hodgkin lymphoma. In the dermatological examination, linear horizontal hyperpigmented plaques under both breasts in the upper abdomen (picture 1) hyperpigmentation in the fingernails and toenails (picture2-3). The case was diagnosed with flagellate dermatitis and nail hyperpigmentation due to bleomycin based on clinical findings and anamnesis. Liver and kidney function tests were normal in the investigations performed in the case. Since it was not severe enough to interrupt the bleomycin treatment, the case was followed up. Topical antihistamine, moderately potent topical corticosteroid and moisturizer were recommended for treatment.



Picture1

Picture 2

Picture 3

Results&Conclusion

Bleomycin is an antineoplastic drug that acts by disrupting DNA in the G2 S phase of the cell cycle. It is metabolized by bleomycin hydrolase, toxication is more common in tissues where this enzyme is relatively low, such as lungs and skin.(2) Bleomycin is rapidly inactivated by the same enzyme in other tissues, particularly the liver and kidneys. However, 50-70% of the total dose is excreted unchanged in the urine. Therefore, there may be an increase in drug accumulation in patients with renal dysfunction and the risk of toxicity increases. (3) It has been reported that cutaneous toxicity usually occurs at total doses of 200 to 300 U, and pulmonary fibrosis occurs at doses > 400 U.(4) The reaction is considered dose-dependent and normally occurs at doses >100 U total and very often at doses >200 U. However, it can occur even at doses as low as 14-15 U.(2) The time between bleomycin administration and the onset of cutaneous side effects can vary between 12-24 hours and 6 months. Although the exact mechanism of flagellate erythema is still unknown, several hypotheses exist, localized increase in melanogenesis, change in normal pigmentation patterns secondary to inflammation; or accumulation of bleomycin in the skin may result in a fix drug eruption due to the direct effects of bleomycin on keratinocytes. In a study, it was concluded that the histopathological findings of flagellate erythema and fixed drug eruption were similar and the relatively low level of bleomycin hydrolase led to the accumulation of this drug. (6) Bleomycin has been associated with nail pigmentation. The pigment grows in horizontal or vertical bands that can be brown or blue and often grows with the nail. (7) On the other hand, it has been suggested that pigmentation occurs in the nail bed.(8) Most drug-induced nail pigmentation is the result of increased melanin production by nail matrix melanocytes. Most drug-induced nail pigmentation is the result of increased melanin production by nail matrix melanocytes. In conclusion, early recognition of these rare specific skin reactions occurring in patients treated with bleomycin by dermatologists is of great importance in preventing the toxication of the drug. We share this case in order to raise awareness .

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A RARE PRESENTATION OF ACTINIC DAMAGE: ACTINIC COMEDONAL PLAQUE OF THE EYELIDS

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Introduction: Favre-Racouchot syndrome (FRS), also known as senile comedones, solar comedones and nodular elastosis with cysts and comedones, is a condition that arises in a background of actinically damaged and atrophic skin as a result of solar degeneration of the skin (1). It is characterized by diffuse a yellowish hue, open comedones, cysts, nodules (1,2). Actinic comedonal plaque is a rare and localized variant of FRS, presenting with a plaque consisting of grouped comedones (3,4). It is common in Fitzpatrick skin types 1-4 (2). Although it was mostly described on upper extremities, it can be found on the face and helix of the ear (4). Here, we describe an unusual case of bilateral actinic comedonal plaques of upper eyelids.

Case: A 58-year-old man was referred to dermatology outpatient clinic from ophthalmology clinic with a 2-year history of purplish black discoloration of the eyelids. The patient was a taxi driver and had been working without any sun protective measures for more than 30 years. He was also a heavy smoker and has been consuming 20 cigarettes per day for 40 years. On dermatologic examination, multiple closely-spaced open comedones forming two well-defined hyperpigmented plaques were located on medial part of both upper eyelids (Figure 1 a,b). Several small fibroepithelial polyps were also present on the upper eyelids and small number of scattered open comedones was seen on the malar areas. Examination of other skin and mucosal sites were normal. Dermatoscopic examination of the lesion revealed multiple black clods with peripheral bluish halo, thus, confirming the presence of open comedones (Figure 1c). The patient was diagnosed with actinic comedonal plaque. Photoprotection was recommended. The patient did not demand treatment.

Discussion & Conclusion: Actinic comedonal plaque was first described in 1980 as confluent plaques, nodules and comedone-like structures (2). In some patients, seropurulent drainage can occur from the lesion (2). Although actinic comedonal plaque is mostly reported in fair skinned individuals, patients with higher Fitzpatrick skin types can also be affected (2,5). Sun exposure, smoking and therapeutic radiation are thought to contribute to development of actinic comedonal plaque (3). Histologically, it is characterized by slightly acanthotic epidermis with orthokeratosis, dilated keratin filled follicles within a matrix of damaged amorphous collagen (2,3). Actinic comedonal plaque should be considered in differential diagnosis of solitary comedonal lesions in elderly men with significant sun damage. These patients should be carefully examined for presence of premalignant and malignant cutaneous lesions (5). Actinic comedonal plaque should also be distinguished from comedonal nevus. However, the latter is typically present at birth or appears during childhood (2,5). Other clinical differential diagnoses include colloid milium, seborrheic keratosis, and amyloidosis among others (5). Treatment options include topical retinoic acids with or without cryotherapy, CO_2 laser treatment, comedone extraction, dermabrasion and curettage, as well as surgical excision (3,5).

Keywords: comedone, Favre-Racouchot syndrome, skin of color, smoker, sun exposure

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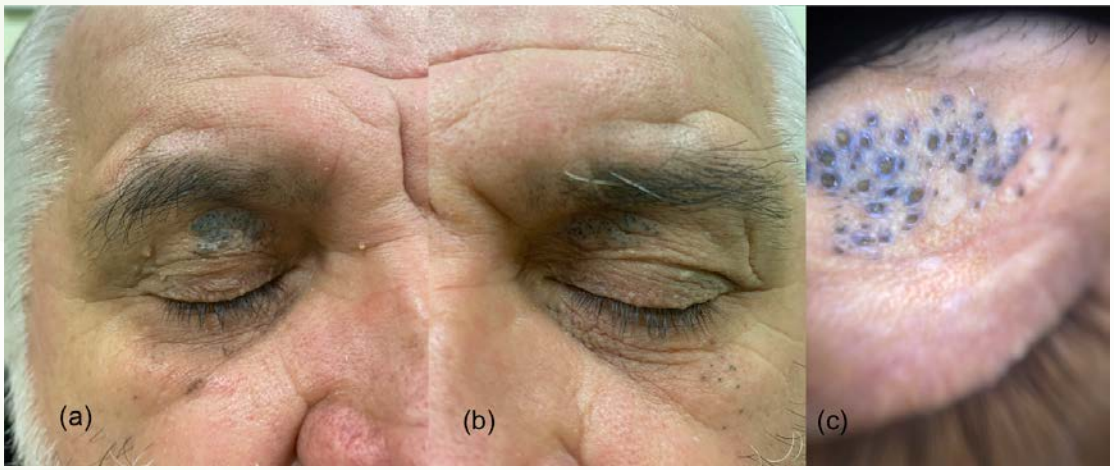

Figure 1 (a-c): Right and left upper eyelids display hyperpigmented plaques composed of grouped comedones while malar region shows several scattered comedones (a,b). Polarized dermatoscopy reveals black clods with peripheral bluish color (c).

INVESTIGATION OF THE RELATIONSHIP BETWEEN FRAILTY, DERMATOLOGICAL QUALITY OF LIFE AND DEPRESSION IN GERIATRIC PATIENTS

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Introduction & OBJECTIVES: Frailty is a geriatric syndrome result of the cumulative decrease in the functions of various systems with aging. Although there are studies showing the relationship between frailty, quality of life and depression, there are few studies examining the effect of dermatological problems on frailty. We aimed to detect the frequency of dermatological diseases in geriatric patients and their relationship with frailty syndrome in terms of dermatological quality of life and depression.

Materials & METHODS: This single center, cross-sectional, observational study was approved by the Ethics Committee of Pamukkale University. A total of 264 patients (126 females,138 males) aged ≥65, were included. Clinic and demographic data of the patients were recorded. The dermatological diseases were categorized into 28 groups after diagnostic evaluation were performed. 'Dermatological Quality of Life Index (DLQI)', 'Edmonton Frail Scale(EFS)' for the assessment of frailty levels and 'Geriatric Depression Scale-30 (GDS-30)' for the assessment of depression were applied to the patients.

RESULTS: Based on the EFS, 0–4 points as 'not frail, robust', 4–10 points as 'frail' and >11 points were evaluated as 'severely frail' patient group. It was determined that 34 (12.9%,mean age 69.5 ± 5.4) patients were robust, 169(64%, mean age 71.9 ± 5.5) were frail and 61(23.1%, mean age 79.4 ± 8.8) were severely frail. The difference between groups was statistically significant (p< 0.005). The most common dermatological diseases observed in decreasing order of frequency were; photodermatoses (87%), premalignant skin tumors (68%), xerosis (68%), pruritus (52%), fungal skin diseases (48%) and eczema (32%). The increase in the DLQI score with the increase of frailty degrees was statistically significant (p <0.001). In the correlation analysis, fragility degrees, GDS-30 scores and DLQI scores were found to be significant positively correlated with each other(p <0.001). Frailty both increases the possibility of depression and affects the dermatological quality of life. According to the results of multivariate logistic regression analysis on fragility; low educational status (aOR=0.156, 95% CI=0.34-0.714), increased DLQI scores (aOR=1,269, 95% Cl=1.073-1.501), the presence of depressive symptoms (probable depression and depression group) according to GDS-30 (aOR=15.055, 95% CI=3.545) were determined as risk factors for frailty.

CONCLUSION: We have obtained data showing that dermatological diseases that affect the quality of life may have an important role in the evaluation of frailty. Considering the close relationship of depression with frailty and DLQI, we think that dermatological diseases may also contribute to depression. In addition to reaching these results in our study, it is difficult to make a definite judgment due to the limited number of publications on the subject in the literature. Therefore, studies including large numbers of patients are needed.

Keywords: Geriatric dermatology, Quality of Life, Frailty, Dermatological Quality of Life Index, Edmonton Frail Scale, Geriatric Depression Scale

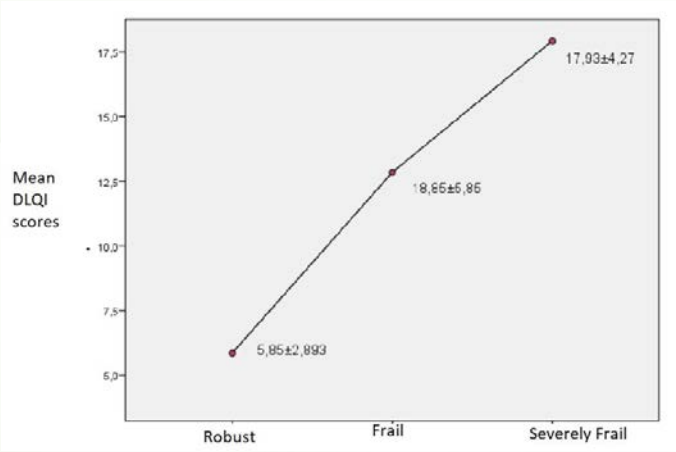


Figure 1:The relationship between frailty degrees and DLQI scores

Table 1: Relationship between Frailty status and demographic characteristics of patients

	Total N=264	Robust N=34(%12,9)	Frail N=169(%64)	Severe Frail N=61 (%23,1)	p-value
Sex Female Male	126(%47,7) 138(%52,3)	10(%7,9) 24(%17,4)	80(%63,5) 89(%64,5)	36(%28,6) 25(%19,1)	<0,005
Age (mean, years)		69,52±5,40	71,94±5,48	79,38±8,84	<0,005
Age group 65-75 >75	180(%68,2) 84(%31,2)	29(%16,1) 5(%6)	122(%67,8) 47(%56)	29(%16,1) 32(%38)	<0,001
EFS scores(mean)		4,11±3,83	7,26±2,57	10,26±1,53	
Mariatal Status Married Single	214(%81,1) 50(%18,9)	32(%15) 2(%0,4)	140(%65,4) 29(%58)	42(%19,6) 19(%38)	0,007
Smoke Yes No	70(%26,5) 194(%73,5)	14(%20) 20(%10,3)	43(%61,4) 126(%64,9)	13(%18,6) 48(%24,7)	0,095
Use of walking aids No Yes	172(%65,2) 92(%34,8)	34(%19,8) 0	119(%69,2) 50(%54,3)	19(%11) 42(%45,7)	0,001
Comorbid diseases No Yes	54(%20,5) 210(%79,5)	15(%27,8) 19(%9)	34(%63) 135(%64,3)	5(%9,3) 56(%26,7)	0,001
Living place Rural Urban	21(%8) 243(%92)	3(%1) 31(%11,8)	13(%5) 156(%59)	5(%2) 56(%21,2)	0,972

Table 2: Relationship between Frailty status and dermatologic diseases

Dermatologic Diseases	Total N=264	Robust N=34(%12,9)	Frail N=169(%64	Severe Frail N=61 (%23,1)	p
Bacterial Infections	16(%6,1)	2(%0,8)	9(%3,4)	5(%1,9)	0,489
Fungal Infections	126(%47,7)	16(%6,1)	83(%34,3)	29(%11)	0,303
Parasitic Infections	11(%4,2)	1(%0,4)	8(%3,1)	2(%0,8)	0,187
Viral Infections	15(%5,7)	1(%0,4)	10(%3,8)	4(%1,6)	0,035
Bening skin tumors	55(%21,2)	11(%4,2)	33(%12,6)	11(%4,2)	0,678
Premalign skin tumors	119(%45,2)	29(%10,8)	53(%20,17)	47(%17,85)	0,098
Malignant skin tumors	33(%12,5)	3(%1,2)	23(%8,8)	7(%2,6)	0,927
Cutaneous lymphomas	8(%3,1)	2(%0,8)	4(%1,5)	2(%0,8)	0,547
Pruritus	137(%51,9)	13(%4,9)	85(%32,2)	22(%14,8)	0,044
Xerosis	180(%68,2)	16(%6,1)	111(%42)	53(%20,1)	0,001
Physical dermatosis	93(%35,2)	9(%3,4)	63(%23,9)	63(%23,9)	0,479
Papulosquamous disorders	15(%5,7)	2(%0,8)	11(%4,2)	2(%0,8)	0,645
Lichenoid skin disorders	1(%0,4)	0	7(%2,7)	2(%0,8)	0,477
Granulomatous dermatitis	1(%0,4)	0	1(%0,4)	0	0,754
Vesiculobullous diseases	8(%3,1)	0	5(%1,9)	3(%1,2)	0,763
Connective Tissue Disease	9(%3,5)	0	7(%2,7)	2(%0,8)	0,771
Eczema	84(%31,8)	6(%2,4)	51(%19,4)	27(%10,3)	0,030
Urticaria and Angioedema	22(%8,3)	4(%1,5)	14(%5,3)	4(%1,5)	0,678
Cutaneous drug reactions	7(%3,2)	3(%1,2)	2(%0,8)	3(%1,2)	0,043
Cutaneous Vasculitis	5(%1,9)	1(%0,4)	4(%1,5)	0	0,453
Panniculitis	1(%0,4)	0	1(%0,4)	0	0,754
Pigmentary disorders	23(%8,8)	4(%1,5)	13(%4,9)	6(%2,4)	0,680
Stasis Dermatitis and ulcers	55(%21,2)	9(%3,4)	13(%4,9)	12(%4,6)	0,807
Acne vulgaris and Rosacea	20(%7,6)	4(%1,5)	14(%5,3)	2(%0,8)	0,399
Hair disorders	46(%17,6)	9(%3,4)	33(%12,7)	4(%1,5)	0,168
Nail disorders	21(%8)	3(%1,2)	13(%4,9)	5(%1,9)	0,982
Behçet's disease and RAS	3(%1,2)	0	1(%0,4)	2(0,8)	0,189
Photodermatoses	230(%87,1)	28(%10,6)	147(%55,6)	54(%20,5)	0,681

Table 3: Edmonton Frail Scale(EFS), 'Dermatological Quality of Life Index (DLQI) and Geriatric Depression Scale-30 (GDS-30) correlation analysis

	E F S Correlation coefficient	p-value
DLQI	0,395	<0,001
GDS-30	0,751	<0,001

Table 3: Multivariable logistic regression analysis of risk factors for frailty

Variables	Univariate OR (95% CI)	p	Multivariate OR (95% CI)	p
Age (y) (>75)	3,034 (1,131-8,145)	0,028	0,820 (0,191-3,511)	0,789
Sex Female	2,242 (1,118-5,336)	0,025	0,969 (0,286-3,279)	0,960
Comorbid Disease	3,866 (1,809-8,264)	<0,001	2,248 (0,724-6,975)	0,161
Low economic status	0,144 (0,067-0,310)	<0,001	1,458 (0,304-6,991)	0,639
Low educational status	0,137 (0,062-0,304)	<0,001	0,156 (0,34-0,714)	0,017
DLQI	1,486 (1,295-1,705)	<0,001	1,269 (1,073-1,501)	<0,005
GDS-30	57,571 (16,685-198,645)	<0,001	15,055 (3,545-65,613)	<0,001

DLQI 'Dermatological Quality of Life Index '; EFS' Edmonton Frail Scale' for the assessment of frailty levels and GDS-30 'Geriatric Depression Scale-30 '

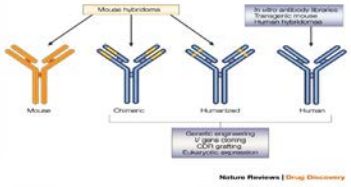
Immunogenicity of Biologics

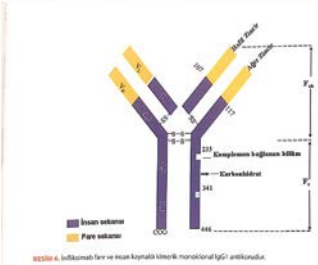
Dr. Zuhal Metin
Ahi Evran University Department of Dermatology

- Biologics are substances whose active component is derived from a biological source using biotechnology by recombinant DNA techniques.
- They have pharmacological effects to mimic normal human proteins or interact with circulating proteins or cellular receptors for treatment.
- They hold a great deal of promise among the therapeutic interventions for a wide range of disorders, including cancer and inflammatory diseases.

- They are divided into 3 groups in terms of structure content
  - Non-human origin
  - Partial human-sequence
  - Complete human-sequence

Monoclonal antibody

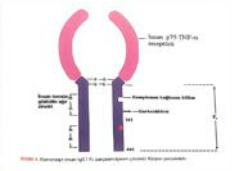




Fusion Proteins

- They resemble an antibody made up of two different components.
- It has two binding loops in one part that recognize specific receptor proteins. This construct binds to and stabilizes a second construct consisting of the Fc portion of a human immunoglobulin molecule.

Etanercept dimeric fusion protein comprised of 2 extracellular portions of p75-TNFR (75-kDa TNF receptor) linked to the Fc portion of a human IgG1.



Recombinant Human Proteins

- Contains copies of normal human proteins or protein parts.
  Insulin, growth hormone, granulocyte-macrophage colony-stimulating factor, factor VIII.
- Their activity is limited to the normal physiological functions of the protein.

- Immunogenicity is defined as the propensity of the therapeutic biologics to generate immune responses to itself and to related proteins or to induce immunologically related non clinical affect or adverse clinical events
- It is complex phenomenon that depends on the interplay between several drug- and patient-related factors (including sex, comorbid conditions, and ethnicity)

Factors contributing to immunogenicity of biologics

Biologic specific	Patient specific
Molecular structure or amino acid sequence differences between native and therapeutic protein (degree of humanization)	Age
Protein aggregation	Other concurrent medication
Protein degradation-oxidation, deamidation, glycosylation	Dose
Impurities/cofactors/adjuvants	Frequency of therapy
Formulation	Route of administration
Subclass of therapeutic IgGs	Genetic predisposition (HLA class and gene defects)
Nature of target protein (endogenous/redundant/unique)	Immune status and competence
Manufacturing process	Disease status (acute/chronic)
	Disease type (immune mediated/non-immune mediated disorders)

- There are two types of immunogenicity of therapeutic biologics
  - Wanted immunogenicity
  - Unwanted immunogenicity
- Wanted immunogenicity an immune response against the pathogen (virus, bacteria, cancer cell…) aims to protect the organism.
- Unwanted immune responses is neutralizing their biological activities and result in adverse events by inhibiting the efficacy of the therapeutic biologics.

- Repetitive administration of these protein-based therapeutics to immunocompetent patients elicit immune responses through the production of anti-drug antibodies (ADA) or cell-based immune responses.
- According to studies in the literature, failure of immune reaction against an exogenous version of an endogenous human protein or immune tolerance against self-antigens is also thought to trigger the development of ADA.

- ADAs consist of
- Low titre, transient IgM
  high titre, persistent IgG (IgG1–IgG4)
  IgE immunoglobulin isotypes.
- It is reported in some studies that the neutralizing property of IgG4 is higher compared to IgG1 and IgG2 ADA.
- IgG4 is usually in response to chronic antigen stimulation and hence is commonly observed in response to long-term treatment with biologics.

- The presence of ADAs may be associated with some clinical consequences
- Reduction in therapeutic efficacy
  Increased risk of adverse events
  Hypersensitivity reaction
  IgE-independent anaphylactic reactions

- **Reduction in therapeutic efficacy**

- ADAs can be either neutralizing or nonneutralizing.
- Neutralizing ADAs (BAb) are predominantly directed against the hypervariable regions of immunoglobulins (antigen-binding site) and competing with the drug's target (e.g., tumor necrosis factor, TNF) they elicit the unique "anti-idiotype" ADA response
- Nonneutralizing ADAs(NAb), binding to other parts of the drug and may alter the drug's clearance and/or reduce its bioavailability (e.g., tumor necrosis factor, Etanercept).
- In both condition, the effectiveness of the biological agent is reduced.

- **Reduction in therapeutic efficacy**

Receptor fusion proteins (ETN) are not associated with neutralizing ADAs, and little or no evidence is found in clinical studies of immunogenicity-related efficacy or safety/tolerability effects with these agents.

This explains why etanercept has consistently exhibited higher drug survival than infliximab or adalimumab.

- **Reduction in therapeutic efficacy**

Sometimes during treatment, ADAs levels may increase over time, and as soon as the drug exceeds the minimum effective concentration level, drug efficacy begins to decline.

Adverse events: breaking of tolerance by immunogenicity

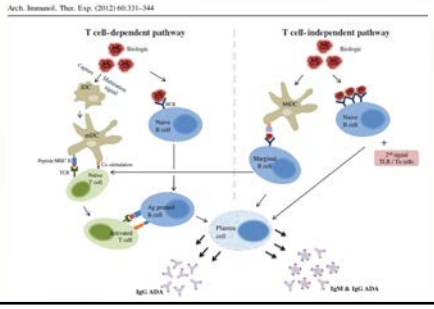
The antigenic structures present in the biologic drug can activate autoreactive B cells against the body's own antigens. This may lead to the development of autoimmunity.

Hypersensitivity reactions

Hypersensitivity reactions associated with treatment-induced ADAs tend to occur at or after the second administration.

First exposure hypersensitivity reactions have also been described and it is associated with the cytokine release that develops against the excipients in its content.

In contrast to ADA-mediated hypersensitivity reactions, ADA-independent cytokine-release syndromes can be managed by short-term cessation of biologic's infusion, by lowering the infusion rate or by the administration of histamine blockers and corticosteroids



Immunological Processes that Underlie Development of ADAs

- Anti-drug antibodies can be generated by both T cell dependent (Td) pathways ⇨ IgG
  T cell-independent (Ti) pathways.⇨ IgM
- T cell subset polarization also determines therapeutic outcome to the ADA
- Th2 response neutralizing ⇨ IgG4 ADA
- Th1 response ⇨ IgG1 and IgG2-based ADA, non-neutralizing in nature

Biological agents or ADA-biologic immune complexes may also activate complement pathways.

Activated complement factors such as C3a, C5a and C3d are potent factors that influence antibody responses.

Complement also influences T cell responses by direct or indirect modulation of Th1/Th2 immunity.

Strategies in predicting and reducing immunogenicity to therapeutic proteins

Prediction	Reduction
Physiochemical characterization	Deimmunization (epitope modifications)
In silico	Humanization
T cell epitope predictions	
B cell epitope predictions	
Tregitopes predictions	
In vitro/ex vivo	Purity and formulations
T cell responses	Modifications
HLA binding assays	Fusion proteins
In vivo models	Combination biologics or combination therapy

Chimeric antibodies, fully human antibodies, and humanized antibodies all have immunogenicity. According to some authors the reason why therapeutic mAbs produced by technological methods have high immunogenicity despite being humanized is due to the nature of ADAs.

Evidence from many studies of biologic agents demonstrate that combining immunosuppressive/anti-proliferative therapy (methotrexate, azathioprine, leflunomide or mycophenolate) reduces ADA levels and immunogenicity due to the immunosuppressive effect of these drugs.

Although it rarely triggers ADA boost in some patients, high biologic doses and induction therapy were also associated with decreased incidence of ADAbs in some published trials.

Increasing the dose may be risky as there is no way to identify which patients are at risk of boosting their ADA response after dose escalation.

