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Primary Cutaneous Diffuse Large B-Cell Lymphoma – a Case Report

DERMOSCOPY CASE OF THE MONTH:
Combined nevus

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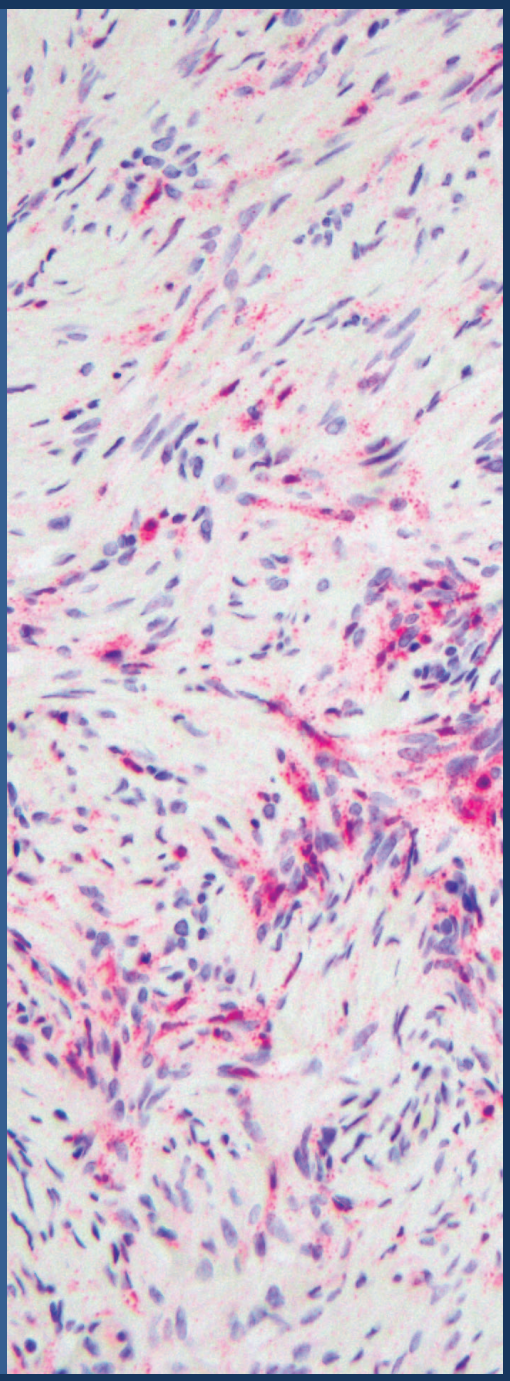

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Partner Notification for Gonorrhea and Syphilis in Belgrade

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Abstract

"Contact tracing" or "partner notification" refers to clinicians' efforts to identify sex partners of infected persons to ensure their medical evaluation and treatment. For many years partner notification has been a cornerstone in the management of patients diagnosed with sexually transmitted infections (STIs) and it is the essential component in the control of these infections. Clinicians' efforts to ensure the treatment of a patient's sex partners can reduce the risk for re-infection and potentially diminish transmission of STIs. Partner notification includes three different approaches for notifying the sexual partners of the person infected with a STI: provider referral, patient referral, and contract referral. The aim of our study was to evaluate the efficacy of partner notification among syphilis and gonorrhea cases registered at the City Institute for Skin and Venereal Diseases in Belgrade in 2016, and its contribution to prevention and control of these diseases. A retrospective chart review of patients with gonorrhea and early syphilis registered in 2016 was undertaken. We analyzed data about the possible source of infection as well as sexual orientation, provided on the official form for notification of syphilis and gonorrhea. The study included 112 male patients, 67 with gonorrhea and 45 with syphilis. Out of three modalities of partner notification offered to patients, only patient notification of sexual partner/s was accepted. Although all patients accepted this type of partner notification, index patients with gonorrhea notified only 17 partners (25.4%) and index patients with syphilis also notified 17 partners (37.8%). The effectiveness of partner notification for gonorrhea and syphilis cases was only 30.4%, and its contribution to prevention and control of these diseases was lower than we expected. National guidelines offering standardized protocols for partner notification service provision can improve this process, as a novel approach with non-traditional method of partner notification such as patient-delivered partner therapy.

Key words: Contact Tracing; Sexual Partners; Gonorrhea; Syphilis; Sexually Transmitted Diseases

Introduction

Sexually transmitted infections (STIs) are a major public health problem due to the high incidence of acute infections, and the frequency and severeness of complications, particularly in women. In 2012, there were an estimated 357 million new infections (nearly one million per day) with one of four curable STIs – chlamydia, gonorrhea, syphilis and trichomoniasis (1).

Gonorrhea and syphilis are common bacterial venereal diseases and their reporting is mandatory in Serbia. During the period 2010 – 2016, the incidence of syphilis increased in Belgrade by 227.5%, from 2.25 per 100,000 in 2010 to 5.12 per 100,000 in 2016, while the incidence of gonorrhea increased by 162.5%, from 2.56 per 100,000 in 2010 to 4.16 per 100,000 in 2016 (2).