Cross reaction

Several reports in the literature also indicate that patients who previously developed ADAs against a biologic agent are more likely to develop ADAs with subsequent agents, although none are cross-reactive.

To know more about biological agents and their immunogenicity may provide essential information to clinicians that can potentially improve treatment, reduce risks and costs.

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- Immunogenicity of Biologics in Chronic Inflammatory Diseases:A Systematic Review Vibeke Strand1 Alejandro Balsa2 Jamal Al-Saleh3 Leonor Barile-Fabris4 Takahiko Horiuchi5 sutomu Takeuchi6 Sadiq Lula7 Charles Hawes8 Blerina Kola8 Lisa Marshall9

  Immunogenicity to Biologics: Mechanisms, Prediction and Reduction Swaminathan Sethu • Karthik Govindappa • Mohammad Alhaidari • Munir Pirmohamed • Kevin Park • Jean Sathish

HYPERPROLACTINEMIA AND GYNECOMASTIA DEVELOPMENT DURING SYSTEMIC ISOTRETINOIN TREATMENT

Introduction

Vitamin A was first used by Straumfjord in 1943 for the treatment of acne. Vitamin A has a narrow therapeutic window. Therefore researches have been started to develop synthetic retinoids with less side effects and higher therapeutic effect. Isotretinoin was produced in 1955. After its production its use for the treatment of various dermatologic diseases had been investigated. Food and Drug Administration had approved its use for the treatment of nodulocystic acne in 1982. Isotretinoin is one of the first generation retinoids. Isotretinoin is produced from vitamin A by manipulation of its polar end group and polyene side chain. Retinoids show their biologic effect by binding to the RAR or RXR retinoid receptors in the nucleus and regulating gene transcription. Retinoid receptors belong to a receptor family in which there are also glucocorticoid, thyroid hormone and vitamin D receptors. In dermatology, systemic retinoids exert their clinical effect through regulating inflammation, cellular differentiation, apoptosis and sebaceous gland activity. Besides nodulocystic acne, isotreinoin has many indications like atrophoderma vermiculatum, condylomata acuminata, cutis verticis gyrata, Darier disease, dissecting cellulitis, epidermolysis bullosa simplex, epidermolytic hyperkeratosis, lichen planus, erosive oral lichen planus, extranodal Rosai-Dorfman disease, Fordyce spots, Fox-Fordyce disease, gram negative folliculitis, granuloma annulare, granulomatous rosacea, Grover disease, hydradenitis suppurativa, HIV associated eosinophilic folliculitis, hyperimmunoglobulin E syndrome, IgA pemphigus, keratoacanthoma, keratoderma, lamellar ichthyosis, Langerhans cell histiocytosis, discoid lupus erythematosus, subacute cutaneous lupus erythematosus, lupus miliaris disseminatus faciei, papular mucinosis, perforating folliculitis, pityriasis rubra pilaris, pyoderma faciale, papulopustular rosacea, cutaneous sarcoidosis, scleromyxedema, sebaceous hyperplasia, ulerythema ophryogenes and chemoprevention of nonmelanoma skin cancers. Side effects of systemic isotretinoin include chelitis, xerosis, pruritus, epistaxis, conjunctivitis, photosensitivity, arthralgia, myalgia, hyperlipidemia, palmoplantar desquamation, alopecia, onycholysis, elevated liver enzymes, visual disturbances, depression, tinnitus, backache, pyogenic granuloma, paronychia, photophobia, headache, nausea, diarrhea, stomach ache, pseudotumor cerebri, osteopenia, osteoporosis, hepatotoxicity, anaphylaxis, allergic vasculitis, teratogenicity, aggression, psychosis, suicidal thoughts, decrease in hearing, cataract, corneal opacities, premature epiphyseal closure, neutropenia, rhabdomyolysis, agranulocytosis, inflammatory bowel disease, pancreatitis and vascular thrombosis. In Litt's drug eruption manual two gynecomastia case reports have been mentioned which are published by Fluckiger in 1992 and by Shelley in 1994. In 2013 Ustun and in 2018 Gualtieri had also published two gynecomastia cases due to isotretinoin. In 2020 fifth case report of isotretinoin induced gynecomastia has been published by Bonifazi. To the best of our knowledge, this is the sixth case report of gynecomastia development during isotretinoin treatment.

Case Report

Our patient was an 18 year old male with nodulocystic acne under isotretinoin treatment. The patient was 63 kg and hds taken 40 mg/day isotretinoin for the first month of treatment. After one month of treatment he had fatigue, epistaxis and onychocryptosis as side effects of the drug and received 30 mg/day isotretinoin for the following two months. The side effects had lapsed and the patient had received 40 mg/day isotretinoin during the fourth month of treatment. At the end of the fourth month he started to complain about an increase in the size of his breasts. He was seen first in the outpatient clinic of the general surgery department. Upon his physical examination he had been found to have a nodular infiltration under his left nipple. The general surgeon had ordered breast ultrasound. The breast ultrasound revealed 5cm x 1cm sized fibroglandular tissue under his left areola and 18mm x 3.5mm sized fibroglandular tissue under his right areola. There wasn't any mass in the breasts and any pathologic lymph node in the axillae. The breast ultrasound had been reported as gynecomastia prominent on the left side. Our patient was sent to the endocrinology department. Endocrinologist had ordered prolactin level. His prolactin level had been found high as 30.32 ng/ml. We terminated his systemic isotretinoin treatment. One month later after stopping his isotretinoin treatment his prolactin level had been found normal as 10.54 ng/ml.

Discussion

Systemic isotretinoin can cause gynecomastia through hyperprolactinemia by inducing hypophyseal hormonal irregularity. Systemic isotretinoin can also induce gynecomastia through downregulation of cutaneous androgen receptors. Gynecomastia is a rare side effect of systemic isotretinoin treatment but must be known by the dermatologists in order to manage the

patients wisely and to avoid unnecessary cranial radiologic investigations.

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MECHANICAL DERMABRASION OF THE UPPER LIP FOR „BAR CODE „ WRIN-KLES: TECHNIC, EXPECTED RESULTS AND PITFALLS

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In this paper, we present a step-by-step demo of the technique of mechani-cal dermabrasion with an electrocautery scratch pad.

The anesthetic technique for superior alveolar nerve block will be presented and then the procedure. The postoperative course will be illustrated by some of the most demonstrative cases. Finally pitfalls and contraindication of the technique will then be exposed and alternative treatments will be dis-cussed.

Reference:

Dupoirieux L. An Affordable and Universal Treatment for 'Barcode' Upper Lip Wrin-kles.doi:https://www.sciencerepository.org/abstract?doi=10.31487/j.SCR.2021.03.09

RELIABILITY AND QUALITY OF YOUTUBE VIDEOS AS A SOURCE OF INFORMATION ON ALOPECIA AREATA

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Introduction: Alopecia areata (AA) is a condition of uncertain etiology mediated by immune response that presents with non-scarring hair loss. It is a common disorder with a lifetime risk of approximately 2%.[1] The course of the disease is unpredictable with range of spontaneous remission reported between 8% and 68%. There are various therapies currently available for AA with variable clinical outcomes and some promising new treatments are being developed.[2] As such, AA remains an enigmatic and burdensome disease; therefore patients frequently search the internet in order to obtain disease-related information.[3]

YouTube is a freely accessible popular video-sharing platform that contains misleading information due to unregulated content.[4] As far as we know, the quality of the content of YouTube videos pertaining to AA was not investigated in prior studies. Our primary objective was to make an analysis of the quality and reliability of the most popular videos on YouTube about AA. Our secondary objective was to compare the quality of the videos according to the source of upload (e.g. independent users vs. healthcare professionals)

Material and Methods: In this cross-sectional study, we searched YouTube (www.youtube.com) on November 25, 2021 in incognito mode for the search term "alopecia areata". First 150 most-viewed videos were retrieved. We limited our analysis to 150 top videos as further videos had low view counts. Non-English, irrelevant and duplicate videos along with videos that lacked sound and advertisements were excluded from the study. Ethical board review was not required, as the study did not contain patient identifiers.

Attributes of each video including video length and age, number of views, number of likes and dislikes, number of subscribers, number of comments and content covered were recorded. Two dermatologists (OC and MCO, OC being European board certified) independently categorized the videos by their upload source into five categories (professional medical society, healthcare provider, health information website, TV program/magazine/YouTube channel, independent user) and evaluated the videos by using reliability scale and global quality score (GQS) scale. In case of disagreement, videos were assessed together by two raters to reach a consensus. Reliability scale adapted from the DISCERN score by Singh et al. was used in our study and included the following questions: (1) Are the aims clear and achieved? (2) Are the sources of information used reliable? (3) Is the information presented in a balanced and unbiased manner? (4) Are additional sources of information listed for patient reference? (5) Are areas of uncertainty mentioned?.[5] We also used GQS scale, a widely used 5-point scale, to rate the content quality and effectiveness of the video from patients' perspective.[7] GQS score included the following statements: 1= Poor quality, poor flow of the video, most information missing, not at all useful, 2= Generally poor quality and poor flow, some information listed but many important topics missing, of very limited use, 3= Moderate quality, suboptimal flow, some important information is adequately discussed but others poorly discussed, somewhat useful, 4= Good quality and generally good flow. Most of the relevant information is listed, but some topics not covered, useful, and 5= Excellent quality and flow, very useful.

Statistical Analysis

SPSS (Statistical Package for Social Sciences; Armonk, NY) version 25.0 was used for the analysis of the data. Descriptive data were shown as numbers (n) and percentage (%) in categorical data and mean ± standard deviation (mean ± SD) in continuous data. Kolmogorov-Smirnov and Shapiro-Wilk test were performed to assess normal distribution in continuous variables. Kruskal Wallis test was used for nonparametric variables when comparing more than two groups. Bonferroni correction was used for pair-group comparison in post-hoc analyses. $p<0.05$ was set as the statistical significance level.

Results

We analyzed 66 videos with a total view count of 6759061 and a mean view count of 102410 views per video. Mean length was 9.35 minutes and mean age was 1596 days. Both reliability score and GQS score had a mean rate of two.

Thirty-one of total 66 videos (47.0%) had GQS score of one while 24.2% of videos (16/66) had GQS score of two. Eight videos (12.1%) had GQS score of three, while seven videos (10.6%) had GQS score of four and only four videos (6.1%) had GQS score of five. Reliability score of videos was also analyzed. Three of total 66 videos (4.5%) had reliability score of zero, while 32 videos (48.5%) had reliability score of one. Ten of videos (15.2%) had reliability score two, eleven videos (16.7%) had score of three, eight videos (12.1%) had score of four and only 2 videos (3.0%) had maximum reliability score as five. We performed a correlation analysis to understand whether the average view count, number of likes and dislikes was correlated to the reliability and GQS scores. Overall the average view count (102410 ± 147003) did not correlate with reliability score (p= 0.329) and GQS (p= 0.720). However, GQS had a positive and very strong correlation with reliability score (p= 0.001, r= 0.87). Mean number of likes (1326 ± 1822) did not correlate with GQS (p= 0.342) and reliability score (p= 0.150). Similarly, mean number of dislikes (62.61 ± 101.19) did not correlate with GQS (p= 0.744) and reliability score (p= 0.355). Reliability score was further evaluated to reveal most common flaws of the videos: Presented data was not evidence-based, additional sources of information were not provided and areas of uncertainty were not discussed.

Content analysis revealed that the clinical features (34%) and treatment (28%) were the most common topics of the videos. Patchy hair loss was invariably mentioned in the videos concerning clinical features. As for treatment, many videos promoted unscientific methods such as stress management, "autoimmune" diet, meditation, and plant oils as main treatment options of AA. Medications including minoxidil, topical and injected corticosteroids were the most commonly mentioned medical treatments. Camouflage techniques (hats, wigs, hair styling, micropigmentation etc.) were also frequently advocated. Topical immunotherapy was only mentioned in two videos.

Regarding the source of the videos, independent users represented 42.4% of upload source, followed by healthcare providers (30.3%). Of note, all of the independent users, except for two, were themselves AA patients. Regarding pair group comparisons, videos of independent users and videos including health care providers showed statistically significant difference concerning length of the video (p=0.001), number of likes (p=0.027), number of comments (p=0.034), reliability scores (p=0.001), and GQS scores (p=0.001). Videos of independent users and videos of professional medical societies showed significant difference between number of comments (p=0.029) and reliability scores (p=0.013), but not GQS scores (p=0.094).

Discussion

With an average of 102410 views and average of 330337 subscribers, our study shows that YouTube has a substantial influence on patients' perspectives about AA. Age of the videos was 4.4 ± 3 years, reflecting continued interest in the subject. Although AA can affect patients of any age, the mean age of disease onset is reported to be between 25.2 and 36.3 years, which corresponds to the biggest proportion of YouTube users. [6,7] However, our data demonstrate that majority of YouTube videos pertaining to alopecia areata mostly contain poor-quality and unreliable medical information for the patients, with 71.2% of all videos having a GQS score of one or two, and 68.2% of them having reliability score of ≤2. This is comparable to other dermatologic studies evaluating YouTube information for various conditions. [8-10]

There was no correlation between the video popularity and GQS/reliability scores. Majority of the videos about AA favored natural or alternative therapies. Potentially harmful practices were also promoted including unnecessary diets prohibiting dairy and/or gluten, and application of irritants such as vinegar or garlic oil. In addition, scientific methods such as topical and intralesional corticosteroids were underrated as useless or with temporary effect.

The majority of most-viewed videos on AA belonged to patients themselves, who are laypersons relating personal histories and supposedly their treatments. Patients seem more likely to prefer videos on first-hand patient experiences, probably because they elicit sympathy in patients. Although they have low reliability score and low GQS scores, videos of independent users had significantly more popularity (significantly more likes and comments) as compared to videos of healthcare providers, which were more concise (less video length) and contained reliable information. Mueller et al. reported a correlation between video length and quality and suggested that short video duration could be a contributing factor to the popularity of low quality videos. [12] In contrast, our data demonstrated that videos of independent users were significantly longer than videos of healthcare providers. We attributed the popularity of low-quality videos to the patients' interest in unconventional content and entertainment in addition to their inability of quality recognition.

In light of our findings, we recommend that dermatologists, as individuals or organizations, should contribute to YouTube with videos, which are reliable, simple and appealing, in order to improve content quality on YouTube videos on AA. Moreover, dermatologists should direct their patients and family members to specific, good-quality videos on AA.

Small sample size and analysis of only English-language videos were the limitations of our study. Furthermore, social media platforms other than YouTube were not analyzed.

In conclusion, our study showed that 71% of most viewed YouTube videos on AA were of low quality and contained misleading and potentially harmful information, most commonly conveyed by independent users. Number of views and likes did not correlate to videos' quality. Our results stress that dermatologists should use YouTube to share patient-directed information on AA.

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A RARE CASE; PEMPHIGUS ERYTHEMATOSUS IN A TURKISH MALE AND TREATMENT WITH RITUXIMAB

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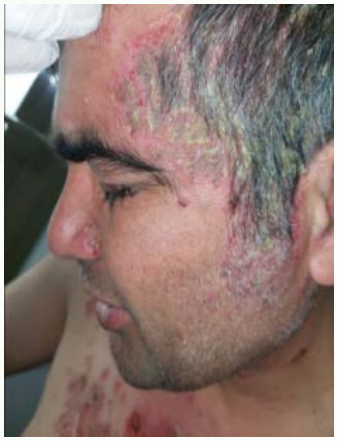
Abstract
Pemphigus erythematosus, also known as Senear-Usher syndrome, is a rare autoimmune skin condition with overlapping clinical, histopathological, and serological features of lupus erythematosus and pemphigus foliaceus.
Patients present with erythematous, scaly and crusted lesions in seborrhoeic distribution. Rash can be triggered by sun exposure. Oral mucosal involvement is not expected. Diagnosis is based on clinical findings, characteristic histopathologic changes, presence of antinuclear antibodies and immunolabelling in direct immunofluorescence test.
We report a middle-aged Turkish male patient, who presented with the complaints of photosensitivity, itchy rash on the cheeks and flaccid blisters and crusted erosions on the chest and back for a few weeks.
A diagnosis of pemphigus erythematosus was made on clinical, histological and immunological findings. To our knowledge, this is the first case reported from Türkiye.

KEY WORDS: Pemphigus erythematosus, Senear-Usher syndrome, Antinuclear Antibody (ANA), Anti-ribosomal P antibody

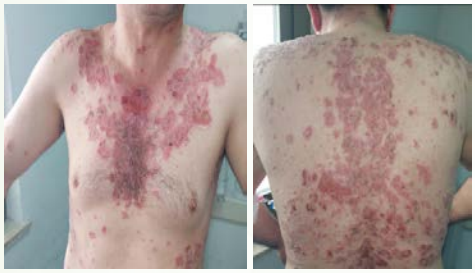
Introduction:
Pemphigus erythematosus (PE) is one of the variants of pemphigus which is an autoimmune bullous disorder. It is characterized by overlapping features of lupus erythematosus and pemphigus foliaceous. Lesions are localized on the face over the nose and cheeks in a butterfly distribution (1). Immunological features of both diseases are also present. 30% to 80% of patiets have positive circulating antinuclear antibodies (ANA)(8). It is a rare condition, has been reported infrequently, with one review in 2021 quoting a total of only 87 cases , and to the best our knowledge, has never been reported from Türkiye. We report a middle aged Turkish male presenting with features of PE(2).

Case Presentation:
A 40-year-old male presented with scaling and painful erosions, and erythematous bullous lesions on the cheeks, ears, scalp, upper back and the chest, present for 20 days. Lesions were associated with sunburn due to sun exposure. There was no hair loss on the scalp and there were no oral or nasal ulcers, and joint pain. He had no neurological symptoms other than headache.
Flaccid blisters containing clear fluid were ruptured within 1-2 days or immediately after manipulation. Rupture of the vesicles resulted in the formation of crusts, which healed with residual hyperpigmentation. Crops of new lesions occurred that followed a similar course, which also left hyperpigmentation.

Medical history revealed neither prior admission to any hospital for medical or surgical reasons, nor any chronic disease. He was not on any medication prior to the eruption of the lesions
A bullous disorder was initially suspected. No abnormalities were detected on systemic examination. Dermatological examination revealed erosions and crusts, present in a seborrheic distribution, including the malar region, with no apparent mucosal involvement at that time.(Figure 1-2a,2b). Nikolsky sign was positive. Oral and genital ulcers were absent.



(Figure 1)



(Figure 2a,2b)

Figure legends:
Figure 1.
Active lesions on scalp and face
2a.2b.
Active lesions on chest and trunk

Laboratory Tests
Serum ANA was weak positive, worked titer: 1/100,Anti-Ribozomal P 2+. Complement 3 (C3) and complement 4 (C4) levels were normal, Anti-ds DNA and other ENA were negative. ESR was 4 mm, Hb was 15,6 g/dL . Chest X-ray, ECG, urinalysis were normal.
Anti-HIV, VDRL, Anti-HBcIgG, HBsAg,Anti-HCV were negative.
Skin biopsy of lesional skin from the chest showed mild
hyperkeratosis, subcorneal acantholysis and small bullae formation with superficial perivascular neutrophile and eosinophile leukocyte infiltration (Figure 3a)
Direct immunofluorescens (Direct IF) of perilesional skin revealed focal deposits of IgG and C3 in the intercellular space of the epidermis (Figure 3b,3c).

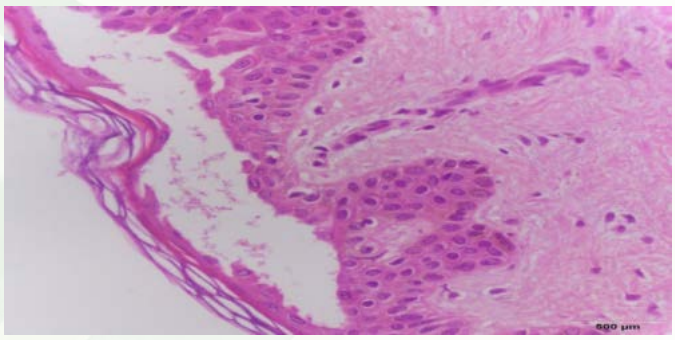


Figure 3a

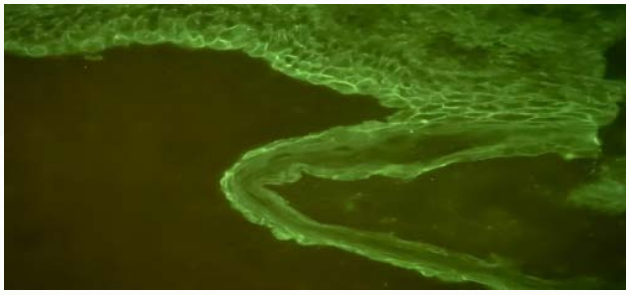


Figure 3b

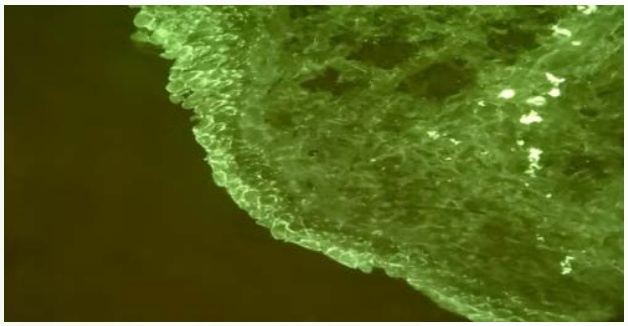


Figure 3c

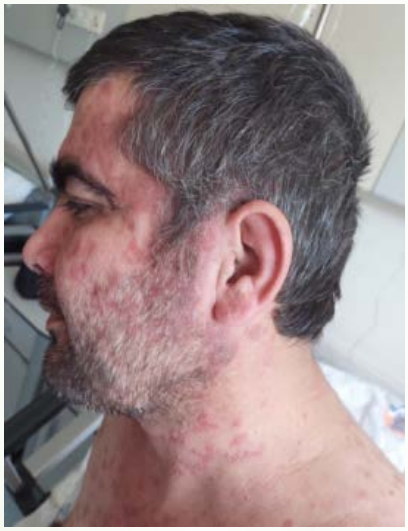
Figure legends:

Figure 3. a. Subcorneal intraepidermal seperation and acantholysis, H&E X 100.
b. Pericellular IgG positivity in the upper part of epidermis, Direct immunofluorescence (Direct IF) X100
c. Pericellular complement 3 (C3) positivity in the upper part of epidermis.
Direct immunofluorescence (Direct IF)X100

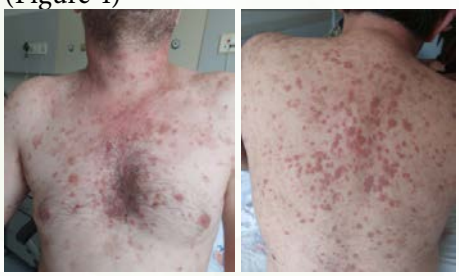
Treatment

He was subsequently diagnosed as pemphigus erythematosus and was put on topical fluticasone propionate, and oral prednisolone at a dose of 1 mg/kg/day for 10 days
Prednisolone was discontinued because the liver enzymes elevated ten fold. He was consulted with gastroenterology department, corticosteroid induced hepatotoxicity was considered.
When the lesions were regressed with topical treatment, the patient was discharged, but came back with recurring lesions 20 days later.
Doxicycline was given for 10 days, but there was no response. Rituxumab treatment was started (1000mg 0,15. day infusion).

On the 15th day, his skin lesions partially regressed.(Figure 4,5a,5b)

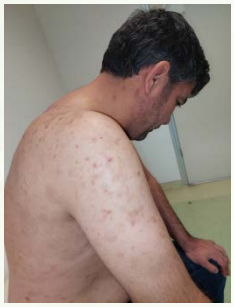


(Figure 4)

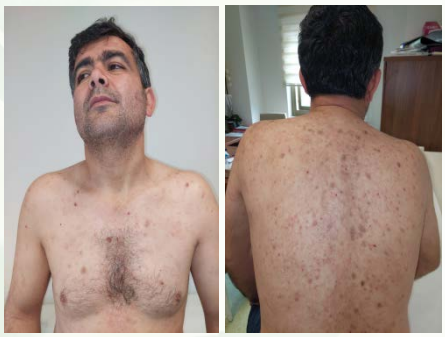


(Figure 5a,5b)

Figure legends:
Figure 4.Regressed lesions on scalp and face 15 days after first rtx infusion
5a.5b.Regressed lesions on chest and trunk 15 days after first rtx infusion



(Figure 6)



(Figure7a.7b)

Figure legends:
Figure 6.Regressed lesions on scalp and face 6 months after first rtx infusion
Figure7a.7b Regressed lesions on chest and trunk 6 months after first rtx infusion

Discussion

Pemphigus erythematosus (PE), is a rare condition that combines the clinical and immunological features of pemphigus foliaceous and lupus erythematosus (3). Clinical features of PE include pemphigus foliaceous-like scattered scaly flaccid blisters with erosions and crusts on 'seborrhoeic' areas of the scalp, face, chest and upper back along with malar rash simulating lupus erythematosus with absence of mucous membrane involvement (4,9). The immunological features include IgG and C3 in the suprabasal layers as in pemphigus foliaceous and along the basement membrane zone similar to lupus erythematosus (5). Many authors have disputed the existence of this condition as a distinct entity and consider it to be an abortive form of pemphigus foliaceous (6). This could be supported by the study done by Oktarina et al., where they demonstrated deposition of antibodies against desmoglein 1 on the basement membrane zone mimicking lupus band test. This could explain the direct immunofluorescence findings when ANA reactivity is negative or weakly positive(7).

Conclusion

Our patient was diagnosed with pemphigus erythematosus based on clinical and immunological findings. He responded promptly to topical and oral corticosteroids but when systemic steroid treatment was stopped, the disease was reactivated and alternative treatment options were evaluated.
Topical and oral corticosteroids along with hydroxychloroquine sulfate, dapsone, tetracycline, adjuvant immunosuppressants
should be considered as the first line treatments of PE. Rapid response to rituximab was reported in treatment resistant patients. [10].

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A Case Report of Uncombable Hair Syndrome Treated with Zinc

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ABSTRACT

Uncombable hair syndrome is a rare anomaly of the hair shaft, that results in a disorganized, unruly hair that is impossible to comb flat. Hair grows unevenly and in different directions. When viewed under the light microscope, the body of the hair should be cylindrical, but rather triangular. The small grooves that go up and down in the triangular shape cause the hair to be uncombable and the hair is irregular, silvery yellow or straw-colored. This syndrome develops between infancy and 3 years of age and begins to appear around the age of 12. There is no definitive treatment, and most cases improve with the onset of puberty. In this poster presentation, we present a 14-month-old baby patient with uncombable hair syndrome who had hair growth and improvement with oral zinc treatment.

INTRODUCTION

Uncombable hair syndrome (UHS) is a rare disorder of the hair shaft of the scalp. There are 100 cases reported worldwide. It is usually characterized by silvery-blond or straw-colored hair that is disorderly stands out from the scalp; and cannot be combed flat. The syndrome appears to be inherited in an autosomal recessive fashion; however, cases inherited in an autosomal dominant manner may also exist, as there are many genes involved in hair formation. Most cases are isolated, but in some cases it has been described in association with other diseases, such as ectodermal dysplasias, Angel-shaped phalangoepiphyseal dysplasia. The syndrome has been found to be caused by genetic changes in the genes PADI3, TGM3, and TCHH. These three genes code for proteins that are involved in hair shaft formation. The condition often spontaneously regress in late childhood.

CASE PRESENTATION

Our patient applied to us because of the irregularity and sparseness of her hair. When our patient was 8 months old, it was noticed that her hair was uneven and sparse. In the microscope, it was seen that the body of the hair is triangular rather than cylindrical. Her twin sister did not have this hair feature, but her grandmother had untidy hair. Although the patient did not have zinc deficiency, oral zinc therapy was recommended. After using 5 milligrams/day for 6 months, our patient's hair increased but untidyness remained.

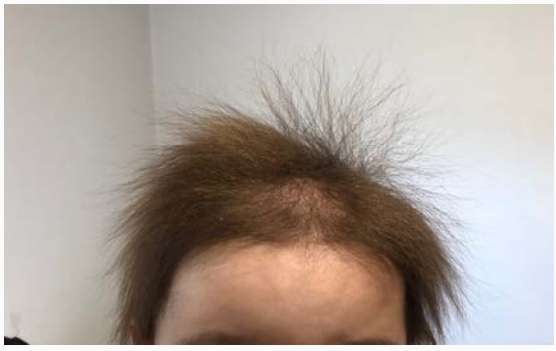

Figure 1. after oral zinc therapy

TEST	RESULTS	REFERENCE VALUES
FERRITIN	54,2 ng/ml	6-67
VIT B12	229 pg/mL	416-1210
Hb	14,2 g/dL	11,3-14,1
VIT D3	38,44 µg/L	25-50
ZINC	94 mg/dL	70-120

Table 1

Figure 2. microscopy of hair fiber

CONCLUSION

Zinc treatment is not routinely used for this disease, but we thought that it could be beneficial for our patient. Oral zinc therapy may be tried in these patients.

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EVALUATION OF INVERS APPROACH'S SPECIFITY AND SENSITIVITY IN DERMOSCOPIC DIFFERENTIAL DIAGNOSIS OF LENTIGO MALIGNA

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Introduction

Lentigo maligna is a subtype of malignant melanoma that occurs in chronically sun-exposed skin areas such as the head and neck region. It may be overlooked until the late stages of its progression, especially because of the other signs of sun damage on the skin and its slow growth rate. According to classical dermoscopic criterias of lentigo maligna, early phase findings such as perifollicular grey dots, short lines, asymmetrical pigmented follicles may have seen focally or unsignificant. Therefore, dermoscopic evaluation algorithms are needed to increase diagnostic sensitivity and specificity. Lallas et all developed a new diagnostic dermoscopic algorithm called inverse approach which points these diagnostic deficiencies. According to inverse approach, six dermoscopic non-melanoma criteria were determined (squam, eryhtema, white and wide follicular openings, brown linear or reticular lines, sharp demarcation, milia like cysts /comedo like openings). If the lesion shows at least one of these non-melanoma dermoscopic criteria predominantly (>%50 of the lesion), this lesion can be diagnosed as actinic keratosis or solar lentigo. However, if the lesion do not show any of these non-melanoma dermoscopic criteria at al lor predominantly, this lesion should be considered as doubtful for lentigo maligna.

Objectives

The aim of this study is to prospectively determine the sensitivity of the newly defined inverse approach in the dermoscopic differential diagnosis of lentigo maligna and evaluate its applicability in dermatology practice.

Materials and methods

Patients who applied to Manisa Celel Bayar University Dermatology Follow-up Outpetient Clinic with hyperpigmented macules in the head and neck region were included in this study with their verbal and written informed consents. All lesions were examined clinically and dermoscopically. Lesions which did not show any of classical lentigo maligna criteria and also show any of inverse approach criteria predominantly were considered as actinic keratosis or solar lentigo depens on predominant finding. Lesions which show any of classical lentgio maligna criteria or did not show any of inverse approach criteria were considered as doubtful for lentigo maligna and excised. Additively, patients age, sex, occupation, risk factors for developing melanoma, sun protection habits, history of persona lor familial melanoma or non-melanoma skin cancer were recorded. The data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 26.0 for Windows.

Results

A total of 68 patients (34 female, 34 male) were included in the study group. Mean age of patients were 59±15,7 [22-84] years. 947 lesions were examined clinically and dermoscopically. Out of a total of 947 lesions, 940 were evaluated benign dermoscopically. 7 lesions were considered doubtful according to inverse approach and only 4 of them (Figure 1) showed classical dermoscopic criterias for lentigo maligna. 6 of the 7 lesions were diagnosed as lentigo maligna and 1 was diagnosed as atypical lentiginous proliferation histopathologically (Figure 2). The sensitivity of the method was found to be 100% and spesifity of the method was found to be %99,8.

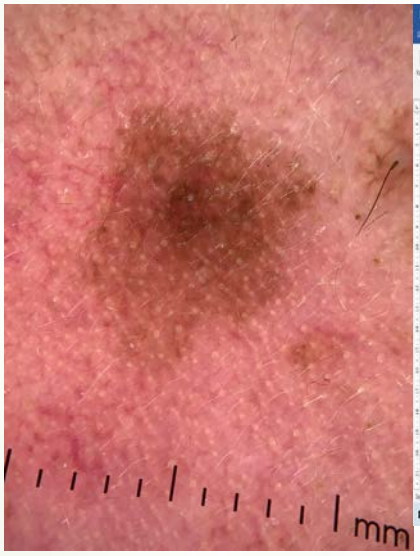

Figure 1. Asymmetrical follicular pigmentation (red circle), rhomboidal structures (blue arrow). Homogenous pigmentation with preserved follicles (green circle). Classical dermoscopic criteria for lentigo maligna are present. Histopathological diagnosis is lentigo maligna.

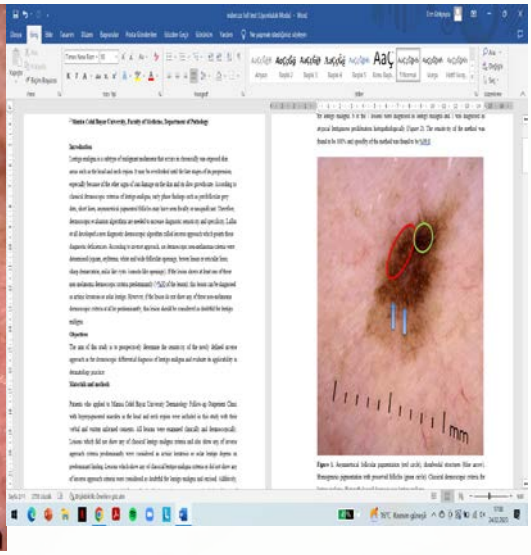

Figure 2. Lesion which do not show any of classical lentgio maligna criteria or did not show any of inverse approach criteria predominantly. Histopathological diagnosis: Atypical lentiginous proliferation.

Conclusion

Despite densitivity and spesifity of classical dermoscopic criteria for diagnosis of lentigo malignant melanoma is high, not that much higher in lentigo maligna. Recetly developed dermoscopic algorithms enhanced correct diagnosis ratios (2), however algorithms and scorring systems became more complicated and hard to apply practically. Inverse approach was developed as an easily applicable diagnostic method by taking into consideration of previous diagnostic algorithms. According to the results of our study, the inverse approach is an easily applicable diagnostic algorithm in the diagnosis of lentigo maligna with high sensitivity and spesifity. Addivitely, in regression period of actinic keratosis and solar lentigo/seborrheic keratosis (lichen planus like keratosis) which are main differential diagnosis of lentigo maligna in inverse approach, symmetrical perifollicular grey dots can be observed (3-8). This finding is also one of classical dermoscopic criteria of lentigo maligna and may lead misdiagnosis in early phase. We suggest perifollicular grey dots should be evaluated in larger series to determine its significance. In addition, inverse approach should be used as an additional algorithm in dermoscopic examinations of patients with chronic sun damage and presenting with multiple hyperpigmented macules in the head and neck region.

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BULLOUS LUPUS ERYTHEMATOSUS: RARE VARIANT OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: A 37-year-old female patient presented with the complaint of watery sores on the body and oral mucosa for 1 month. The patient who was diagnosed with bullous pemphigoid in another center applied to our center. She has no known disease. She's on prednol therapy for her lesions. In his dermatological examination, excoriated eroded areas on the shoulders, axilla, breast and legs, and eroded areas on the oral mucosa were observed.

Diagnosis: In the microscopic examination; In the epidermis, compact hyperkeratosis, subepidermal separation, dense fibrin material with band-like distribution on the base of the bulla, as well as mixed type inflammatory cell infiltration, rich in neutrophil leukocytes and accompanied by clasia findings, were observed. In immunofluorescence examination; granular staining of the basement membrane was observed with IgG and fibrinogen.

In the serological examination of the patient, ANA +++, Antidsdna ++, antiRNP +++ were detected. With these clinical, serological and histopathological findings, the patient was diagnosed with Bullous Lupus Erythematosus. The patient was diagnosed with lupus nephritis class 3 in the kidney biopsy performed afterwards.

Discussion: Bullous lupus erythematosus is a rare variant of systemic lupus erythematosus. It most commonly affects African-American women. It most commonly affects the trunk, proximal arms, face and neck. Patients must fulfill the American College of Rheumatology criteria for the diagnosis of systemic lupus erythematosus. It is characterized by pruritic tense vesicles and bullae. Mucosal involvement may be seen. Lesions respond dramatically to dapsone [1]. There are autoantibodies against type VII collagen [2] . Dermatitis herpetiformis, linear IgG A bullous dermatosis and acquired inflammatory epidermolysis bullosa can be considered in the differential diagnosis.

Keywords: Bullous, Lupus, band-like distribution

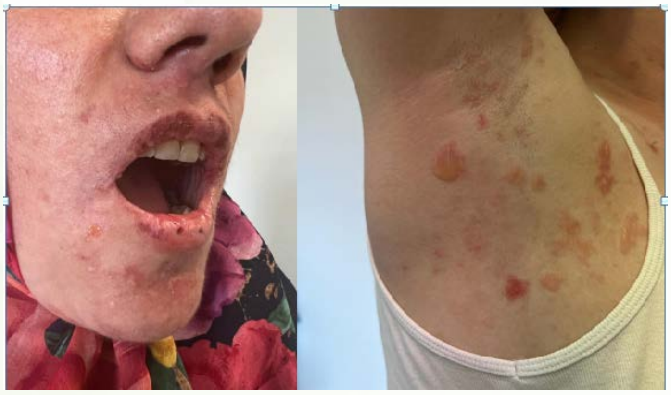

Figure 1: Excoriated eroded areas on the axilla and oral mucosa

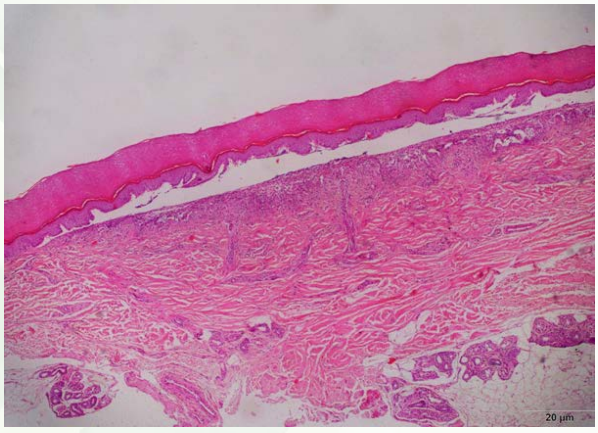

Figure 2: In the epidermis, compact hyperkeratosis, subepidermal separation, HE;x40

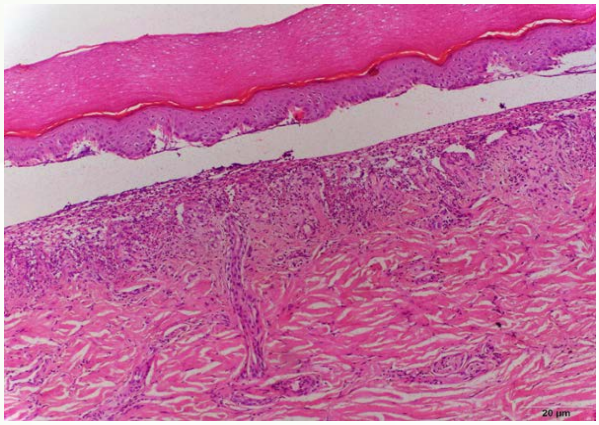

Figure 3: Dense fibrin material with band-like distribution on the base of the bulla, as well as mixed type inflammatory cell infiltration, rich in neutrophil leukocytes and accompanied by clasia findings HE; x100

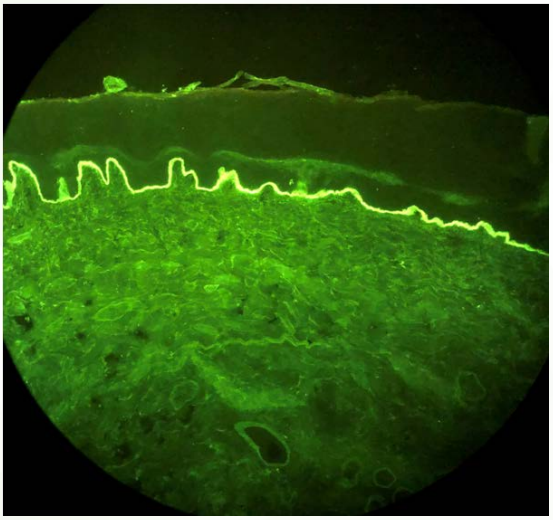

Figure 4: Granular staining of the basement membrane was observed with IgG, x40

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ECTOPIC HIDRADENOMA PAPILLIFERUM OF NECK: A RARE LOCALIZATION

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Introduction

A 63-year-old male patient was admitted to the dermatology clinic with the complaint of nodular pigment resolution in the right side of the neck, behind the ear. The patient's lesion was excised with preliminary diagnoses of dermal nevus, fibroma, skin tag and nodular basal cell carcinoma.

Diagnosis

On histological sections, there were papillary structures lined with cuboidal cells within the well-circumscribed cystic structures without any connection with the epidermis (Figures 1 and 2). Focal areas of apocrine differentiation and decapitation secretion were seen in the lesion (Figure 3). Diffuse, moderate-to-strong cytoplasmic staining with CK7, EMA and GCDFP-15 was observed in the cuboidal cells lining the lesion without atypia and significant mitotic activity. No staining was observed with CK20, mCEA, CK5/6, Amacr, Pax8, TTF-1 and p63 (Figure 4). The lesion which was not associated to the epidermis was reported as Hidradenoma papilliferum.

Discussion

Hidradenoma papilliferum (HP) is a benign adnexal tumor that can show apocrine differentiation (1). Since the apocrine sweat glands are predominantly located in the anogenital region and axilla, most cases of HP have been reported in these regions. Rare ectopic forms of HP have been described in various locations, including the head and neck, chest, and extremities (2,3,4). In contrast to anogenital HP, approximately half of the patients with ectopic HP are male and the lesions are located mainly on the head and neck (5). Although malignant transformation is rare, it can be confused with a malignant tumor due to its complex papillary pattern. The overall prognosis of this neoplasm is good with total excision, regardless of location (4). Syringocystadenoma papilliferum (SP) should be considered in the differential diagnosis, but SP is associated with the epidermis and shows cystic invaginations extending downwards. Other histopathological differential diagnoses include tubular apocrine adenoma, clear cell (apocrine) adenoma, and intraductal carcinoma (6).

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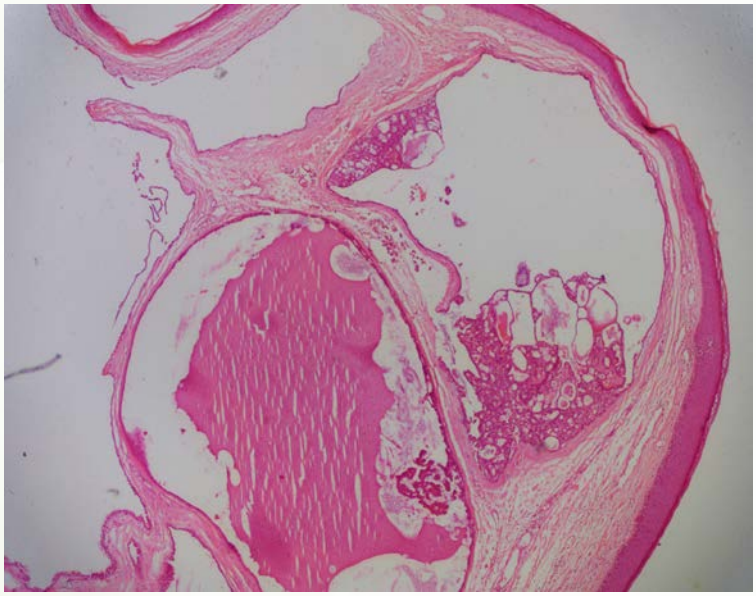

Figure 1: Cystic papillary structures located in the dermis, not connected with the epidermis (H&E, x40)

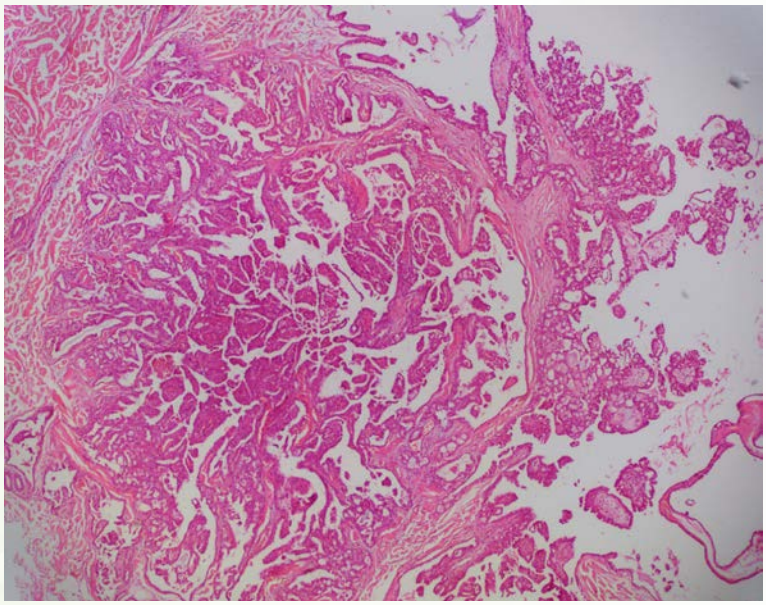

Figure 2: Papillary structures containing central fibrovasculary cores (H&E, x40)

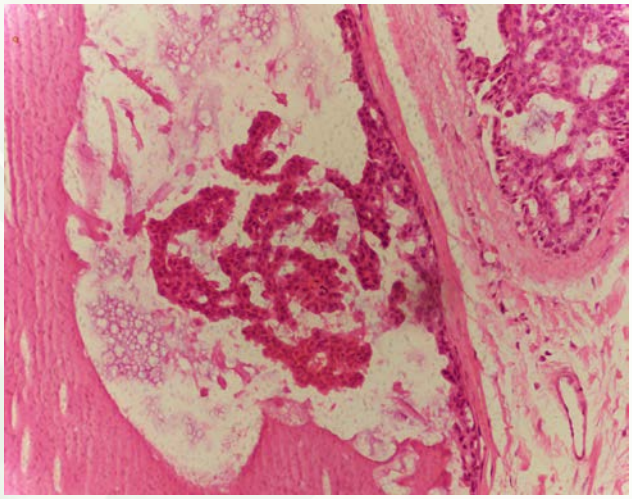

Figure 3: Focal area of apocrine differentiation and decapitation secretion on the left (H&E, x200)

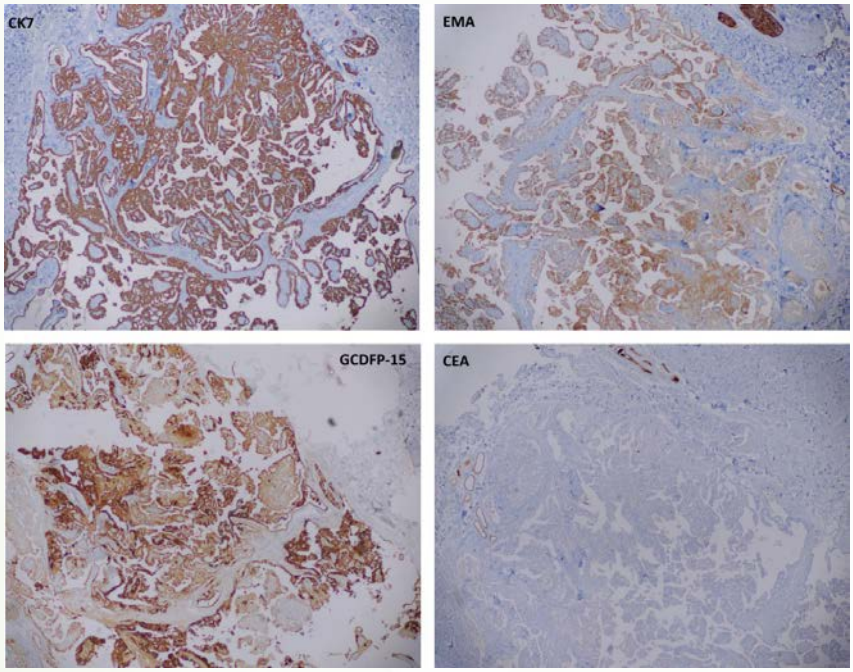

Figure 4: Cytoplasmic staining was observed with CK7, EMA and GCDFP-15. No staining was observed with CEA (x40).

A RARE ACANTHOLYTIC GENODERMATOSIS: HAILEY HAILEY DISEASE

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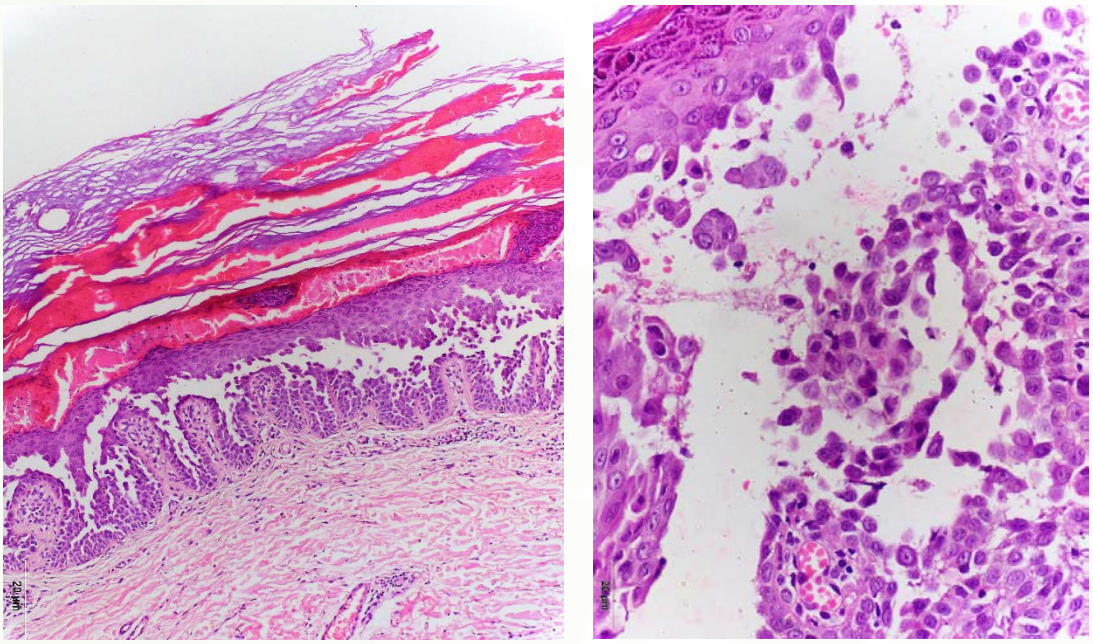
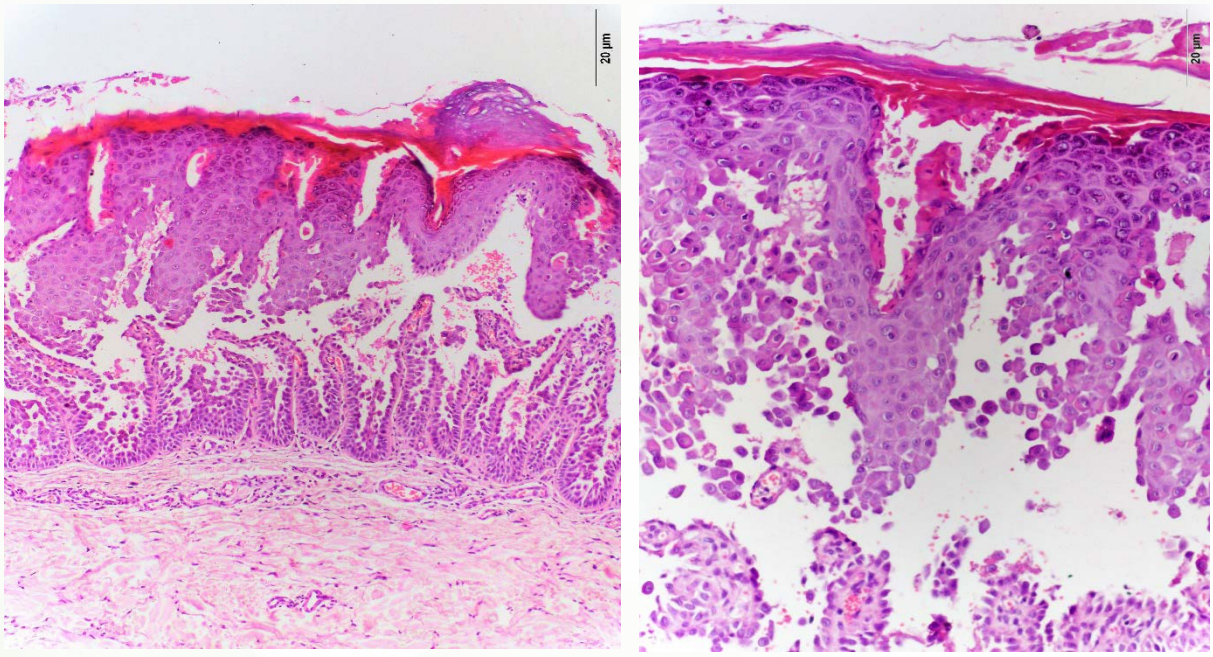
Introduction: A 48-year-old female patient was admitted to the dermatology clinic with itchy lesions that started 30 years ago, were aggravated by heat and friction and predominantly localized flexural areas. In dermatological examination, there are erythematous, eczematized, eroded, bullous lesions located in the neck, axilla and inguinal region.

Case: Biopsies wer taken from the patient, which would allow direct immunofluorescent examination with localization of the neck and inguinal region. Similar histomorphological findings were observed in samples from both localizations in hematoxylin-eosin examination. In biopsy specimens with mild orthokeratosis and parakeratosis in the epidermis, large areas of intraepidermal suprabasal acantholytic dehiscence were noted(Photograph 1). Villi or elongated dermal papillae lined with a single layer of basal cells protruded into the bulla. Dyskeratotic keratinocytes were seen in the corneal layer, more prominently in the inguinal region localized sample(Photograph 2). Mild lymphohistiocytic inflammatory cell infiltration accompanied by sparse neutrophil leukocytes, eosinophil leukocytes and melanophages was observed around partially congested vascular structures in the superficial dermis. No specific accumulation was observed in the direct immunofluorescence examination. When the case was evaluated together with clinical and pathological findings, Hailey-Hailey Disease was considered primarily, considering the early onset and family history.



Photograph 1: Orthokeratosis and parakeratosis in the epidermis, large areas of intraepidermal suprabasal acantholytic dehiscence, H&E, x100, x200



Photograph 2: Elongated dermal papillae lined with a single layer of basal cells protruded into the bulla and subcorneal dyskeratotic keratinocytes H&E, x100, x200

Discussion: Hailey-Hailey disease (HHD), also known as benign familial pemphigus, is a rare autosomal dominant genodermatosis caused by mutations in the ATP2C1 gene that encodes a calcium pump of the Golgi apparatus firstly described in 1939 by the Hailey brothers[1]. HHD is a chronic disease with a relapsing-remitting clinical course. Exacerbations are mainly triggered by sweating, minor trauma, and secondary infections. HHD is characterized by ruptured vesicles and blisters that tend to form eroded, erythematous plaques with painful "rhagades" in flexural areas[2]. Histologically, well-developed lesions are characterized by incomplete acantholysis, resulting in a "dilapidated brick wall" appearance[3]. Chronic lesions present epidermal hyperplasia with ortho- and parakeratosis. The parakeratotic crust sometimes contains neutrophils and bacteria. The superficial dermis can contain focal perivascular lymphohistiocytic infiltrate[2]. Direct immunofluorescence is negative[3]. Hailey–Hailey disease can be recognized clinically based on the distinctive distribution pattern and the usual presence of a positive family history[4]. There is no curative treatment. Mild cases can be controlled successfully with intermittent courses of topical corticosteroids and antibiotics[2].

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Keywords: Hailey Hailey, genodermatosis, acantholytic

BACLOFEN-INDUCED DYSHIDROSIFORM BULLOUS PEMPHIGOID IN A TETRAPLEGIC PATIENT

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Dyshidrosiform bullous pemphigoid is a rare variant of bullous pemphigoid, and it usually presents as itchy, potentially hemorrhagic, or purpuric blisters on the palms and soles of elderly individuals; subsequently, typical bullous lesions of bullous pemphigoid appear on other body sites.

Case report:

A 62-year-old tetraplegic male patient presented with a history of tender blisters on the hands and feet for 1 month. Over time, erythema spread all over the body, red itchy lesions on the legs and arms began to form. He had gliclazide, which he had been using for 2 years due to diabetes, and betanecol, which he had been using for 1 month due to neurogenic bladder. Gabapentin was discontinued due to increasing pain and rash, and he was switched to baclofen. He had been using baclofen for 2 months.

On skin examination there were hemorrhagic vesiculobullous lesions on the erythematous ground on the hands and feet including the palms and soles. There were also erythematous urticarial plaques on the trunk and extremities, and several hemorrhagic bullous lesions on the arms and legs.

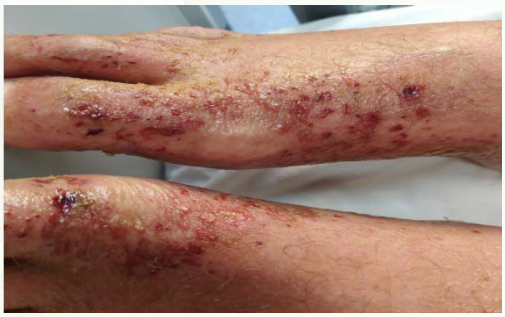


Figure1: hemorrhagic or purpuric blisters,vesiculobullous lesions on erythematous ground on the dorsum of the foot

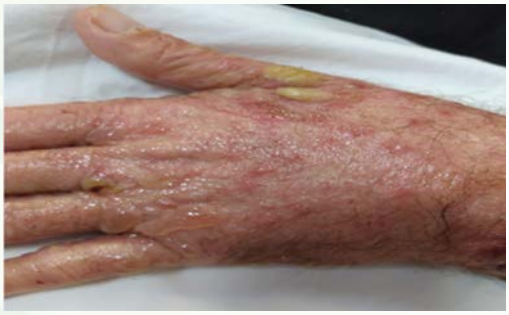


Figure 2: vesicubullous lesions on the dorsum of the hand

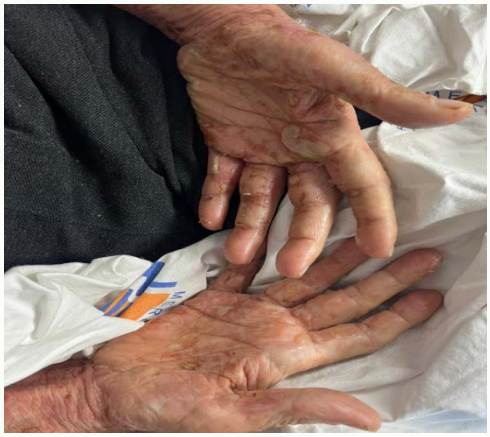


Figure 3: flattened and deroofed blisters on the palm

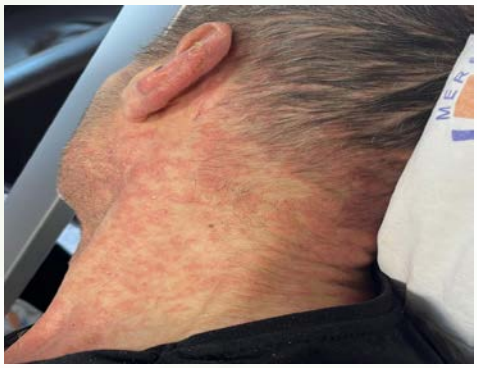


Figure 4: urticarial plaques on the neck

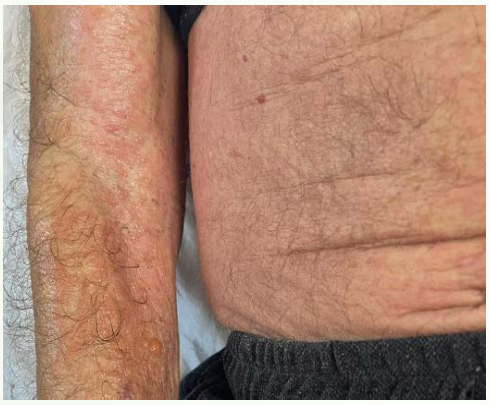


Figure 5: Tense bullae in the erythematous area on the arm and trunk

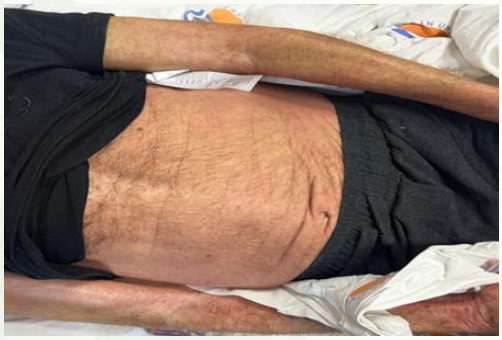
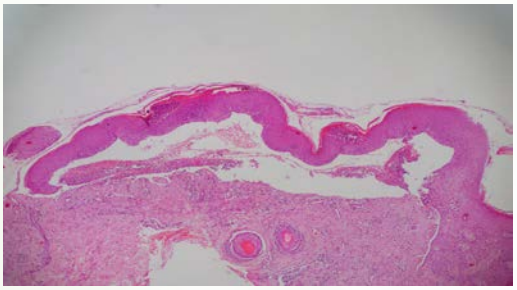


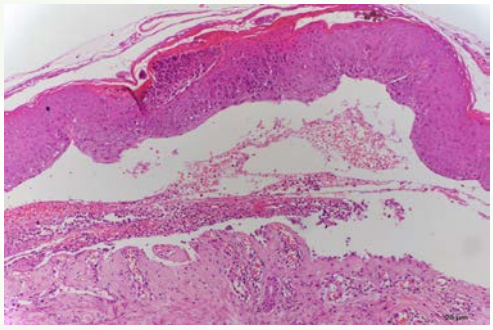
Figure 6: erythema on trunk

In the microscopic examination of the skin biopsies of the lesions in the right ankle there was subepidermal bulla formation and mixed-type inflammatory cell infiltration rich in eosinophil leukocytes in the perivascular and periadnexal area of the dermis.

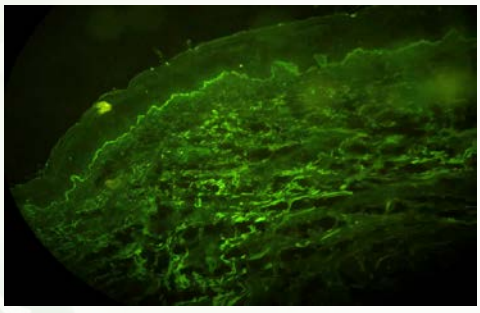
A second biopsy was performed immediately adjacent to the right foot lesion for direct immunofluorescence. Staining for immunoglobulin G (IgG) and C3 showed a flat band of linear immunoreaction deposition at the dermo-epidermal junction. The staining was negative for immunoglobulin A (IgA), immunoglobulin M (IgM), and fibrinogen. Both (direct immunofluorescence) biopsies of the left ankle (hematoxylin and eosin) were diagnostic for bullous pemphigoid. Correlation of clinical history with histopathology and immunopathology diagnosed dyshidrosiform bullous pemphigoid



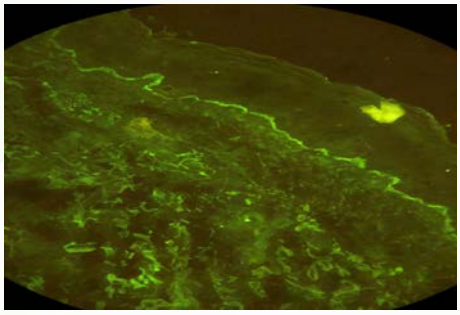
Photograph 1: Subepidermal bulla formation, HE, x40



Photograph 2: Inflammatory cells rich in neutrophil and eosinophil leukocytes on the fibrin background in the bulla lumen, HE, x100



Photograph 3: Linear granular staining of basement membrane with IgG, x40



Photograph 4: Linear granular staining of basement membrane with C3, x100

The patient's eosinophil count was 2900cells/mcl.serum immunoglobulin E (IgE) level was very high at 738 UI/ml (normal: <115 UI/ml).

IV methylprednisolone (60 mg/day) and topical clobetasol propionate 0.05% ointment (2 times a day). Betanechol was discontinued with urology consultation. IV prednisone treatment was continued. Azathioprine 50 mg twice a day (after confirming normal thiopurine methyltransferase enzyme activity) was started as a corticosteroid sparing agent. New blisters continued to appear despite the discontinuation of betanechol. Baclofen was discontinued with neurology consultation. The patient's eosinophil count was from 2900 cells/mcl (microliter) to 900 cells/mcl. declined. Within 2 weeks, the lesions on the hands and feet began to regress; There were no new blisters after four weeks. Currently, methylprednisolone and azathioprine treatment continues. Started reducing prednisone by 10mg every other week

Discussion:

Dyshydrosiform bullous pemphigoid is a rare type of bullous pemphigoid. The morphology of the lesions mimics vesicular hand or foot dermatitis, chronic bullous disease of childhood, mainly lesions and irritant contact dermatitis, cutaneous T-cell lymphoma (vesicular palmoplantar diseases), dermatophyte infection (bullous), epidermolysis bullosa acquisita, erythema multiforme, herpes gestationis, lichen planus (bullous) linear IgA disease includes scabies.(1) There are also few reports of palmoplantar involvement without further spread to other skin areas, and rarely DP may be limited to plantar areas only. (2) In a study of 20 bullous pemphigoid patients conducted in Sweden, it was observed that two of nine patients with dyshydrosiform bullous pemphigoid had lesions of the palm and/or sole only. They emphasized that dyshidrosiform bullous pemphigoid patients had prodromal symptoms such as eczematous rash in 3, papular rash in 3 patients, eczematous and papular rash in 1 patient, intertriginous rash in 1 patient, and urticaria and papular rash in 4 patients.(3) In our case, it had a classical appearance with lesions on the palms and soles.

As in our case, the literature also emphasized the association of hemorrhagic blisters or purpuric lesions with dyshydrosiform bullous pemphigoid. This may help differentiate DP from pompholyx.(4) In contrast, only one (5%) of 20 patients in a large series of patients had hemorrhagic lesions.(5) Oral lesions were defined in only five patients in the literature. Oral lesions were not detected in our patient. One patient with dyshydrosiform bullous pemphigoid with oral lesions had only accompanying acral blisters.(6) DP mostly affects older adults, and reports in young adults are extremely rare. In the literature, the expression of BP antigens was found to be greatest in plantar skin, which may be the reason for localization to the soles and palms.(7)

An association between bullous pemphigoid and neurological or psychiatric disorders has described. Especially associated with neurological disorders such as epilepsy or Parkinsonism.(8) In addition, there are publications in the literature indicating that dyshidrosiform bullous pemphigoid patients are associated with cerebrovascular events, Parkinsonism, peripheral neuropathy, senile dementia, and patients with manic depression syndrome.(2, 9-11) In our case, our patient had tetraplegia that developed after trauma. Whether there is an increased incidence of neurological and psychiatric conditions in patients with dyshydrosiform bullous pemphigoid compared with individuals with bullous pemphigoid without dyshydrosiform-like lesions remains to be determined.(9)

Numerous drugs are known to trigger bullous pemphigoid. Lugovic-Mihic et al. suggest that baclofen induces dyshydrosiform bullous pemphigoid in his patients. baclofen was not listed as a triggering agent in the major studies of drug-induced bullous pemphigoid. The patient had paraplegia secondary to ischemic transverse myelitis. The drug was started two years

before the onset of dyshydrosiform bullous pemphigoid.(6) Our case had a recent history of baclofen use. We found rapid regression in the eosinophil level and lesions of our patient after baclofen was discontinued. Therefore, we suggest that baclofen-associated dyshidrosiform bp may be present

Conclusion:

Drug-induced dyshydrosiform bullous pemphigoid resolves after discontinuation of the associated agent; however, systemic treatment was also necessary to allow the bubbles to dissolve. New onset of recurrent or persistent blisters on the palms, soles, or both should prompt the clinician to consider the diagnosis of dyshidrosiform bullous pemphigoid.

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ACRODERMATITIS ENTEROPATHICA

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Case report

A 21-year-old female patient with a diagnosis of celiac disease presenting with cachexia, diarrhea, vomiting, diffuse brownish erythematous hyperpigmented papules and plaques on the dorsum of the feet and hands, arms, knees and legs, desquamation and erythematous plaques in the nasolabial, medial eyebrows and perioral area, and hair loss.

In the microscopic examination, hyperkeratosis, parakeratosis (Figure 1), mild irregular acanthosis were observed in the epidermis, cytoplasmic paleness and keratinocyte dismaturation (Figure 2) were noted in the upper half of the epidermis. In the biopsy sample, in which the papillary dermis was observed in an edematous appearance, mild lymphohistiocytic inflammatory cell infiltration was observed around the vascular structures with endothelial prominence in the superficial dermis (Figure 3).

Discussion

With these histomorphological findings, a diagnosis of Acrodermatitis Enteropathica was considered. Acrodermatitis Enteropathica is an autosomal recessive metabolic disorder affecting the uptake of zinc through the inner lining of the bowel, the mucous membrane. It is characterized by inflammation of the skin (dermatitis) around bodily openings (periorificial) and the tips of fingers and toes (acral), hair loss (alopecia), and diarrhea. It can also be related to deficiency of zinc due to other, i.e. congenital causes.

Keywords: diarrhea, dermatitis, hair loss

Reference: National Library of Medicine, Acrodermatitis Enteropathica, Soumya Jagadeesan; Feroze Kaliyadan.

Figure 1: Hyperkeratosis and parakeratosis *(H&E, x200).*

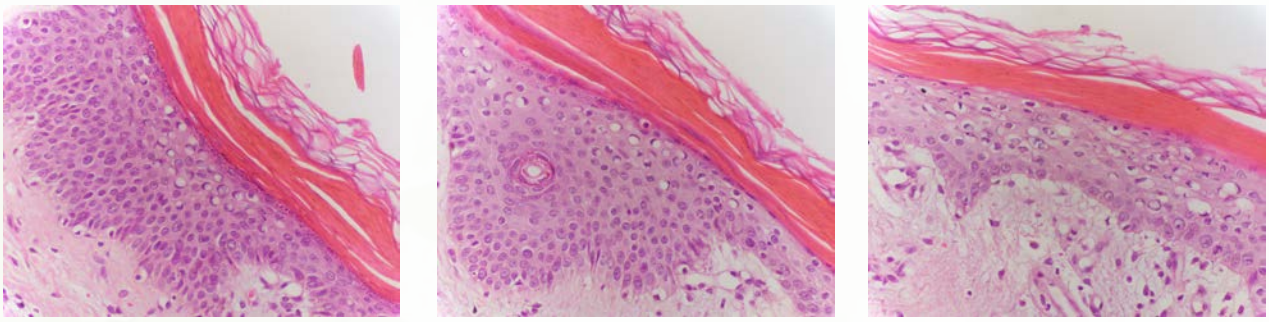

Figure 2: Cytoplasmic paleness and keratinocyte dismaturation *(H&E, x400).*

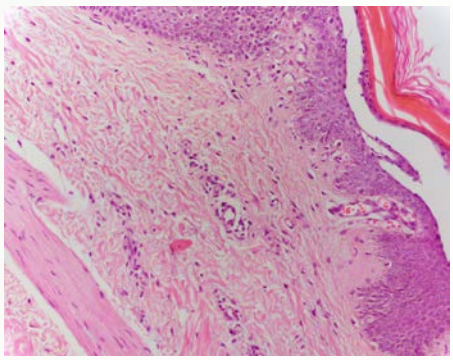

Figure 3: Mild lymphohistiocytic inflammatory cell infiltration was observed around the vascular structures with endothelial prominence in the superficial dermis *(H&E, x200).*

ASSOCIATION OF MYCOSIS FUNGOIDES AND KAPOSI SARCOMA: IS ONLY A COINCIDENCE ?

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INTRODUCTION: Mycosis fungoides (MF) is the most common form of cutaneous T cell lymphoma that arise from skin-tropic memory T lymphocytes[1]. Kaposi Sarcoma (KS) is a multifocal angioproliferative neoplasm that develops due to Human-Herpes virus 8 (HHV-8), which often occurs on the skin. Patients with KS are at risk of lymphoma, such as Hodgkin‘s lymphoma, Castleman‘s disease and plasmablastic lymphoma[2]. However, the coexistence of MF and KS in the same patient is a rare phenomenon especially in HIV negative patients. Herein we report a patient with concurrent diagnosis MF and Classic KS in an elderly man.

CASE REPORT: An 68 year old man applied to our hospital because of infective scar tissue that was not healing on his right foot. Histopathological examination of excisional biopsy of the lesion taken by Department of Plastic Surgery revealed CD30 positive T cell lymphoproliferative disease. Then he was consulted to our department. Physical examination found both brown atrophic macules (Fig. 1) and purple macular lesions (Fig. 2) on his thighs. Histopathological examination of these lesions were compatible with MF and KS (patch stage) respectively. He was consulted to Department of Oncology and Hematology. Positron emission tomography was taken and reactive lymph nodes 2 cm diameter were observed in inguinal region. Histopathological examination of reactive lymph nodes were Grade 1 according to Dutch system. Peripheral blood smear and flow cytometric analysis were compatible with B0 according to EORTC classification. The patient was considered as stage 2a MF with large cell transformation in one lesion. Oral acitretin (25 mg/day) and pegylated interferon alfa 2a was started. Clinical and histopathological improvement was achieved in six months.

DISCUSSION: In the literature, mostly cases of KS developing with MF includes patients who received therapy such as phototherapy and nitrogen mustard for MF or who had previous chemotherapy exposure for another lymphoma[3-6]. Immunosupression induced by either MF itself or treatment modalities including photoherapy or chemotherapy for another cancer are proposed mechanisms in these reports. In our case, MF and KS diagnosis was made concurrently with no history of immunosupression or phototherapy. In the literature only one 88 year old patient was reported with concurrent MF and KS with no previous immunosupression. In this case they proposed that the development of MF, induced an immunosuppressive state and in combination with immunosenescence due to advanced age of that patient along with HHV-8 positivity contributed to the development of KS [7]. In conclusion coexistence of MF and KS in a patient is a rare condition. However it should be kept in mind that this association may be present especially in elderly patients.

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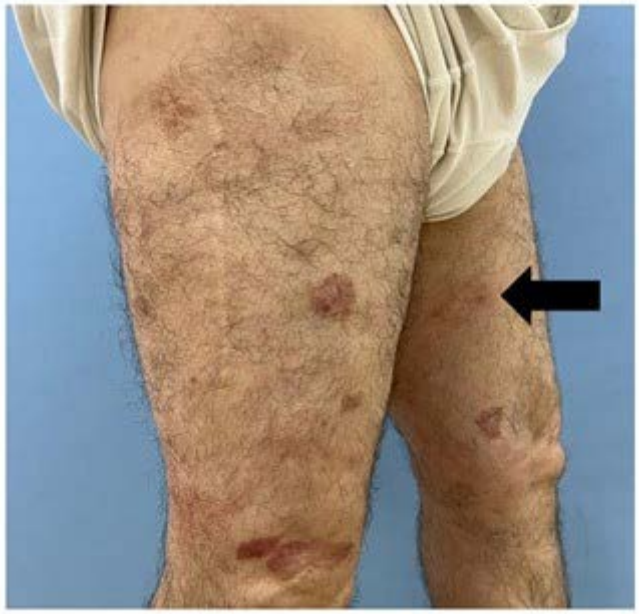
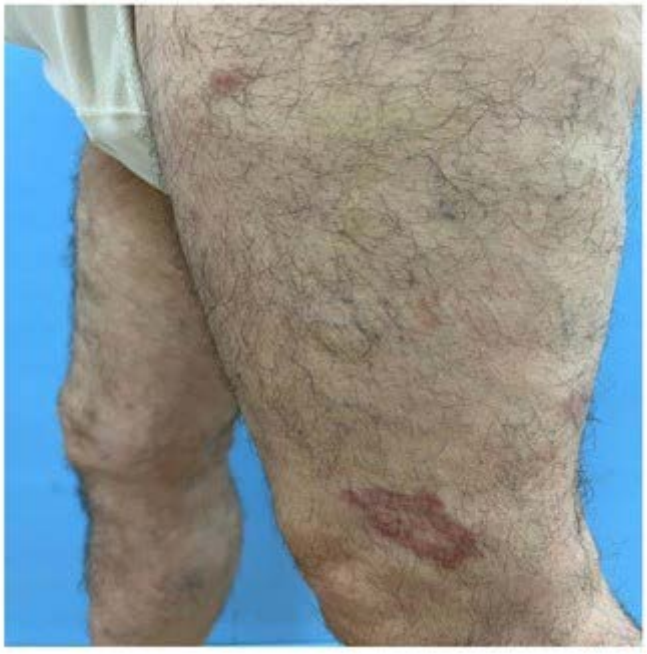
Keywords: mycosis fungoides, kaposi sarcoma, coexistence of mycosis fungoides and kaposi sarcoma

Figure 1



Atrophic macular lesion (arrow)

Figure 2



Purple macular lesions on his thighs

AN UNEXPECTED CAUSE OF HYPERPIGMENTATION: A CASE OF BERLOQUE DERMATITIS

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INTRODUCTION: Berloque dermatitis is a phototoxic reaction due to using bergamot oil. Phototoxic effect of bergamot arise as a result of bergapten (5-methoxypsoralens). Bergapten and UVA contact results melanogenesis and hyperpygmentation. Bergamot are used for perfumes, colognes, fragrances. Using of these products may cause hyperpygmented lesions.

CASE: A 15-year-old patient was admitted to the dermatology outpatient clinic with hyperpygmented skin lesions. Dermatological examination revealed irregulated border, hyperpygmented patchy skin lesions on the neck and chest areas (Figure 1). İncisional biopsies performed from the neck. Actinic Lichen Keratosis, Acanthosis Nigrikans and Berloque dermatitis were considered as preliminary diagnosis. Histopathological examination revealed basal vacuolar degeneration and necrotic keratinocytes on the dermoepidermal junction (Figure 2). Melanophages accompanying lymphohistiocytic infiltrate were detected in the papillary dermis (Figure 3). Considering localization and anamnesis finally diagnosis were determined Berloque Dermatitis.

DISCUSSIONS AND CONCLUSIONS: Berloque dermatitis occurs after cosmetic products containing bergamot are applied to the skin followed by exposure to UVA. After that detection, using for cosmetic purpose of bergamot was decreased. However bergamot is stil using in colognes, aromatherapy oils. Nowadays aromatherapy very popular as a consequence of several cases were reported related bergamot aromatherapy oil in the literature. Additionaly there is a case report of berloque dermatitis mimicking child abuse in the literature. Berloque dermatitis was caused by perfume in the our case. The aim of the present this case was attrack attention phototoxic effects of bergamot and hyperpigmented lesions.

Keywords: PIGMENTATION, BERLOQUE DERMATITIS, BERGAMOT

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Figure 1: *Hyperpigmented patchy skin lesions on the face and neck in the dermatologic examination*

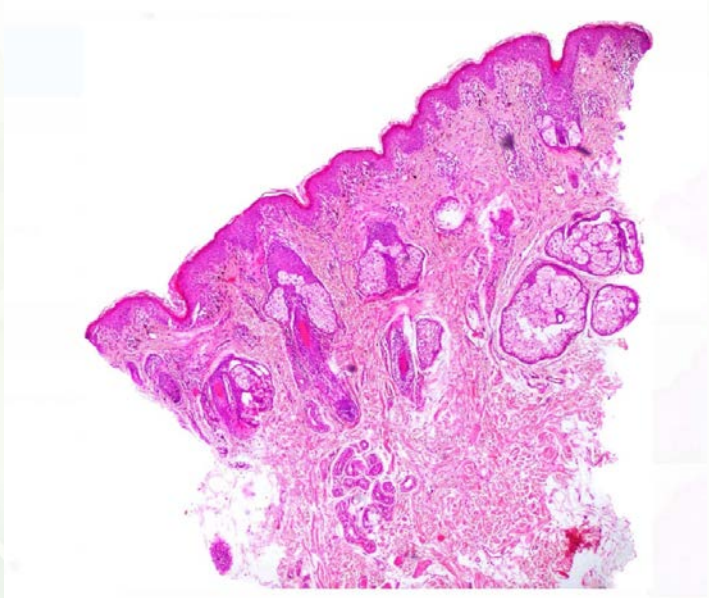

Figure 2: Basal vacuolar degeneration, necrotic keratinocytes, and an increasing number of melanocytes on the dermoepidermal junction (H&E, x40).

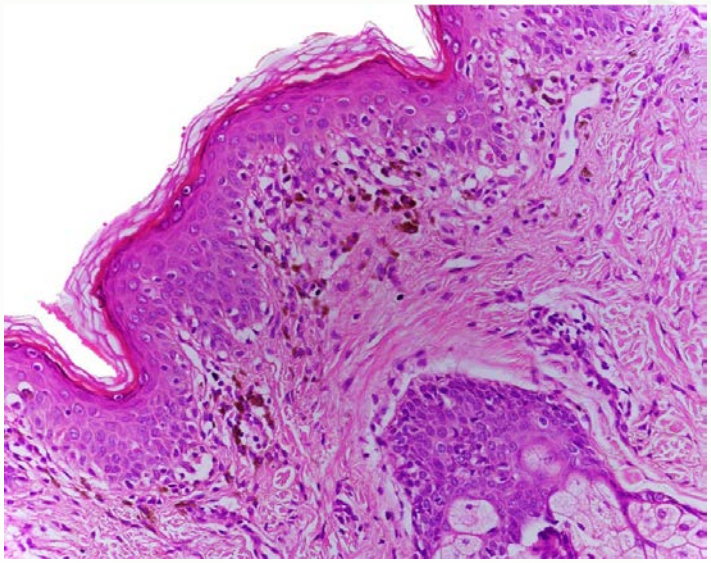

Figure 3: Prominent basal vacuolar degeneration in the dermoepidermal junction. Lymphohistiocytic infiltrate and melanophages in the papillary dermis (H&E, x400).

EFFICIENCY OF SQUARIC ACID DIBUTYL ESTER THERAPY IN TREATMENT RESISTANT CASES OF VERRUCA VULGARIS AND VERRUCA PLANTARIS

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Introduction: Verrucae are benign lesions that develop as a result of infection of the skin and mucous membranes with human papillomaviruses (HPV). In general, its prevalence in the population is 10%, and it is seen equally in men and women. Verrucas are transmitted from person to person by direct contact. Although there are various treatments against HPV, a specific antiviral agent has not been developed yet. The difficulty in the treatment of verruca vulgaris and verruca plantaris is that the treatment process of the disease is long and requires patient compliance. Invasive treatments, on the other hand, often involve some problems such as requiring multiple sessions, causing treatment non-compliance especially in pediatric patients, and the frequency of recurrence(1,2,3,4).

Squaric acid dibutyl ester (SADBE) is a chemical molecule used in the treatment of various diseases in dermatology and can cause allergic contact dermatitis when applied topically. The advantage of SADBE is that it does not have mutagenic effects observed in other sensitizing molecules, therefore it can be used safely in the pediatric age group and can be easily applied by the patient at home. In our study, SADBE was administered to one group of cases with verruca vulgaris and verruca plantaris resistant to other treatment methods, and placebo to the other group, and the effectiveness of SADBE was investigated by quantitative measurement methods.

The results were compared with the results of other studies using SADBE in the treatment of verruca vulgaris and plantaris, and the advantages and disadvantages of SADBE over other treatment methods were discussed(5,6,7).

Materials and Methods: The cases were selected from patients with verruca vulgaris and plantaris who applied to Haydarpaşa Numune Hospital Dermatology Outpatient Clinic. A total of 46 patients who were resistant to previous treatments or could not tolerate invasive interventions were included in the study. The ages of the patients, of which 29 were female and 17 were male, ranged from 9 to 49 (mean: 21.24). The duration of Verruca lesions ranged from 2 to 480 months (mean: 37.41 months). Individuals with verrucas in cosmetic areas such as the face and anogenital region, having a systemic disease, diagnosed with chronic allergic contact dermatitis, receiving immunosuppressive therapy, children younger than 2 years of age, and pregnant or lactating women were not included in the study.

Complete blood count, anti-HIV and serum immunoglobulin levels (IgA, IgG, IgM, IgE) and immune systems of all patients were evaluated and those with normal results were included in the study. Verbal and/or written consent was obtained from the patient or the patient‘s parents, by giving information about the rationale and duration of the treatment, and possible side effects of the drugs to be used. Approval of the local ethics committee was obtained for this study

The study was designed as controlled and prospective. Two groups of 23 people were formed. SADBE was administered to one group and placebo to the other group.

In the study, a solution of 3% SADBE in acetone was first applied to an area of 1 cm2 on the inner surface of the upper arm to the SADBE group. After 1 week , the patient was checked for sensitization. The development of erythema, papule and vesicle in the area where SADBE was applied was evaluated as a sign of sensitization. 0.3% SADBE solution was applied to the patients in weekly periods by the physician directly on the verruca lesions with a cotton applicator. In the placebo group, 10% trichloroacetic acid solution was applied to an area of 1 cm2 in the forearm area in the first week. The patients were seen again 1 week later. Liquid Vaseline solution was applied directly on the verrucae with a cotton applicator for 7 sessions at one-week intervals by the doctor.

Verrucae lesions were photographed at the beginning and end of the study. Verrucae areas were calculated before and after treatment with geometric morphometry analysis software (Tpsdig V2.04 2005, F.James Rohlf, Ecology & Evolution,SUNY at Stony Brook) to evaluate response to treatment. At the end of the 7-week treatment, the patients were followed up for

recurrence at monthly intervals for 3 months.

Results: In the study, the efficacy of SADBE treatment was evaluated in a total of 46 patients. SADBE and placebo groups were treated once on sensitization and 7 times on verruca lesions in 8 weeks. As a result, a 27% reduction in the total area of verruca lesions was found in all patients at the end of the treatment in the SADBE group, compared to 20% in the placebo group. Sensitization occurred in 20 (86%) of 23 cases in the SADBE group.

After SADBE application, limited angioedema of the lip and intolerable extensive allergic contact dermatitis developed in 3 patients.

Complete response to treatment in 2 (8%) patients (5), good response in 3 (13%) (4), moderate response in 2 (8%) (3), 4 (17% had minimal response(2), 6(26%) did not respond to treatment(1), 6(26%) showed an increase in lesions(0). Of the patients given placebo treatment, 3 (13%) had complete response(5), 1(4%) had good response(4), 1(4%) had moderate response(3), 13. (56%) did not respond to treatment(1), and 5 (26%) had an increase in lesions(0). (Graph 1, Photo 1, Photo 2)

Discussion: SADBE is a molecule that was first synthesized in 1979 and has gained popularity in Europe and South East Asia for the treatment of alopecia areata and verruca vulgaris. Since SADBE dissolved in acetone is an unstable molecule, it should be kept in the refrigerator when not in use. Not mutagenic according to Ames classification(6)

The difference of our study from other SADBE studies is that it is a placebo-controlled study. In addition, in the publications we mentioned, subjective methods depending on the observer were used in the evaluation of lesions. In our study, morphometric analysis software, which is an objective evaluation method and not based on subjective observation, was used.

Conclusion: As a result of our study, it has been shown that SADBE is not superior to placebo in terms of treatment efficacy in treatment-resistant verruca vulgaris and verruca plantaris cases. Unlike other publications on this subject, only topical SADBE treatment was applied to the patients during the course of the study. The difference in treatment efficacy may be due to the fact that other treatment methods were not applied together with SADBE, and that SADBE was applied relatively longer and more frequently in other studies. Although the treatment of verruca lesions is mentioned as one of the problematic areas in dermatology in the current period, we think that immunization methods that will provide a specific immune response against HPV lesions can be used in the treatment of verruca lesions.

In conclusion, SADBE was not found to be more effective than placebo in treatment-resistant verruca vulgaris and verruca plantaris lesions. However, if it is used for a longer time and at more frequent intervals or combined with other exfoliating agents, the success of the treatment may increase. Additional controlled studies are needed, especially in the pediatric age group, as it is an alternative to painful and traumatic procedures, can be easily administered by the patient at home, and is a safe treatment because it is not mutagenic.

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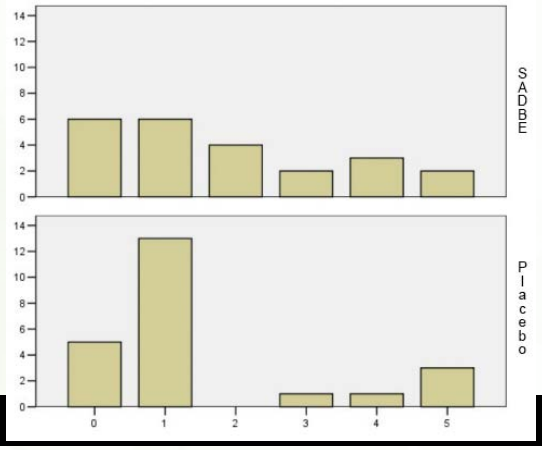
Figures



Graph 1 . Response to Treatment

Photo 1 . Verruca vulgaris lesions before SADBE application

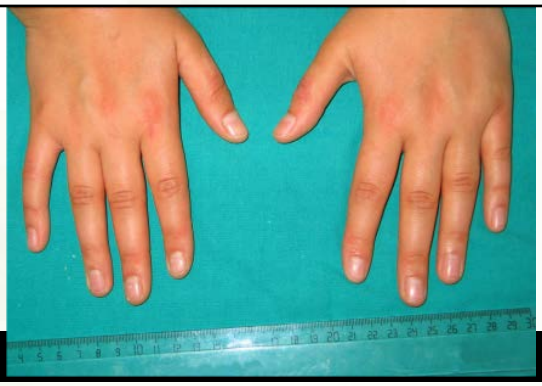


Photo 2 . Verruca vulgaris lesions resolved after SADBE treatment sessions

NASOLABIAL AREA CORRECTION WITH MULTI-LEVEL FILLER PLACEMENT.

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Abstract: We used 2 types of fillers for the nasolabial area correction with placement of each filler to a different plane.

1. Teoxane Teosyal RHA3 filler was placed into subdermal plane of the nasolabial areas followed by

2. Teoxane RHA Redensity filler placed superficially in the same areas

Standard precautions were used with aspiration prior to injections.

Explanation: Nasolabial creases have dermal and epidermal defects which make this area difficult to correct. Acceptable techniques recommend subdermal plane for the filler placement. But because nasolabial area also has sub epidermal volume loss, filler that is placed in the deep plane may not provide adequate correction. Hence using thicker filler for the subdermal placement and thinner filler for the superficial plane would improve overall appearance with a higher level of patient satisfaction.

Keywords: fillers, subdermal plane, superficial placement, nasolabial creases

1. Introduction

Correction of the Nasolabial area is a difficult task. (1)

Multiple approaches including placement of filler into subdermal plane or placement of filler into Ristow's space will improve general appearance. But considering that nasolabial grove presence is a result of multiple processes it would be prudent to explore other approaches for correction.

Nasolabial groove appearance related to a loss of fat volume in multiple facial fat pads and thinning and loss of elasticity of the overlaying skin.

Numerous therapeutic options address loss of volume with placement of dermal filler or fat grafting into deeper layers.

Skin defect treated with subcision (2), rhytidectomy or skin tightening with Nd:YAG laser or radiofrequency devices.

Understanding that nasolabial area needs correction at multiple planes we suggest placement of fillers with different properties to a deep plane and superficial plane.

2. Technique

We used Teosyal RHA Teoxane fillers.

Teosyal RHA Teoxane Resilient Hyaluronic Acid fillers are gels with long HA chains stabilized by natural and chemical crosslinks. (3)

RHA 3 would fall into a category of a hard filler with a higher viscosity and elasticity, those type of fillers provide lift and support with minimal product migration.

RHA 1 or RHA Redensity would represent soft filler with lower viscosity and elasticity with ability to spread into soft tissues.

Teoxane Teosyal RHA 3 filler was placed into subdermal plane of the nasolabial areas followed by

Teoxane Teosyal RHA Redensity (used as RHA 1 on the European market) filler placed superficially (sub

epidermal) in the same areas.

We used standard company supplied needles. Aspiration was utilized in order to avoid vascular occlusion. Filler placement was with small boluses followed by manual distribution.

There were no complications after procedures and patients expressed high level of appreciation due to instant correction of the nasolabial creases.

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A CASE OF BREAST LOBULAR CANCER DIAGNOSED WITH CUTANEOUS METASTASES

E. Kaplan, Y. Yuyucu Karabulut, S.Çakır, Ü.Türsen

İntroduction

In women, breast cancer is the leading cancer diagnosis and the second leading cause of cancer-related death(1), as well as the most common malignancy to metastasize to the skin(2). Cutaneous breast carcinoma may present as cutaneous metastasis or can occur secondary to direct tumor extension. Five percent to 10% of women with breast cancer will present clinically with metastatic cutaneous disease, most commonly as a recurrence of early stage breast carcinoma(2).

Case Report

A 49-year-old female patient with no known disease was admitted to our clinic with conglomerate nodular lesions lasting 1.5 months, forming diffuse sclerodermoid indurations on the chest wall and abdomen and neck.The lesions were not itchy or painful. There were no symptoms suggestive of malignancy such as weight loss or night sweats.

The mother had a history of breast cancer. This was the patient's first admission to the hospital due to skin lesions and the patient had not received any treatment before.

Atypical cells and lymphocytes were seen in the tzanck test. Cutaneous lymphoma and cutaneous metastasis, leukemia cutis, sarcoidosis are included in differential diagnosis. Biopsie was performed. Hematoxylin and eosin staining revealed a relatively monomorphic epithelioid cell infiltrate extending from the superficial reticular dermis into the deep dermis and displaying an open chromatin pattern and pink cytoplasm was observed, as well as dermal collagen thickening. Linear, single-filing cells along with focal irregular nests and scattered cells were observed.

Immunohistochemical staining was positive for cytokeratin 7, estrogen receptor, progesterone receptor; focal gross cystic disease fluid protein 15 positivity also was present. Cytokeratin 20, LCA, CD3, CD20, e-cadherin, mammoglobulin stains were negative. Findings identified were consistent with metastatic cutaneous lobular breast carcinoma.

PET CT was performed on the patient. In PET CT, In addition to left axillary lymphadenopathy, heterogeneous bilateral multiple nodular lesions were detected on breasts, the largest of which was in the upper inner quadrant of the left breast with a diameter of approximately 2.5 cm.

Conclusion

Invasive lobular breast carcinoma represents approximately 10% of invasive breast cancer cases. Compared to invasive ductal carcinoma, there tends to be a delay in diagnosis often leading to larger tumor sizes relative to the former upon detection and with lymph node invasion. These findings may be explained by the greater difficulty of detecting invasive lobular carcinomas by mammography and clinical breast examination compared to invasive ductal carcinomas (3-5). Cutaneous metastases of breast cancer most commonly are found on the anterior chest wall and can present as a wide spectrum of lesions, with nodules as the most common primary dermatologic manifestation (6). Providers should be aware of the varying clinical presentations that may arise in the setting of cutaneous metastasis. When faced with lesions suspicious for cutaneous metastasis, biopsy is warranted to determine the correct diagnosis and ensure appropriate management.

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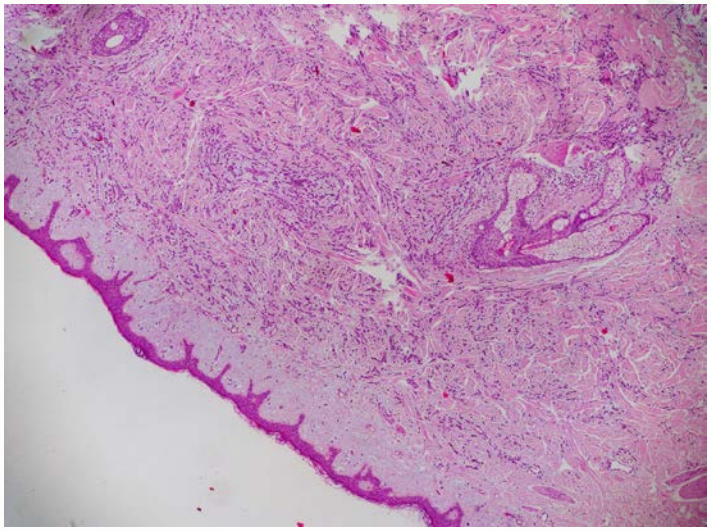

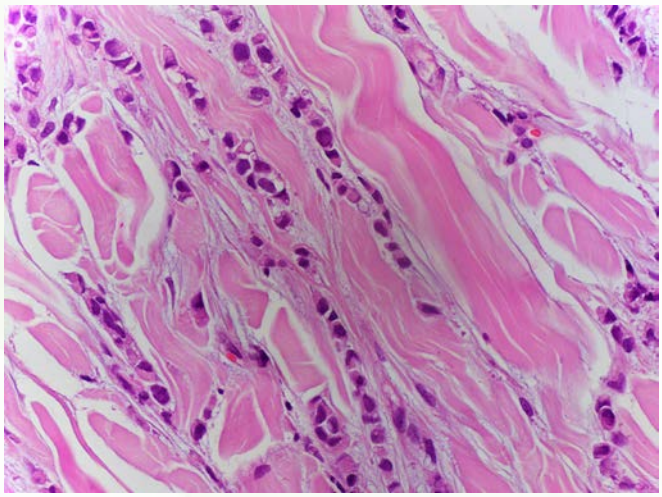

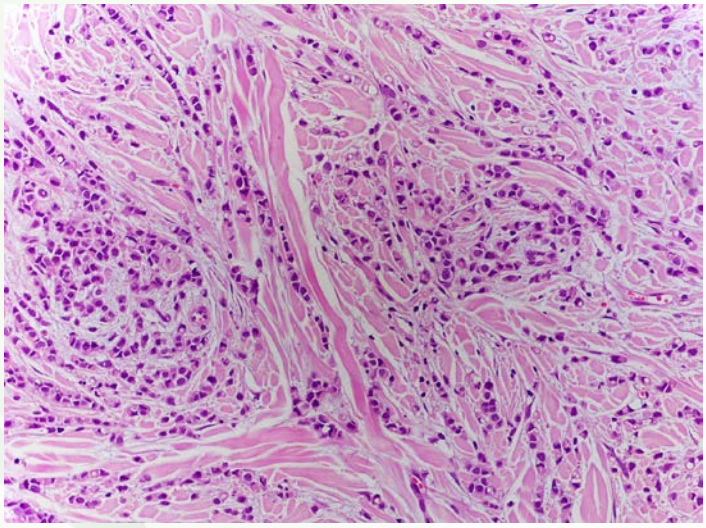

A RARE CASE OF CUTANEOUS LEIOMYOSARCOMA

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CASE PRESENTATION

A 77 year old male patient presented to the dermatology outpatient clinic with a lesion located at his left gluteal region. Physical examination revealed a verrucous looking plaque lesion which felt hard with palpation. Preliminary diagnoses from the clinician were calcified pilomatrixoma, verrucous carcinoma and dermatofibrosarcoma protuberans (DFSP). The patient underwent an incisional biopsy. Histopathologic examination showed a cellular lesion that consisted of relatively uniform, spindle shaped cells that had eosinophilic cytoplasm, forming fascicules located in the dermis (Fig.1). The cells had nuclear enlargement and cigar shaped nuclei. Brisk mitotic activity and atypical mitoses were observed. The lesion infiltrated into the neighboring dermis and focally involved the subcutaneous adipose tissue (Fig.2).

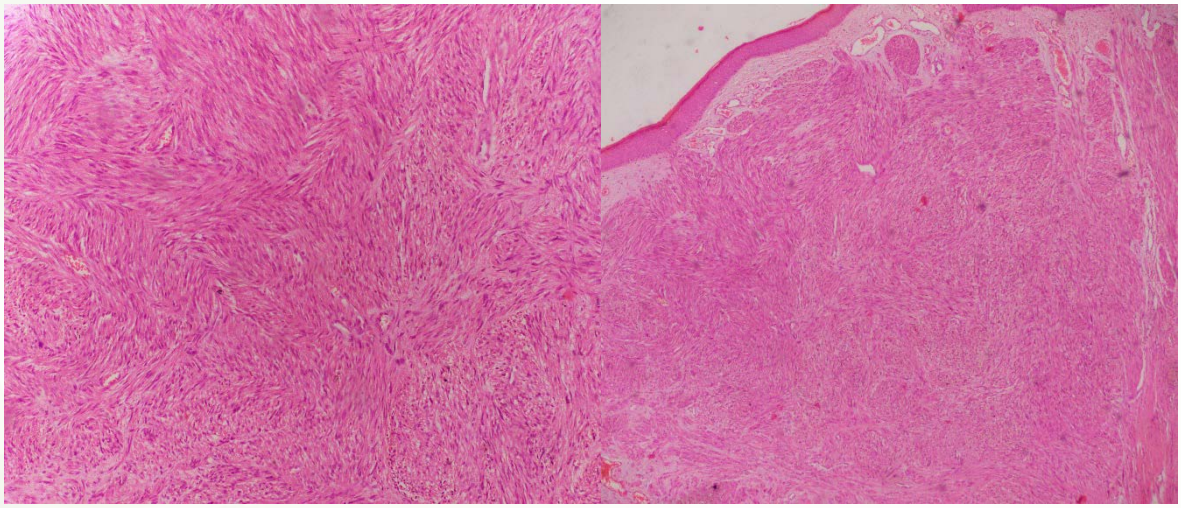

Fig.1 The lesion is composed of spindle shaped cells that forms fascicules located in dermis.

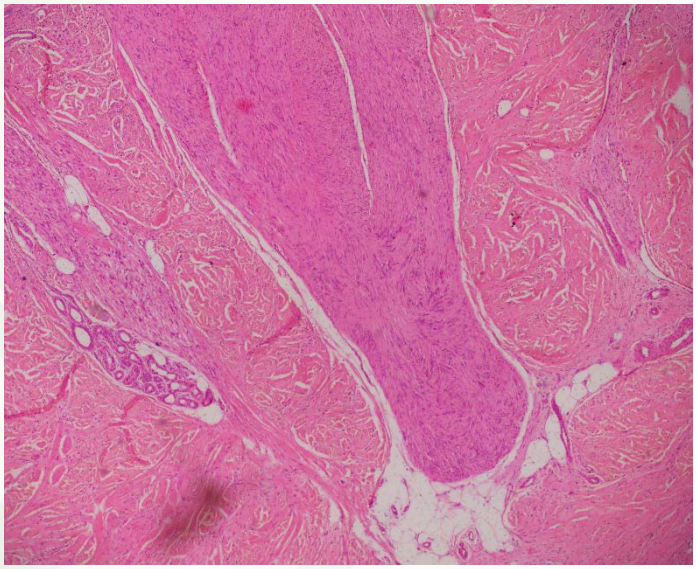

Fig.2 The lesion focally infiltrates subcutaneous adipose tissue.

On detailed immunohistochemical analysis, the tumor cells showed diffuse strong positivity with h-caldesmon (Fig.3) and desmin. There was no staining with CD34. Ki67 proliferative index was approximately %30 (Fig.4). According to the microscopical examination of the biopsy sample and immunohistochemistry analysis, the lesion was reported as Cutaneous leiomyosarcoma (Atypical smooth muscle tumor). Later the patient underwent total excision of the lesion. The findings were also consistent with Cutaneous Leiomyosarcoma and therefore confirmed the initial diagnosis.

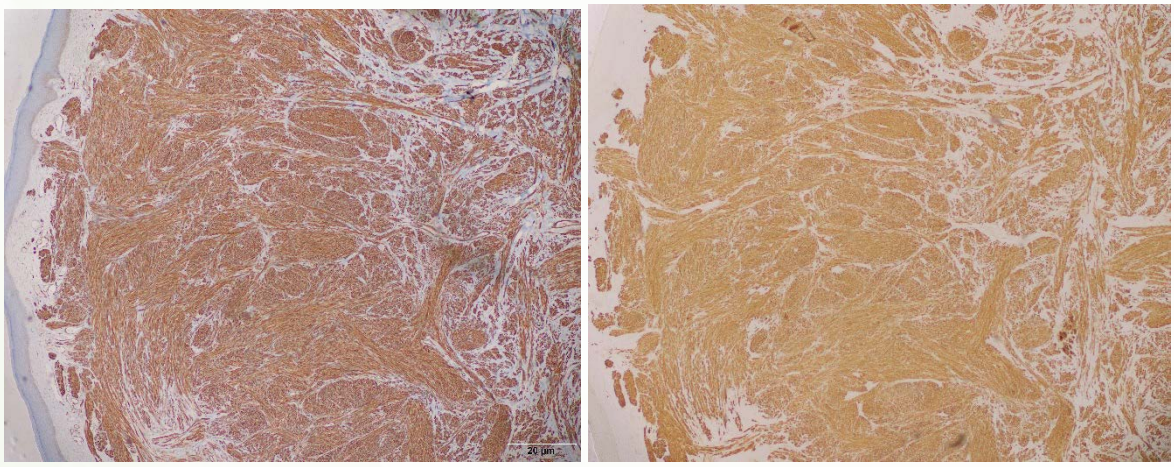

Fig.3 Tumor cells show diffuse strong immun reactivity with h-caldesmon and desmin.

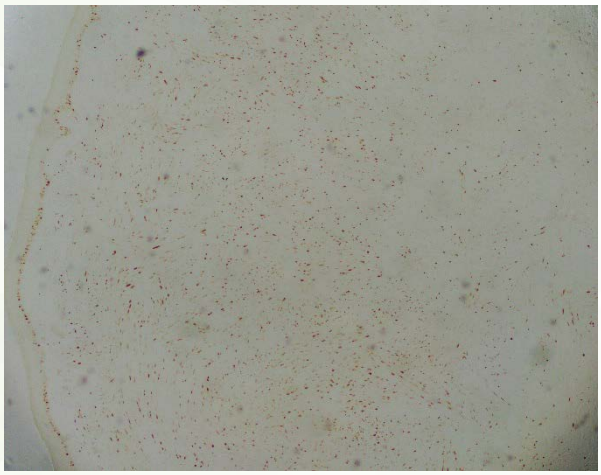

Fig.4 The Ki67 proliferation index of the tumor was %30.

DISCUSSION

Leiomyosarcomas are tumors derived from smooth muscle that arises in deep soft tissue, the uterus, and, more rarely, the dermis(1). It accounts for approximately 5-10% of all sarcomas(1). Cutaneous Leiomyosarcoma is a rare malignant neoplasm with a muscular origin, representing around 2%-3% of all cutaneous soft tissue sarcomas and 0.04% of all skin tumors.(3) Cutaneous Leiomyosarcoma can occur at any age, but it mostly affects older adults, with a peak incidence between 60 and 70 years(4). Ionizing irradiation, sunlight, antecedent traumatic injury, chemicals and lupus vulgaris have been previously associated with this type of tumor. It is more common in males and appears to be more common in whites. It can occur at a wide distribution, the most frequent locations being the head and neck region as well as the extremities(2). Histologically, Cutaneous Leiomyosarcoma is characterized by a dermal proliferation of elongated spindle-shaped cells arranged in interweaving fascicles with blunt-ended, cigar-shaped nuclei and eosinophilic cytoplasm. Mitotic figures are usually easily identifiable(3). Morphologic differential diagnosis includes a large variety of other malignant spindle cell neoplasms like desmoplastic malignant melanoma, spindle cell synovial sarcoma, spindle cell angiosarcoma, fibrosarcoma, malignant fibrous histiocytoma and malignant peripheral nerve sheath tumor. Immunohistochemistry studies are therefore auxiliary to a definitive diagnosis(5).

On immunohistochemical examination, the neoplastic cells show reactivity to smooth muscle actin and vimentin. More

than half of the lesions show positive reaction for desmin(4). Caldesmon staining is positive in a vast majority of cases(5). Standard treatment is surgical resection with free lateral margins of 3–5 cm including subcutaneous tissue reaching the fascia (2).

In conclusion, although leiomyosarcomas usually occur in deep soft tissues, cutaneous leiomyosarcoma should also be kept in mind if there is a spindle cell lesion located in the dermis. Immunohistochemistry studies combined with histological examination are crucial for differential diagnosis because cutaneous leiomyosarcomas could resemble a wide array of other tumors.

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A case of lichen planus pemphigoides

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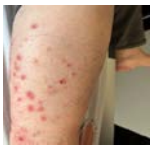
Abstract:

Lichen planus pemphigoides (LPP) is a rare, acquired autoimmune disease. It is characterised by coexistence of lichenoid and bullous pemphigoid-like lesions. The bullous lesions of LPP are typically located outside of LP lesions on normal skin, but sometimes these blistering lesions can be restricted to the lichenoid plaques. It is thought that the basement membrane damage seen in lichen planus triggers autoimmune bullous diseases by causing some antigens to be exposed. Histopathologic examination shows subepidermal bulla formation and direct immunofluorescence examination reveals band-shaped IgG and C3 deposition in the basement membrane of lesional and normal skin. This picture is the same as for bullous pemphigoid. In this case, we present a 69-year-old patient with recurrent lichenoid papules and bullous lesions on the tibial area for six years.

Case Report:

A 69-year-old woman presented to our outpatient clinic with a six-years history of recurrent rash and pruritus. Previously, various topical treatments were given at an external center, but they did not help. She has hypertension, diabetes and bronchial asthma. She uses irbesartan, sitagliptin/metformin, gliclazide, salbutamol and tizanidine. Dermatologic examination revealed excoriated areas on the abdomen, bullous lesions on the abdomen and both anterior tibiae with papular onset that were described to enlarge over time and eroded areas. A biopsy was taken with a prediagnosis of lichen planus pemphigoides. The biopsy specimen showed subepidermal separation and lymphohistiocytic cell infiltration in a lichenoid pattern in the superficial dermis. Systemic and topical steroid, topical antibiotic treatment was started The lesions were gradually decreased.



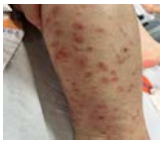


Figure 1 and 2: Papular, plaque, lichenoid and eroded lesions on the tibial areas

Discussion:

LPP is a rare disease. In addition to bullous pemphigoid and bullous lichen planus, differential diagnosis of LPP includes several other dermatoses such as subacute cutaneous lupus erythematosus, paraneoplastic pemphigus, erythema multiforme, pemphigoid nodularis. It should be considered in cases where both lichenoid plaques and bulla formation are observed in normal skin. Systemic corticosteroids usually result in remission but 20% of recurrence rate is inevitable. Second-line treatment agents include hydroxychloroquine, mycophenolate mofetil, tetracyclines, nicotinamide, dapsone, and isotretinoin (1). Tumor necrosis factor-alpha and other proinflammatory cytokines are thought to play an important role in the pathogenesis of LPP. Therefore, immunosuppressive drugs such as ustekinumab may also be beneficial (1).

Conclusion:

LPP is a unique dermatosis and must be differentiated from similar conditions to provide appropriate treatment.

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PINK, PURPLE NODULAR LESION IN THE GLUTEAL REGION: PRIMARY CUTANEUS B CELL LYMPHOMA

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Introduction: Primary cutaneous lymphomas are unique, heterogeneous group of lymphoproliferative disorders which have primary cutaneous manifestation in the absence of systemic involvement of lymph nodes, bone marrow, or visceral organs at the time of diagnosis. Among the primary cutaneous lymphomas, B-cell lymphoma is much less common and accounts for 20%–25% of cases. Primary cutaneous diffuse large B-cell lymphomas (PCDLBCLs) are rare but aggressive neoplasms with poor prognosis, most commonly affecting elderly women and manifesting with rapidly enlarging nodule(s) on one or both legs[1, 2]. In this article, we present a case of PCDLBCL diagnosed on the basis of clinical features, histomorphology, and characteristic immunohistochemical expression.

Case Report: An 80-year-old male patient was admitted to our clinic with the complaint of a rapidly growing purple-colored swelling on the left hip for one year. On clinical examination, there were firm purple nodular lesions and pink plaques in the left gluteal region (Fig. 1). A biopsy was taken and histopathological and immunohistochemical analysis revealed diffuse large B cell lymphoma.

The patient was referred to the Department of Hematology. Positron emission tomography, complete blood cell count, peripheral smear examination were made and no systemic involvement was observed. He had no weight loss, fever, night sweats, and additional complaints. R-CHOP (rituximab, doxorubicin, vincristine sulfate, cyclophosphamide) chemotherapy was started for the patient. Clinical and radiological response was achieved and he was decided to be followed-up.

Discussion: Primary cutaneous B-cell lymphomas (PCBCL) were previously classified into three distinct subtypes; primary cutaneous marginal zone lymphoma, primary cutaneous follicle center lymphoma and primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL, LT). [3] In an update in 2018, a new provisional entity of Epstein–Barr virus positive mucocutaneous ulcer was included. [4] Among all the PCBCLs, PCDLBCL, LT has the worst prognosis, with a 5-year disease-specific survival between 40 and 60%. Recurrences and extracutaneous progression are common. [5] In our patient, after chemotherapy, the lesion regressed and no recurrence was observed in 6 months follow-up period.

The term PCLBCL, LT is preferred for both lesions on the legs and similar lesions at the other sites. [6] Lesions outside of the lower extremities develop in 10% to 15% of cases. [7] Our case is PCLBCL, LT with gluteal region involvement.

In conclusion, primary cutaneus B-cell lymphoma should be considered in the differential diagnosis of pink-purple nodular lesions in the elderly. Collaboration with the Department of Hematology and screening for systemic involvement should be considered.

Keywords: primary cutaneous B-cell lymphoma, primary cutaneous diffuse large B-cell lymphoma, pink-purple nodular lesions

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PEMBROLIZUMAB RELATED LICHENOID DRUG ERUPTION

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Introduction

Pembrolizumab is humanized monoclonal antibody that inhibit the interaction between the programmed death-ligand 1(PD-L1) and PD-L2 ligands on tumor cells and PDL-1 receptor on T-cells. (1) Pembrolizumab is used in the treatment of many cancers such as advanced melanoma, non-small cell lung cancer, Hodgkin lymphoma, Primary Mediastinal B-cell lymphoma and urethral carcinoma. (2) Pembrolizumab triggers T-cell reaction and it is causing T cells to attack healthy cells. This leads to appear of various autoimmune diseases. (1) Among the cutaneous immune mediated side effects, maculopapular rash, pruritus, psoriariform and lichenoid eruption are the most reported types.(3) Here we report a case of patient with non small cell lung cancer undergoing pembrolizumab therapy who developed a lichenoid drug eruption.

Case Report

A 65-year-old female patient presented with pruritic erythematous scaly papules and plaques. These lesions started 1.5 months ago on the trunk, bilateral arm flexor regions, dorsum of the hand, and bilateral legs. Her medical history include breast carcinoma, psoriasis and non-small cell lung cancer diagnoses in remission. She had a history of using 16 courses of pembrolizumab every 3 weeks for 1 year for the treatment of non-small cell lung cancer. She had not received any treatment for these rashes. Histopathology study of performed biopsy was reported as “interphase dermatitis compatible with drug eruption”. Treatment was started by single dose of ıntramuscular betamethasone dipropionate and betamethasone sodium phosphate and topical methylprednisolone aceponate . Significant regression was observed in the lesions of the patient at the follow-up 3 weeks later under these treatments.

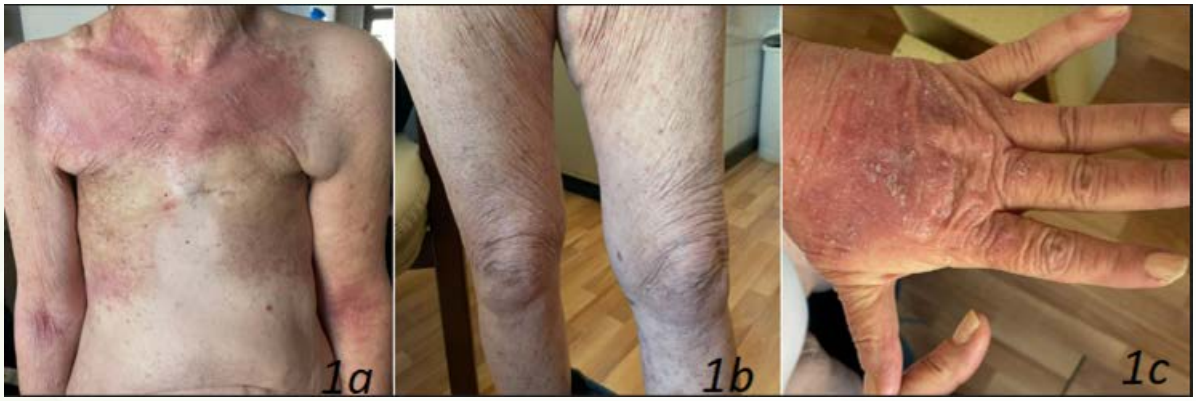

Image 1a/1b/1c: Erythematous scaly papules and plaques on the trunk, bilateral arm flexor regions, on the dorsum of the hand, and on the bilateral legs

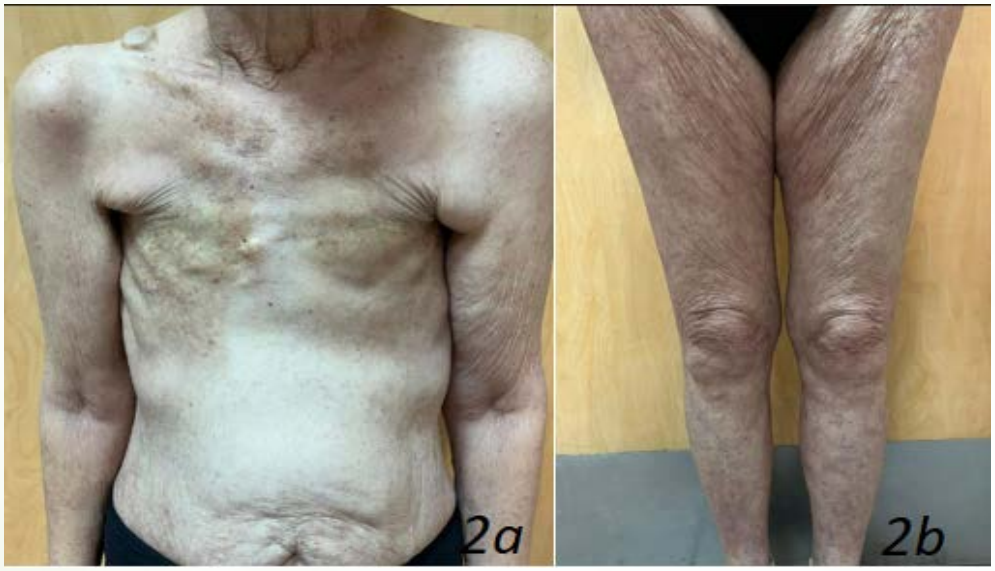

Image 2a/2b: Significant regression was observed in the lesions 3 weeks after topical and systemic corticosteroid treatment.

Discussion

Pembrolizumab, an immune checkpoint inhibitor, is a revolutionary immunotherapeutic agent in cancer treatment. (4) Anti PD1 treatments are generally well tolerated, but cutaneous side effects are observed in 18-42% of patients.(5) Among the cutaneous immune mediated side effects, maculopapular rash, pruritus, psoriariform and lichenoid eruption are the most reported types. (3) The risk of autoimmune diseases due to PD1 inhibitors also increases. (1) In this case we report lichenoid drug eruption that started at the 16th cycle of pembrolizumab treatment. In the literature, it has been recommended to use topical steroids in mild cases, systemic steroid therapy in advanced stages, and to interrupt immunotherapy in advanced stages where life-threatening results may occur.(3) In this case, similar to the literature, the patient responded to systemic and topical steroid combination and the rashes regressed significantly. Early recognition and treatment of immunotherapy associated adverse drug eruption are critical to provide patient safety.(6) In this case report, it is aimed to draw attention to pembrolizumab-related cutaneous side effects and to provide early diagnosis and management.

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A TREATMENT OPTION IN THE ACUTE GVHD: MESENCHYMAL STEM CELL THERAPY

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Introduction: Allogeneic Hematopoietic Stem Cell Transplantation (allo-HSCT) is an effective treatment option for many malignant and non-malignant hematological diseases by stimulating the Graft-Versus-Leukemia (GvL) immune response. However, as a result of this treatment, Graft Versus Host Disease (GVHD), may occur when the donor T cells recognize the recipient's tissue as foreign. GVHD can be life-threatening. .(1) GVHD is an immune phenomenon that can occur with blood transfusion, solid organ transplantation, autologous HSCT and allogeneic HSCT. It may present acutely or chronically. It is a multisystemic picture that can involve many organs; including the lung, hepatobiliary system, gastrointestinal tract, and skin.(2) The first and most common manifestation of GVHD is a maculopapular eruption of the skin. While mild skin involvement tends to regress spontaneously; In cases with severe skin involvement, bulla formation, desquamation or erythroderma may be observed.(3) The mortality rate in this potentially fatal disease can reach up to 15%. (2) Topical and systemic corticosteroids are the first-line treatment option in the treatment of GVHD, while various immunosuppressive and immunomodulatory treatments are used in resistant cases. (1) Here we report a case of patient with acute GVHD that was resistant to systemic steroid therapy and benefited from mesenchymal stem cell (MSC) treatment.

Case Report: A 21-year-old patient who had allo-HSCT 20 days ago due to the diagnosis of AML; admitted to our outpatient clinic with diffuse maculopapular eruption which was more prominent on the trunk. The patient had itching and fever. The histopathologic finding of skin showed "minimal perivascular dermatitis characterized by sparse neutrophil leukocytes". Since GVHD was considered clinically, the patient was administered cyclosporine, mycophenolate mofetil and methylprednisolone treatments by hematology for a month. In addition to all, ruxolitinib was used for control skin rashes. However, the skin rashes were resistant to all of these treatments. Therefore, we performed rebiopsy and it was reported as compatible with GVHD Grade 2. The patient had no other system involvement, except skin involvement. Extracorporeal photopheresis (ECP) treatment was started for the patient 2 days in a week. 4 weeks later, once a week MSC treatment was added to the treatment. Significant regression was observed in the lesions at the follow-up 2 weeks later.

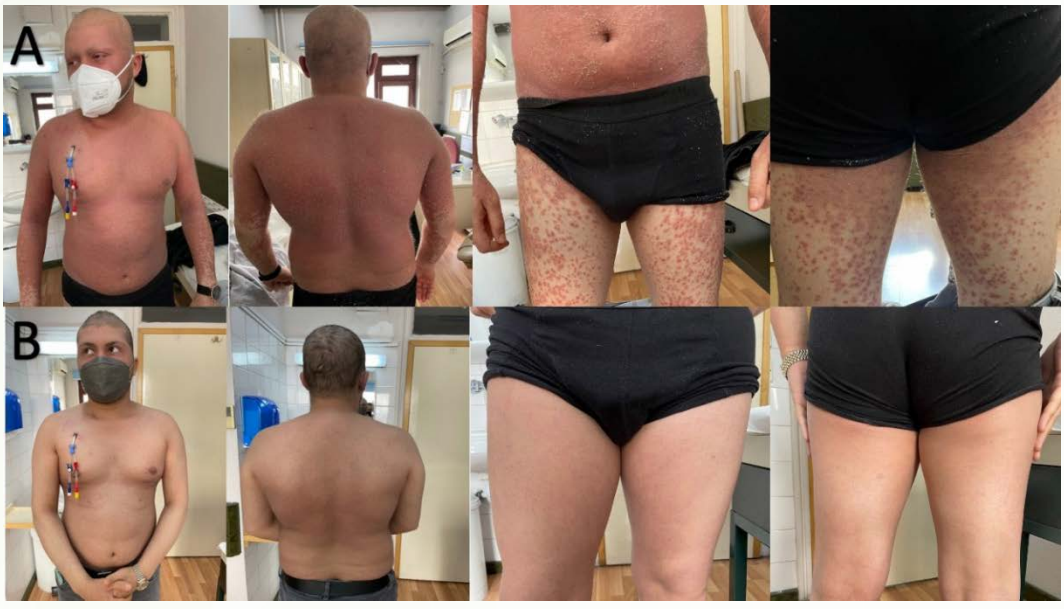

Image A: Before Treatment

Image B: 2 weeks after Mesenchymal Stem Cell Therapy

Discussion

GVHD is an important immune-mediated complication following allogeneic hematopoietic stem cell transplantation. Depending on host and donor-related factors, it affects 40-60% of patients ant it has 15% mortality rate after HSCT.(4) GVHD is classified as acute and chronic. Acute GVHD occurs 100 days or less after HSCT. Persistent, recurrent, or late-onset acute GVHD occurs over 100 days. Chronic GVHD can occur at any time after HSCT.(5) The skin, gastrointestinal tract and hepatobiliary system are the main sites of involvement in acute GVHD. The combination of classic maculopapular eruption, diarrhea and high bilirubin levels strengthens the diagnosis. However, most of the involvements are not observed at the same time, which makes diagnosis difficult. Skin involvement is the first and most common symptom. Classically, it starts as a maculopapular eruption and may turn into erythroderma, as in this case.(4) In cases with only skin lesions, acute GVHD may be confused with drug eruptions and viral exanthema. This makes diagnosis difficult. (6) According to the European consensus recommendations, routine skin biopsy is recommended. There is no direct relationship between clinic and histopathology. Histopathology may not always yield definitive results in clinically compatible patients. Treatment should not be delayed because early treatment affects the prognosis. In this case, the first biopsy was inconsistent with the clinic. However, treatment was started due to clinical suspicion. Control biopsy was reported as compatible with GVHD Grade 2. (7)The histopathological grading, clinical staging and grading of acute GVHD are as shown in the table below.

Histopathological Grading (4)		Skin Staging (4)		Clinical Staging (4)	
0	Normal skin	0	No GVHD rash	1	Skin Stage 1-2
1	Mild vacuolization of epidermal cells	1	Maculopapular rash less than 25% of body surface area (BSA)	2	Skin stage 3 or liver/intestinal stage 1
2	Diffuse vacuolization and dyskeratotic bodies in basal cells	2	Maculopapular rash in 25-50% of BSA	3	Skin stage 3 or liver stage 2-3/ intestinal stage 2-4
3	Subepidermal separation	3	>50% of BSA maculopapular rash	4	Skin stage 4 or Liver stage 4
4	Complete epidermal separation	4	Generalized erythroderma + bullous formation		

Based on the table, this case was histopathologically grade 2; clinically it is stage and grade 3.

Topical corticosteroids and calcineurin inhibitors are used in grade 1 cases in the treatment of acute GVHD. Systemic corticosteroids are the first-line treatment in cases with grades 2-4. Extracorporeal photopheresis (EKF), mycophenolate mofetil, Anti-Tumor Necrosis Factor, rapamycin inhibitors, ruxolitinib, methotrexate, pentostatin, alemtuzumab and MSC treatments can be used in patients who do not benefit. MSCs are a population of undifferentiated pluripotent stem cells that modulate the immune and inflammatory response and facilitate the repair of connective tissues. MSC is an undifferentiated pluripotent stem cell population that modulates the immune and inflammatory response and facilitates connective tissue repair. In 2004, Blanc et al. demonstrated the efficacy of MSCs in the treatment of GVHD for the first time. Again, Blanc et al. 2008 showed that it is also effective in corticosteroid-resistant cases. No significant side effects were observed in the studies. (8)

In this case, systemic steroid, mycophenolate mofetil, cyclosporine, ruxolitinib, and ECF were used, and MSC treatment was given when it did not show any benefit. The patient was receiving cyclosporine, ruxolitinib, and ECF treatments simultaneously with mesenchymal stem cell therapy. Significant regression was observed in the lesions in the control follow-up 2 weeks after the start of mesenchymal stem cell therapy. It is difficult to predict whether this regression is due to MSC treatment or the additive effect of other treatments. Since early and effective treatment of GVHD positively affects the prognosis, new treatment options should be evaluated in corticosteroid-resistant cases. (1) MSC treatment can be considered as an effective and safe option in resistant cases.

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CARCINOMA ERYSIPELOIDES: A CASE REPORT

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Introduction: Cutaneous metastases are observed in 5.3% of cancers and usually occur within 3 years of diagnosis. Cutaneous metastases from breast cancer tend to be located in the thoracic region. The dermatological pattern of cutaneous metastases of breast cancer is papulonodular lesions, but erysipeloid infiltration is also possible. Carcinoma erysipeloides is a rare condition observed in 3% of all cutaneous metastases. It presents as a fixed, well-circumscribed erythematous patch or plaque resembling cellulitis or erysipelas. Differential diagnoses include cellulitis, eczema, inflammatory breast cancer, radiation dermatitis, and breast Paget's disease. Here we will present a case of carcinoma erysipeloides, which appeared as the first sign of metastasis in a patient diagnosed with breast cancer that was in remission.

Case: A 49-year-old female patient was admitted to our clinic with an erythematous patch observed on the anterior trunk for 1 month. Systemic and local symptoms were absent. During dermatological examination of the patient, there was a 25 cm surgical scar on the anterior side of the trunk and a widespread erythematous patch around the scar that faded with pressure.(Picture 1) After diagnosis of breast cancer, she underwent left total mastectomy in 2012 and right total mastectomy in 2020. She had been treated by letrazole for 18 months. No recurrence or metastasis was observed 3 months ago. Considering the cellulite/erysipel diagnoses in another center, she was started on amoxicillin/clavulanic acid, topical isoconazole and fusidic acid+betamethasone valerate cream treatments. Despite this treatment for a week no improvement was detected. According to current clinical data, 5 mm punch biopsy was performed considering Carcinoma Erysipeloides. In histopathological examination and immunohistochemical studies, diffuse nuclear staining with GATA-3 was observed in tumor cells . Estrogen and progesterone receptors were negative. Staining was detected in tumor cells with C-ERBB2. Proliferative activity was observed with Ki-67 at a rate of 10-15% in invasive tumor cells.(Picture 1) Since the patient had a clinical history of breast carcinoma, breast carcinoma metastasis was considered first. The fact that the primary tumor of the patient was C-ERBB2 positive supported the diagnosis of metastasis. The patient was evaluated as Carcinoma Erysipeloides with the pathology result and was referred to medical oncology.

Discussion: Carcinoma Erysipeloides is easily confused with erysipel or cellulite, causing delay in diagnosis. (4) In this case, too, the patient developed a well-defined cutaneous lesion resembling an acute infectious process such as erysipel and/or cellulitis. It was misdiagnosed as cellulite and given the wrong treatment. The diagnosis of carcinoma erysipeloides requires rapid diagnosis and treatment in order to increase patient survival. Response to induction chemotherapy is the most important prognostic factor. The prognosis varies according to the underlying cancer type, but generally low survival is observed. (2) While patients with breast cancer have a better prognosis than other cancers, the estimated survival after diagnosis of cutaneous metastases is 50% at 6 months. (1) The median survival for all forms of cutaneous metastasis in breast cancer is 13.8 months, with a 10-year survival rate of 3.1%. Treatments include surgery, chemotherapy, hormonal treatments, and radiotherapy. Topical chemotherapeutic agents may be useful in small thin carcinomas. Electrochemotherapy combines electrical current pulses and intralesional or systemic chemotherapy agents. Photodynamic therapy is another option. (3) Therefore, a multidisciplinary evaluation is important for the rapid initiation of treatment. This case report highlights the need for accurate differential diagnosis of carcinoma erysipeloides and prompt initiation of treatment.

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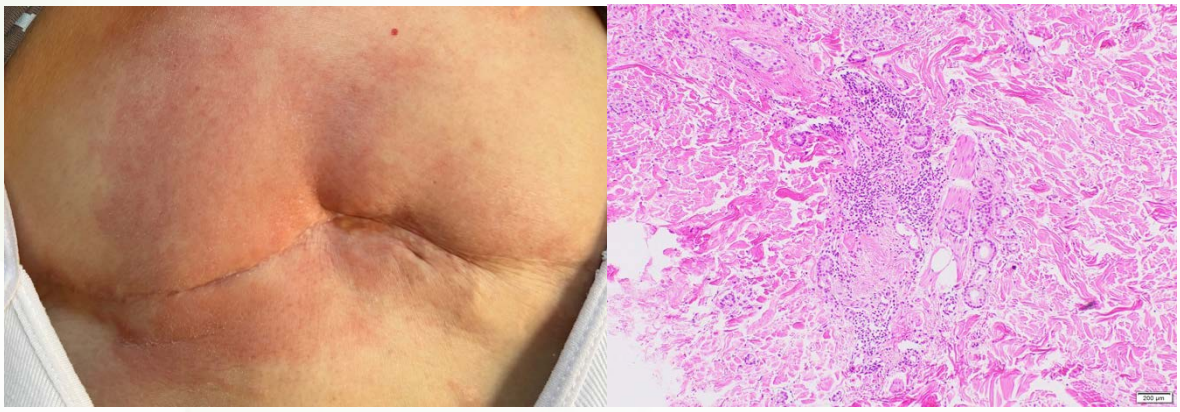

Picture 1

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DEMOGRAPHIC, CLINICAL, AND HISTOPATHOLOGICAL FEATURES OF MERKEL CELL CARCINOMA: A SINGLE-CENTER RETROSPECTIVE STUDY

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Introduction & Objectives: Merkel cell carcinoma (MCC) is an extremely rare neuroendocrine carcinoma of the skin with an aggressive clinical course. MCC is more common in Caucasians and data from Asian countries appears to be limited to a small number of case reports. Our study aimed to define the demographic, histopathological features and predisposing factors of patients diagnosed with MCC.

Materials & Methods: We reviewed the records of 6 patients diagnosed with MCC between 2003 and 2022 at our institute and re-evaluated the histologic slides of the cases.

Results: All patients were over 50 years at diagnosis (mean age 77.5 years). Most patients were female (M: F = 1/2). The most common tumor site was the head and neck region (n=3), followed by the upper extremities (n=2), and the lower extremities (n=1). Tumor diameters ranged between 1.1 and 8 cm. Two patients had lymph node metastasis and three had distant metastasis. 2 patients had previous malignancy, one with prostate cancer and the other with chronic lymphocytic leukemia (Table 1).

Conclusions: MCC clinically appears as a small, red-purple colored, painless, firm, solitary dermal nodule with a shiny surface and telangiectasias. The most common anatomical site of the primary lesion is the head and neck region, followed by the arms and legs. Advanced age, immunosuppression, hematological malignancies, and presence of other cutaneous tumors are risk factors. Immunosuppression and hematological malignancies are also associated with a worse prognosis. Histopathological examination is essential for diagnosis. MCC typically exhibits sheets and nests of uniform small round blue undifferentiated cells with scant cytoplasm,large lobulated nucleoli, high mitotic rate and occasional necrotic cells. Immunohistochemical markers, especially cytokeratin-20, which are positive in approximately 95% of cases and are useful in differentiating from other neuroendocrine tumors, are required for diagnosis. First-line therapy for primary or regional MCC is wide local excision supported by adjuvant radiotherapy. Advanced MCC requires chemotherapy and emerging immunotherapeutic agents. The incidence of MCC is increasing gradually. Large-scale epidemiological studies are needed to determine the tumor's demographic, clinical, and histopathological features, especially for non-Caucasian countries.

Keywords: merkel cell carcinoma,dermatopathology,skin tumors

Introduction & Objectives: Merkel cell carcinoma (MCC) is an extremely rare neuroendocrine carcinoma of the skin with an aggressive clinical course. Despite its rarity, it is noteworthy that an epidemiologic study found a 95% increase in incidence between 2000 and 2013 [1]. MCC was first described as trabecular carcinoma by Toker et al. in 1972 [2]. In later years, it was renamed as MCC due to the overlap between the immunohistochemical profile of these tumors and Merkel cells, which act as mechanoreceptors of the skin. MCC occurs mostly in the later years of life (usually in the 7th and 8th decades). It is more common in males than females [3]. The most common localization is the head and neck, followed by the extremities and trunk. Risk factors include older age, immunosuppression, pale skin and ultraviolet (UV) exposure [1,4].

In the pathogenesis, especially in the northern hemisphere, approximately 80% of cases are related to Merkel cell polymavirus (MCPyV). MCPyV integrates into host cell DNA and plays a role in oncogenesis by inactivating the tumor suppressor gene Retinoblastoma (RB) [5,6]. In non-virus-associated tumors, UV-induced progressive DNA damage plays a role and high mutation burden is observed in these tumors. Contrary to its name, MCC does not originate from Merkel cells of the skin. In virus-associated MCCs, the tumor originates from pro- and pre-B lymphocytes and dermal fibroblasts; in virus-negative MCCs, it originates from epidermal precursor cells [1,7].

Its clinical features are summarized by the synonym AEIOU (Asymptomatic, Expanding rapidly, Immunosuppression, Older than 50 years and UV-exposed area) [8]. It usually presents as a well-circumscribed, firm, skin-colored cutaneous nodule. Ulceration may be seen.

Histopathologic examination shows a small blue round cell morphology consisting of cells with salt and pepper chromatin pattern and indistinct nucleoli, growing as solid islands and sheets in the dermis and subcutaneous tissue. Although initially termed trabecular carcinoma, the trabecular growth pattern is rarely seen [8]. Mitotic figures are observed quite frequently. On immunohistochemical examination, perinuclear dot-like staining with CK20 is quite characteristic and neuroendocrine markers such as Chromogranin, Synaptophysin and CD56 are (+). MCPyV antibody is (+) in the majority of cases.

Radiotherapy plays an important role in the treatment as well as wide resection of the primary tumor. In recent years, studies on immunotherapy have increased and a positive response has been reported in approximately 50% of patients [5].

In our study, we aimed to define the demographic, histopathological features and predisposing factors of patients diagnosed with MCC.

Materials & Methods: We performed a retrospective study revealing the clinicopathologic features of a total of 6 patients diagnosed with MCC between 2003 and 2022 in our institute. Important clinical information (including age, sex, tumor site, tumor diameter, stage of the disease, distant or lymph node metastasis, multifocalty and clinical history) of the patients were collected from computerized medical records of our hospital. Follow-up information was obtained from routine outpatient visits or by telephone.

Formalin-fixed, paraffin-embedded and hematoxylin-eosin (H&E) and immunohistochemically-stained tumor samples were re-examined microscopically. Histopathological features such as surgical margin status, tumor thickness, Clark level, lymphovascular and perineural invasion, growth pattern, presence of ulceration, lymphocytes infiltrating the tumor, presence of necrosis and mitotic index were evaluated. Immunohistochemical stains CK20, synaptophysin and chromogranin were present in all cases and were re-evaluated as ‘positive’ or ‘negative’.

Results: All patients were over 50 years at diagnosis (mean age 77.5 years). Most patients were female (M:F = 1/2). The most common tumor site was the head and neck region (n=3), followed by the upper extremities (n=2), and the lower extremities (n=1). Tumor diameters ranged between 1.1 and 8 cm. Two patients had lymph node metastasis and three had distant metastasis. Two patients had previous malignancy, one with prostate cancer and the other with chronic lymphocytic leukemia.

On histopathologic examination, the tumor was confined to the dermis in 2 cases, while the rest showed invasion to the subcutaneous adipose tissue (and 2 of them to the striated muscle). Two of the cases had positive surgical margins. Nodular and infiltrative growth patterns were seen together in half of the cases. Lymphovascular invasion was observed in three cases and perineural invasion was noted in 4 cases. Mitotic index was quite high and the number of mitoses per mm2 ranged between 8 and 43. There was only one case in which tumor-infiltrating lymphocytes were not observed.

Immunohistochemical examination revealed perinuclear dot-like CK20 (+) as well as chromogranin and synaptophysin positivity for all cases. TTF-1 immunohistochemistry was performed in all but 1 case and all were negative. MCPyV antibody was not available for any case.

Conclusions: MCC is a primary cutaneous neuroendocrine carcinoma with a high mortality rate. Recurrence and lymph node metastasis are common. Advanced age, immunosuppression, hematological malignancies, and presence of other cutaneous tumors are risk factors. Immunosuppression and hematological malignancies are also associated with a worse prognosis.

MCC clinically appears as a small, red-purple colored, painless, firm, solitary dermal nodule with a shiny surface and telangiectasias. Biopsy and histopathologic examination are diagnostically critical since the clinical impression is benign in a significant proportion of cases. Since cutaneous metastatic neuroendocrine neoplasms of different origins are important in the histopathologic differential diagnosis, immunohistochemical examination (TTF-1, Cdx-2, NKX3.1, etc.) is also useful.

First-line therapy for primary or regional MCC is wide local excision supported by adjuvant radiotherapy. Advanced MCC requires chemotherapy and emerging immunotherapeutic agents. The incidence of MCC is increasing gradually. Large-scale epidemiological studies are needed to determine the demographic, clinical, and histopathological features of the tumor especially for non-Caucasian countries.

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A CASE OF SKIN MANIFESTATION OF RICHTER'S TRANSFORMATION IN A PATIENT WITH CHRONIC LYMPHOCYTIC LEUKEMIA

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Abstract: Cutaneous lesions are seen in 30%-50% of patients with chronic lymphocytic leukemia. Specific cutaneous findings are seen less frequently in these patients, presenting as a wide spectrum of skin lesions. Specific skin lesions can be seen in the form of skin involvement of leukemia cutis and richter syndrome. In our case, an 80-year-old woman who had CLL for 2 years was presented with diffuse lobular lesions on the right lower leg. A biopsy was taken and the histopathological examination revealed diffuse large b-cell infiltration, consistent with cutaneous involvement of richter syndrome. The patient was referred to the department of hematology and oncology. Eevaluation of skin lesions of patients with lymphoma for primary infiltration or secondary malignancies will provide early diagnosis and treatment of the disease and may have a positive effect on the patient's survival.

Keywords: cutenous lymphoma, chronic lymphocytic leukemia, richter's syndrome

İntroduction: Cutaneous lymphomas are a group of skin malignancies. Pathophysiologically, they are characterized by uncontrolled accumulation and proliferation of B and T cells in the skin. They may be primarily cutaneous in origin or may present as a cutaneous manifestation of a systemic lymphoma. Skin involvement of Richter syndrome, one of the specific skin lesions of chronic lymphocytic leukemia patients, is a rarely seen entity.

Case presentation: An 80-year-old woman presented to our clinic with ulcerated and infected lobular lesions on her right lower leg for 2 months. She was diagnosed with chronic lymphocytic leukemia 2 years earlier, and the lesions on the leg have appeared in the last 2 months. In the complete blood count analysis, chronic disease anemia, thrombocytopenia and leukocytosis were present and there was a history of B symptom for the last 6 months. She received 7 cycles of bendamustine treatment in the last 2 years with the prediagnoses of lymphoma kutis and Richter's tranformation. An incisional skin biopsy was taken from the lesions. Histopathological and immunohistochemical evaluation of the biopsy revealed high grade diffuse large B cell lymphoma characterized by B cell accumulation with increased expression of CD20, MUM1, Bcl-2, Bcl-6, loss of CD5 and CD23, and Ki-67 proliferative index of 90%. PET-CT imaging of the patient showed hypermetabolic activity in the right leg region (SUVmax 38). The patient was considered as cutaneous involvement of Richter syndrome, an aggressive form of CLL, and was referred to the hematology-oncology clinic for re-staging with PET imaging.

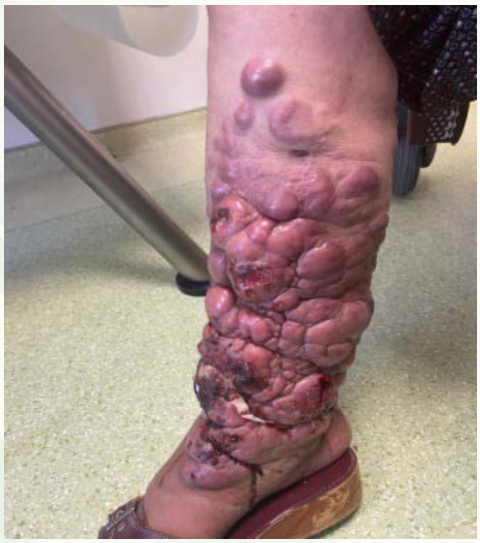

figure: infected lobular lesions on the patient's right leg

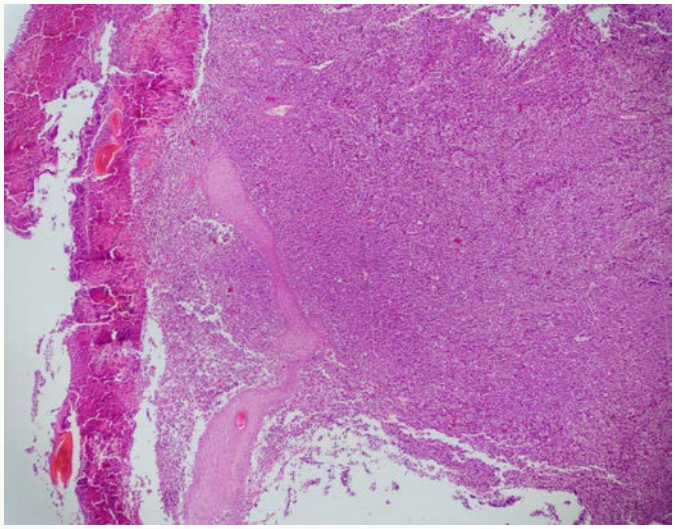

Figure1: Cutaneous infiltration of diffuse atypical lymphoid cells and squamous epithelial fragments within the lymphoid infiltration (H&E, x40)

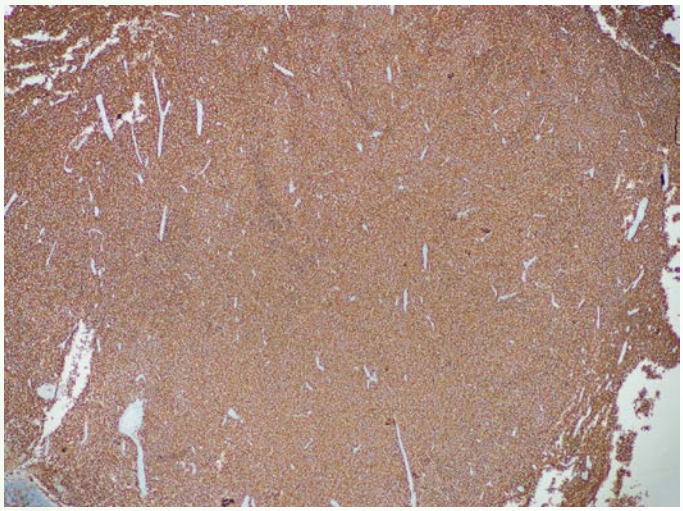

Figure: Diffuse strong membranous staining of tumor cells with CD20 (x40)

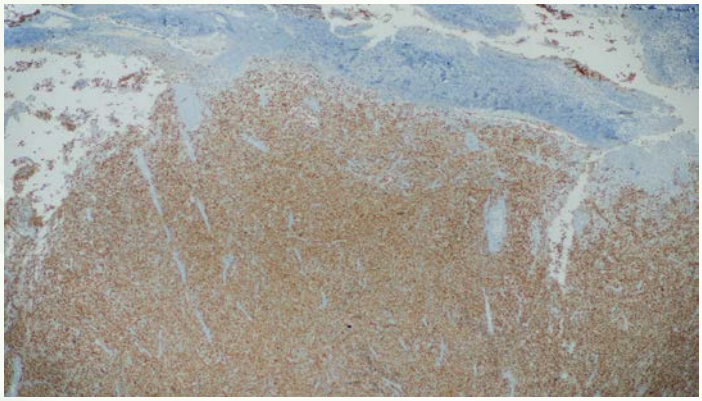

Figure: Diffuse moderate nuclear staining of tumor cells with MUM1 (x40)

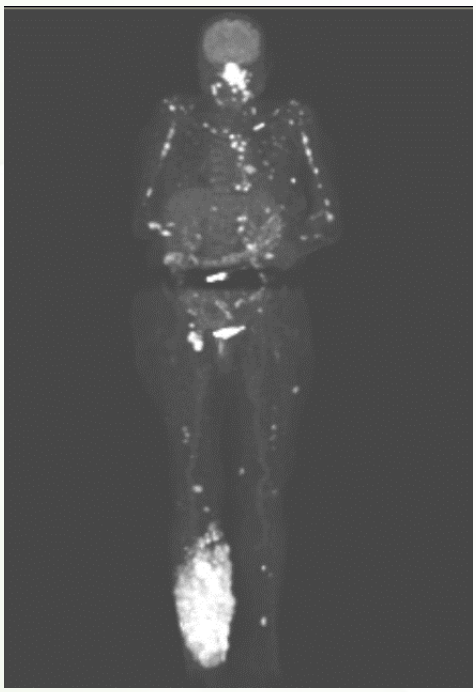

Figure: Diffuse increased metabolic activity in the right leg on PET-CT imaging.(SUVmax :38)

Conclusion: Cutaneous involvement of Richter syndrome, which can be aggressive and resistant to treatment, is rare in patients with chronic lymphocytic leukemia. In our case of diffuse large B-cell lymphoma, which is a common variant of Richter syndrome, which is considered to be an aggressive form of chronic lymphocytic leukemia, R-CHOP treatment, which has a relatively lower risk of side effects, was planned in the hematology-oncology department in the first plan. Among Hodgkin's lymphoma and DBBCL variants, the most common type associated with the DBBCL variant may be more aggressive and chemo-refractory. Therefore, it is of great importance in terms of survival to be careful in the follow-up of CLL patients in terms of B symptoms or laboratory tests and to be referred to the relevant department in case of changes.

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EFFICACY OF OMALIZUMAB IN ELDERLY PATIENTS WITH CHRONIC SPONTANEOUS URTICARIA: A MULTICENTER OBSERVATIONAL STUDY

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Introduction & Objectives: Treatment with omalizumab is used effectively and safely in patients with chronic spontaneous urticaria (CSU) who do not respond to non-sedating antihistamines. [1] Chronic spontaneous urticaria can affect elderly patients and impair their quality of life. However, comorbidities in elderly patients and their use of multiple the presence of drugs limit treatment options. [2] Our study evaluated the efficacy of omalizumab treatment in patients with CSU over the age of 60.

Materials & Methods: A total of 163 CSU patients treated with omalizumab at a dose of 300 mg every four weeks for 12 weeks were enrolled in our study. The patients were divided into two groups: < 60 years and ≥ 60 years. The patients' sociodemographic characteristics, duration of diagnosis, presence of concomitant angioedema, hemogram parameters, serum immunoglobulin E (Ig E) levels, d-dimer levels, antinuclear antibody (ANA) results, and concomitant comorbidities were examined. The Urticaria Activity Score 7 (UAS7) was used to evaluate the efficacy of omalizumab treatment for these patients. Patients with UAS7 scores of 0 on the seventh day of omalizumab treatment were classified as early complete responders (ECR); patients who achieved UAS7 scores of 0 during the first three months of treatment were classified as late complete responders (LCR); and patients whose UAS7 scores decreased by 50% after three months were classified as partial responders (PR). If patients' UAS7 scores did not decrease by 50% after three months, they were classified as nonresponders (NR).

Results: There was no statistically significant difference between the ages of the males and females who participated in this study. The female-to-male ratio was nearly 2/1 (Table 1). In addition, no statistically significant difference was found regarding gender, presence of concomitant angioedema, duration of diagnosis, or number of applications (Table 2). Twenty-eight (17.2%) of the patients were 60 or older. The UAS7 scores were similar in both groups at the baseline and at the fourth and twelfth weeks of treatment (Table 3). There was a statistically significant decrease in the UAS7 scores in both age groups at the fourth and twelfth weeks in comparison to the baseline ($p = 0.000$, $p = 0.001$) (Table 4). Hypertension was the most common comorbidity in the group that was 60 or older, and autoimmune and psychiatric diseases were the most common comorbidities in the under 60 group. It was observed that 20.7% of patients under 60 and 32.1% of patients 60 or older achieved an ECR (Table 5). We also observed statistically significant differences in the platelet counts, serum IgE levels, and d-dimer results between the two groups (Table 6).

Discussion: Chronic spontaneous urticaria is a heterogeneous, inflammatory skin disease with a high prevalence in females. Studies have observed that the female-to-male ratio regarding the commonality of this disease varies between 2-4/1. [3] Although the peak incidence of CSU occurs between 20 and 40 years of age, it can affect people of all ages. The prevalence of CSU in elderly patients (65 years or older) has been reported as 9.9%. The sociodemographic data of our study are similar to the data presented in the literature.

In a study evaluating the efficacy of omalizumab in elderly patients, rates of change in UAS-7 scores were found to be similar between patients aged 65 and older and patients under 65 in the beginning, fourth week, and twelfth week. However, in Kitao et al.'s study, older patients showed much less response to omalizumab. Our study is consistent with the literature, as the efficacy of omalizumab was proven once again in patients aged 60 and over. Similarly to our study, Martina et al. found that ECR was more common in the elderly population during the use of omalizumab. [4] Based on these data, it can be said that elderly patients respond faster to omalizumab.

The most common comorbidity in CSU in elderly patients is hypertension. It is emphasized that chronic urticaria may facilitate hypertension with oxidative stress in the vessels, leading to systemic inflammation. [5] Our study showed similar results, but the absence of a healthy control group in our study makes the interpretation of this data difficult. The predictors

used to determine the severity and course of CSU (serum IgE levels, basophil counts, eosinophil counts, and d-dimer levels), when evaluated together with the patients' ages, showed no statistically significant difference between the two age groups in Kitao et al.'s study. [1] However, compared to aged 60 and older patients, in our study, platelet counts and serum IgE levels were found to be higher, and d-dimer levels were found to be lower in patients under 60.

Conclusions: Our study demonstrated that the response to omalizumab in patients 60 and older was similar to that in patients under 60. It was concluded that omalizumab is also an effective treatment for the elderly population.

Keywords: Chronic spontaneous urticaria, elderly, omalizumab.

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Table 1. Mean and median age distrubiton of patients by gender

			Age			
Gender	n	%	Average.±SD	Median (Min.-Max.)	Z	p
Male	54	33.1	42.89±16.56	41 (20-87)	-0.291	0.771
Female	109	66.9	43.15±15.69	43 (17-78)		
Total	163	100.0	43.06±15.94	43 (17-87)		

Mann Whitney U analysis. Abbreviations: SD, standart deviation; Min, minimum; Max, maximum.

Table 2. Distribution of gender, presence of concomitant angioedema, duration of diagnosis and number of applications by age groups

	<60 years (135 (%82.8))	≥60 years (28 (%17.2))	p
Male	44 (32.6)	10 (35.7)	0.749
Female	91 (67.4)	18 (64.3)	
Presence of concomitant angi-oedema			
No	95 (70.4)	16 (57.1)	0.172
Yes	40 (29.6)	12 (42.9)	
Duration of diagnosis	18.34±30.78	15.54±13.91	0.496
Number of application	10.94±4.94	13.14±6.17	0.086

Pearson Chi-Square, Mann Whitney U analysis.

Table 3. Distribution of mean of UAS7 scores in both age groups

	<60 years	≥60 years	p
UAS7 scores at baseline	19.79±12.13	15.46±9.55	0.072
UAS7 scores at week 4	7.27±6.87	5.54±6.04	0.179
UAS7 scores at week 12	3.41±6.08	4.89±9.47	0.826

Mann-Whitney U analysis. Abbreviation: UAS, urticaria activity score.

Table 4. Change from baseline in UAS7 scores at weeks 4 and 12 in two patient age groups

	Change in UAS7 from baseline to week 4	p	Change in UAS7 from baseline to week 12	p
<60 years				
Mean (SD)	12.23±10.31	**0.000**	16.08±12.01	**0.000**
Median (Min-Max)	10 (-7-42)		14 (-28-42)	
≥60 years				
Mean (SD)	9.93±8.42	**0.000**	10.57±14.42	**0.001**
Median (Min-Max)	10.5 (-7-24)		12 (-28-42)	

Wilcoxon Signed Ranks Test. Abbreviation: UAS, urticaria activity score; SD, standard deviation; Min, minimum; Max, maximum.

Table 5. Comparison of omalizumab treatment responses in both age groups

	<60 years	≥60 years	p
ECR	28 (20.7)	9 (32.1)	0.190
LCR	39 (28.9)	7 (25)	0.677
PR	55 (40.7)	8 (28.6)	0.229
NR	13 (9.6)	4 (14.3)	0.497

Pearson Chi-Square test, Fisher's Exact test. Abbreviations: ECR, early complete responders; LCR, late complete responders; PR, partial responders; NR, non-responders.

Table 6. Change of laboratory findings in two patient age groups

	<60 years	≥60 years	Z / X^2	p
Hb	13.34±1.92	13.52±1.23	-0.222	0.824
WBC	9.47±2.36	8.84±1.78	-1.199	0.231
PLT	292.41±77.39	253.71±52.86	-2.517	**0.012**
Neu	5.8±1.82	5.28±1.57	-1.703	0.089
Lym	2.69±0.81	2.56±0.75	-0.354	0.723
Mon	0.65±0.2	0.7±0.19	-1.175	0.240
Eos	0.18±0.17	0.17±0.19	-0.560	0.576
Bas	0.06±0.09	0.07±0.07	-0.859	0.390
IgE	409.78±495.46	221.35±282.76	-2.026	**0.043**
D-Dimer	0.38±0.35	0.55±0.42	-3.175	**0.002**
ANA	15 (11.1)	7 (25)	3.832	0.067
Thyroid autoantibodies	18 (13.3)	6 (21.4)	1.21	0.256

Mann Whitney U analysis, Fisher's Exact test. Abreviations: Hb, hemoglobin; WBC, white blood cell count; PLT, platelet count; Neu, neutrophil; Lym, lypmhocyte; Mon, monocyte; Eos, eosinophil; Bas, basophile; IgE, immunoglobulin E; ANA, anti nuclear antibody.

A SLOWLY GROWING MASS ON THE TONGUE

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INTRODUCTION: Traumatic Ulcerative Granuloma with Stromal Eosinophilia (TUGSE) is a reactive benign ulceration of the oral mucosa with unknown etiopathology. TUGSE may be easily mistaken for cancer or microbial infection. Therefore, awareness of this entity is important to emphasize the correct diagnosis of indurated ulcerated lesions.

CASE PRESENTATION: A 67-year-old female with a known history of coronary artery disease presented with a slowly growing indurated and well-demarcated ulcerative lesion of the lateral side of the tongue. The lesion was present for 2 months and growing slowly since then.

The patient denied any symptoms of pain, itch or burning sensation. She described no history of trauma, dental procedure, consuming irritating foods or any other drug administration.

In the past, the patient was prescribed with topical analgesics, and topical antibacterial and antifungal sprays with no improvement.

On clinical examination, an erythematous ulcer of 1.8 cm diameter with a gray-white surrounding halo was seen. The ulcer was smooth, tender, and firm in consistency. There was no fixation to the deeper structures or any regional lymphadenopathy. After examination, the patient was consulted to the ENT clinic for performing incisional biopsy with preliminary diagnosis of squamous cell carcinoma and traumatic ulceration.

HISTOPATHOLOGY: The histopathologic analysis showed hyperplastic epithelium with central ulceration. a mixed inflammation containing mainly eosinophils and other inflammatory cells in the submucosa, mucosa, and extending deep into the musculature of the tongue. The infiltrated tissue was well vascularized. No atypical cells were seen. And the diagnosis of Traumatic Ulcerative Granuloma with Stromal Eosinophilia (TUGSE) was made.

MANAGEMENT: After the diagnosis, topical triamcinolone acetonide was prescribed. The lesion showed regression on the first follow-up.

DISCUSSION: TUGSE has been known by different names, Riga-Fede disease in infants and neonates, sublingual granuloma, traumatic granuloma, eosinophilic granuloma, eosinophilic ulcer, and ulcerative eosinophilic granuloma. It is a rare, benign, and self-limiting lesion of the oral mucosa. Although trauma seems to trigger the development of TUGSE, the majority of cases has no history of trauma. The tongue is the most commonly affected location, although other areas of oral mucosa may also be involved. The lesion usually regresses spontaneously or after removal of possible triggers for microtrauma (e.g., artificial denture), within weeks to months.

CONCLUSION: Diagnosis of TUGSE is made by the combination of clinical and histopathological features. The pathogenesis of this condition remains uncertain and controversial and this condition is considered self-healing with a benign course.

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3 CASES OF MORHPEA LIKE ATROPHIC LESIONS DEVELOPED AFTER ABOBOTULINUMTOXIN A TREATMENT: A NEW THEORY FOR A RARE COMPLICATION

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Introduction : Botulinum toxin injections for facial rejuvenation are at the forefront of non-surgical aesthetic treatments. In particular, for the rarity of complications and the duration of action it is preferred frequently. In the three cases we presented, morphea-like skin atrophies occurred after botulinum toxin injection treatment and healed within 3-4 weeks without the need for additional treatment. While presenting these cases, we also wanted to present a new hypothesis for the etiology of complication.

Case reports: Case 1: A 43-year-old female patient presented one week after the Abobotulinumtoxin A injection. A treatment applied to active wrinkles in the frontal, periorbital and glabellar region. After 1 weeks of first injection , 4 units of Abobotulinumtoxin A injection were applied to the remaining active streaking area in the middle right forehead. The patient stated that 12 hours after the touch up injection, local intense redness without pain and itching occurred, and after 24 hours of injection the redness disappeared and pitting occurred. There were no signs of inflammation with any ecchymosis or nodular formation. Due to its epithelialising properties, the patient was advised to apply the cream containing the active ingredient Hamamelis virginiana (1) twice a day and no other intervention was made. It was observed that the lesion disappeared within 4 weeks.

Case 2: A 34-year-old female patient developed a clearly circumscribed atrophic area of approximately 1 cm in diameter in the frontal area 3 weeks after the injection of Abobotulinumtoxin A between the frontal, periorbital and glabellar area. The lesion completely disappeared after 1 month without any intervention or topical treatment.

Case 3: A 72-year*old female patient had an atrophic area of 1 cm in diameter on the frontal region after one week of touch up injection. She had been treated with Abobotulinumtoxin A for frontal, glabellar and periorbital wrinkles for the first time in her life. This lesion also regressed without any topical treatment of interventions in 1 month period.

Discussion: There are only five reported cases in the English literature describing atrophy or morphea-like lesions after cosmetic injection of botulinum toxin.

Three similar cases were reported by Landau M. et al., reported three cases and no morphea-like findings were found in the pathological evaluation performed by biopsy due to the differential diagnosis of morphea from the case with linear atrophy(1). In his histopathology, epidermis and dermis were seen in normal structure, but deeper tissues could not be evaluated due to the depth of biopsy. In 3 cases, botulinum toxin activity regressed within the period without the need for any additional intervention. Although the author presented his hypotheses that localized muscular atrophy due to neural stimulus deficiency and the silicone oil remaining in the injectors pass into the tissue and cause a reaction, silicone oil creates a granulomatous foreign body reaction (3,4), and in some studies, contrary to tissue atrophy, it has been used as a high-safety soft tissue filler. is indicated(5). In addition, similar injectors have been used for injection to the face area in many aesthetic procedures, but lesions with similar characteristics have not been reported.

Nyckowski T. et al. presented 2 cases of atrophy after Onabotulinumtoxin A injection. In one case, it was stated that a green-blue discoloration accompanied by circular net-demarcated atrophy, and in the other case a linear atrophy was described, which was attributed to aberrant contraction of the subcutaneous branches of the frontal muscle in the region.(6) There are various theories about the etiology of atrophy in botulinum toxin A application. According to our evaluation, in the only case of linear atrophy evaluated by biopsy, the pathology is not in the epidermis and dermis layer. Our recommendation is to distinguish a possible muscular or adipose tissue pathology by detecting the depth of the pathology that causes the atrophic image non-invasively with high-frequency ultrasound in cases encountered in the future.(7)

In the cases we reported, we think that it is a pathology originating from adipose tissue, since there is no pigment change and a faster recovery course than normal botulinum toxin resolving timing. Also the lesion is static and not affected by facial mimics.(8) Humans have white adipose tissue in the facial region and there is no parasympathetic innervation, and the lipolysis process is managed by the sympathetic system (9,10). Parasympathetic system blockade in the presynaptic space by retrograde transport due to injection of toxin into the supraophthalmic or supratrochlear branch of the ophthalmic nerve or close to the neuromuscular plate may cause hyper-activation of the sympathetic system in the regional innervation area. Most cases in the literature have been reported in locations close to the innervation areas of these nerves.

In the treatment of this unique complication, saline injections applied every 1-2 weeks are effective for temporarily eliminating the aesthetic problem. Informing the patient that the temporary nature of atrophy is important while it takes approximately 1-6 months according to the reported cases.

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Figures:

	
Photo 1 : Case 1	**Photo 2 :** Case 2
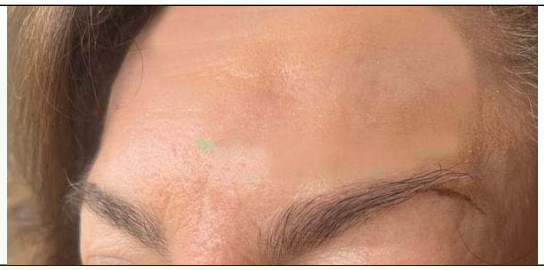	
Photo 3 : Case 3	

CD30 - POSITIVE ANAPLASTIC LYMPHOMA KINASE - NEGATIVE SYSTEMIC ANAPLASTIC LARGE CELL LYMPHOMA PRESENTING WITH CUTANEOUS LESIONS

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INTRODUCTION&OBJECTİVES: Anaplastic large-cell lymphoma (ALCL) is a CD30- positive non-Hodgkin lymphoma of T-cell origin. Cutaneous ALCL presents either as primary cutaneous disease or as secondary skin involvement due to systemic disease[1]. Herein, we present a rare case of ALK (anaplastic lymphoma kinase)-negative S (systemic)-ALCL, was evaluated for rapidly growing nodules and an evolving ulcers on the left leg for about 2 months.

MATERIAL& METHODS: A 60 years of male presented with a two months history of rapidly growing nodules and an evolving ulcers on his left leg (Fig. 1). Dermatological examination revealed numerous nodules which have ulcer on top of them on the lateral aspect of the upper leg (Fig. 2). There are also two distinct ulcerated tumoral lesion which completely involves the ankle.The lesion was violaceous in colour and firm on palpation and had necrotic crusts. Lymphadenopathy was detected on the left inguinal region via physical examination (Fig. 3). The patient also complained of fever and weight loss. All laboratory tests were negative, including complete blood count, biochemistry, routine urine examination, except elevated C-reactive protein(CRP), erythrocyte sedimentation rate (ESR) and lactate dehydrogenase (LDH). Serology tests for viruses were negative, except anti-HBC immunoglobulin G positive. A skin biopsy specimen from the tumor showed infiltrate of atypical mononuclear cells with large nucleoli and hyperchromatic nucleus in the dermis. Also a few atypical cells with multinucleation were present (Fig. 4a). These atypical cells stained positive for CD30 (Fig. 4b) and CD4, but negative for ALK. FDG-PET/CT revealed abnormal FDG uptake in skin tumor at the left lower extremity and also bilateral inguinal region, suggesting the systemic involvement of lymphoma cells. The features were consistent with ALK negative systemic ALCL with skin metastasis and the patient was referred to Department of Hematology.

DISCUSSION: Anaplastic large cell lymphoma (ALCL) is a CD30-positive T-cell neoplasm characterized by large lymphoid cells with pleomorphic nuclei and abundant cytoplasm. The majority of cases (90%) are primary systemic ALCL with systemic disease usually present within the lymph nodes[1]. Systemic ALCL accounts for 30% of non-Hodgkin lymphomas in adults. It is most often seen in young men younger than 35 years of age, with the presence of lymphadenopathy in stages 3 and 4. B symptoms, characterized by fever, night sweats, and weight loss, are seen in 75% of patients [2-3].

Cutaneous involvement is seen in approximately 20% of patients with systemic ALCL. Skin lesions in anaplastic ALK -negative S-ALCL have been rarely reported in the literature. Miyagawa et al. reported a 48-year-old woman who presented with redness and swelling of her breast. After further examinations, the patient was diagnosed as ALK -negative S-ALCL [4]. In another reported case, who was 9-year-old Korean boy, presented with with itchy erythematous maculopapules and an erosive nodule on the trunk area. Based on histopathological and immunohistochemical examinations CD30-Positive ALK-negative S-ALCL was detected in the patient. The authors suggested that in the presence of eczematous lesions, an underlying malignant disease should be suspected [5]. Our patient had refractory nodules and ulcers unresponsive to treatment. He had also systemic symptoms. Therefore we considered the possibility of malignancy.

The most important prognostic marker of systemic ALCL is ALK positivity seen in 85% of the cases. ALK-1 in systemic ABHL is expressed as a result of translocation [t(2,5)] of the nucleophosmin 'NPM' gene on the 5th chromosome to the ALK gene on the 2nd chromosome. ALK positivity indicates a good prognosis in systemic ALCL. While the 5-year median survival is 71-100% in ALK-positive systemic ALCL, this rate is only 15-45% in ALK-negative systemic ALCL[2-

[3]. IPI (International Prognostic Index), age, LDH, CD56 expression, ALK status are the prognostic factors for ALCL. Back bone of the treatment is anthracycline containing protocols (CHOP/CHOEP). Except low risk ALK+ ALCL, most of the patients are consolidated with autologous stem cell transplantation. Brentuximab (vedotin), anti-CD30, is favored second-line therapy for relapsed and refractory patients. GDP (Gemcitabine, Dexamethasone, and Cisplatin) is the preferred combination chemotherapy for the salvage therapy due to low adverse event profile and non-inferior efficiency. Allogeneic stem cell transplantation is one of the treatment option for selected patients who have relapsed and refractory disease. Crizotinib and Ceritinib are the novel agent ALK inhibitors can achieve durable response with low adverse event profile. Considering low median survey rate and current treatment options, early diagnosis and aggressive treatment are important[4].

RESULTS: Skin involvement in systemic ALCL is relatively rare. Our case was evaluated due to initial skin lesions. Dermatologists should be aware that systemic lymphomas may present as skin lesions such as nodules, ulcers and erythematous plaques. Necessary examinations and biopsy procedures should be made almost immediately to avoid delayed diagnosis.

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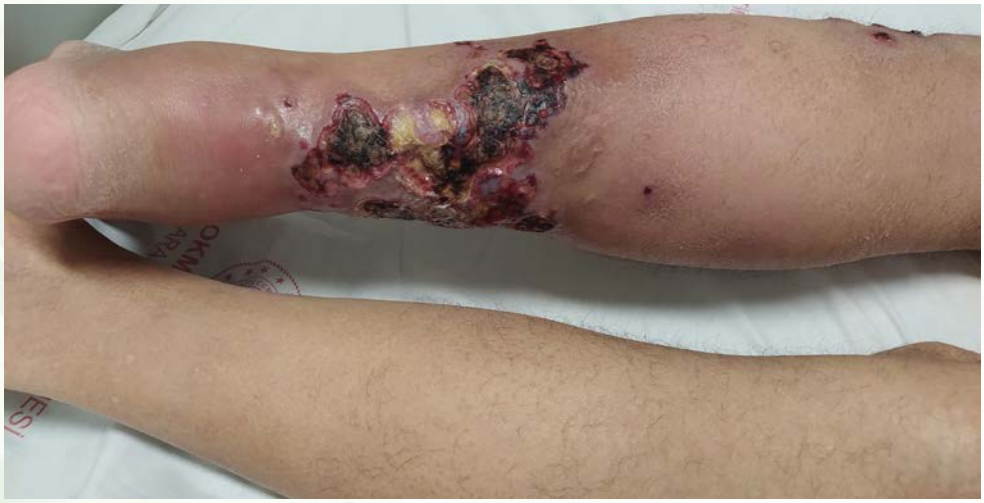

fig 1

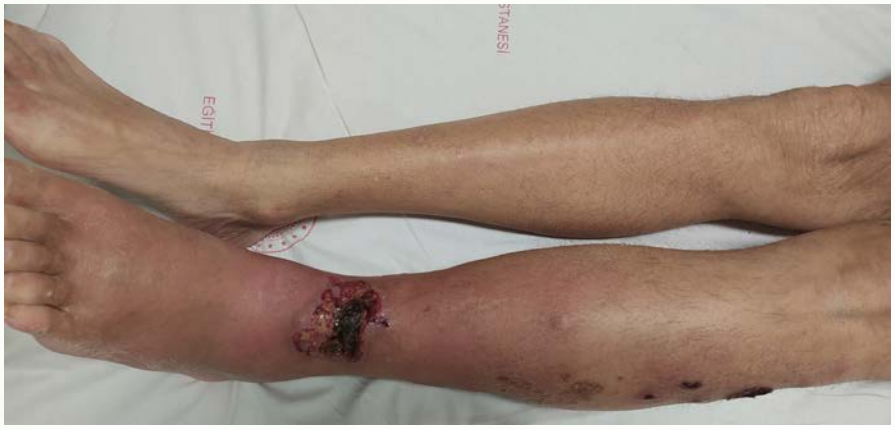

fig 2

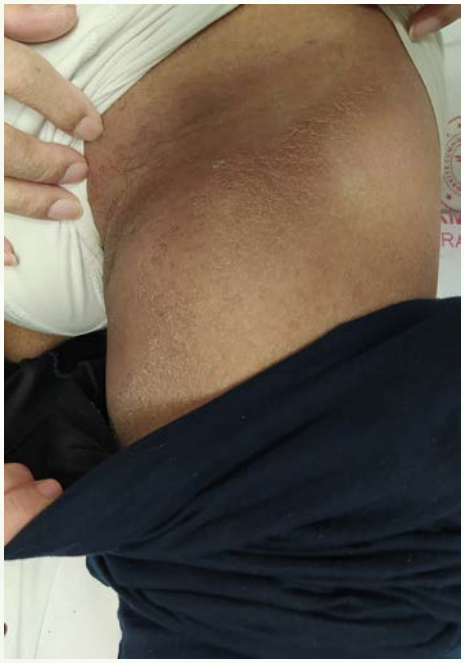

fig 3

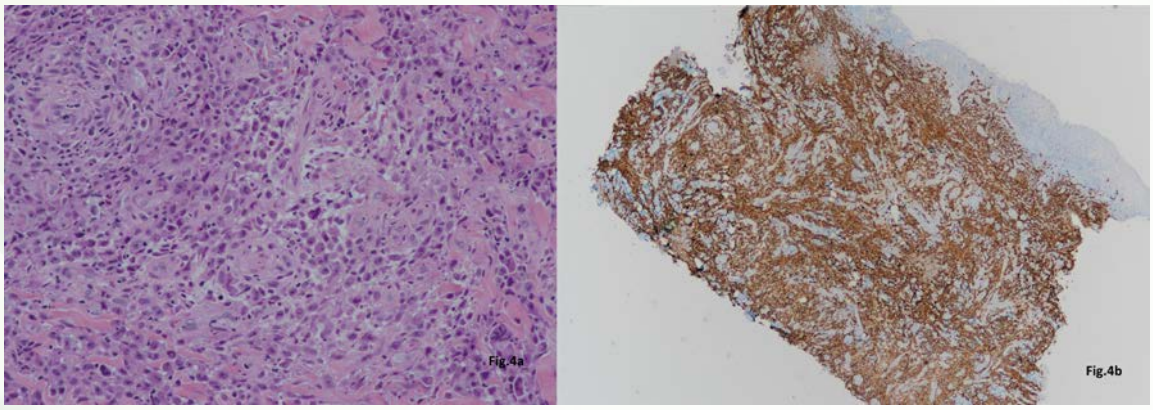

fig 4

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