Prevention and control of STIs is based on the following five major strategies: education and counselling of persons at risk in order to avoid venereal diseases through changes of sexual behaviours and use of recommended prevention services; pre-exposure vaccination of persons at risk for vaccine-preventable STIs; identification of asymptomatic infected persons and symptomatic persons unlikely to seek health care; effective diagnosis, treatment and counselling of infected patients and evaluation, treatment and counselling of sex partners of patients infected with a STI (3).

The last one, known as "contact tracing" or "partner notification", refers to efforts of clinicians to identify sex partners of infected persons (index patients) to ensure their medical evaluation and treatment. For many years,

partner notification has been a cornerstone in the management of patients diagnosed with STIs, and is considered an essential component in the control of these infections. Clinicians' efforts to ensure the treatment of patient's sex partners can reduce re-infection risks and potentially diminish transmission of STIs (4).

Partner notification includes three different approaches to notify the sexual partners of a person infected with an STI (5): provider referral, patient referral and contract referral. Provider referral means that healthcare professionals elicit information from index patients about their sexual contacts, notify these contacts about possibly being at risk of acquiring a STI, and recommend screening and treatment for such infection. Clinicians inform the partner confidentially, without disclosing the identity of the index patient. This is a method of choice when an individual fears a violent reaction (6).

Patient referral involves patients notifying their sexual partners. Various methods of partner notification can be provided by an index patient such as verbal contact (face to face), telephone or email communication, and notification card delivery to sexual partners. Contact referral is an approach when the index patient agrees to notify his partner(s) within a specified time period and if this is not done, the health adviser will proceed to provider referral. However, the stigma attached to venereal diseases makes partner notification difficult (7).

Partner notification actions in the case of index patients with syphilis, gonorrhea, chlamydia and HIV in most European countries are priorities and the main responsibility of specialty health providers from reference clinics (5).

Partner notification was probably practiced for many years before it became formally introduced as a means of STIs control in different countries around the world. In Britain and Sweden, partner notification for venereal diseases has been practiced since the 19th century (8, 9), while in the US contact tracing had become a central feature of syphilis control programs by the 1940s (10).

There are various processes to measure partner notification efficacy such as the number of contacts notified, the number of contacts presented for screening, the number of contacts identified who tested positive, and the number of contacts treated for a STI (11).

The aim of our study was to measure the efficacy of partner notification among syphilis and gonorrhea cases registered at our institution in 2016 and its contribution to prevention and control of these diseases.

Material and Methods

A retrospective chart review of patients with gonorrhea and early syphilis (primary, secondary and early latent syphilis) registered in 2016 was undertaken at the City Institute for Skin and Venereal Disease in Belgrade. Data about the possible source of infection as well as sexual orientation, provided on the official syphilis and gonorrhoea notification form were analyzed.

Case definitions of gonorrhea and early syphilis were in line with STD Surveillance case definitions (12). To diagnose early syphilis, Venereal Disease Research Laboratory (VDRL) and Treponema pallidum hemagglutination assay (TPHA) tests were used. To diagnose gonorrhea, standard laboratory examination was done, i.e. microscopy, while inoculation on culture media was technically limited.

One dermatologist interviewed all patients and gave them detailed explanations about the importance of referring their sexual contacts for screening and treatment, because they were unaware of infection and its serious reproductive and general health consequences. In order to identify other persons at risk, the infected patients were asked to refer their sexual partners in the last two months for gonorrhea cases. The infectious period for syphilis was estimated based on the syphilis stage: 3 months plus duration of symptoms for primary syphilis, 6 months plus duration of symptoms for secondary syphilis, and 1 year before the diagnosis for early latent syphilis. The patients were offered all three modalities of partner notification by their dermatologist.

The research was approved by the Ethics Committee of the City Institute for Skin and Venereal Diseases in Belgrade. Data are presented by counts and percentages, while data analysis was based on proportions and χ^2 test and Fisher exact probability test.

Table 1. Number of notified sexual partners by patient referral

Sexually transmitted disease	Number of index patients	Number (%) of notified sexual partners
Gonorrhea	67	17 (25.4)*
Syphilis	45	17 (37.8)
Total	112	34 (30.4)

* 11 index patients notified one sexual partner and 3 index cases notified two partners

Results

The study included 112 male patients, 67 with gonorrhea and 45 with syphilis. Out of the three partner notification modalities offered, only patient notification of sexual partner/s was accepted. Index patients with gonorrhea notified 17 partners (25.4%), as well as index patients with syphilis who notified 17 partners (37.8%) (Table 1). The difference was not statistically significant.

Out of 112 index patients, 63 were heterosexual and 49 were homosexual. Gonorrhea was more frequent among heterosexual men (82.5%) and syphilis among homosexual men (69.4%). In the group of patients with gonorrhea, homosexuals notified their sexual partner/s significantly more frequently than heterosexuals ($p < 0.05$). In contrast, among patients with syphilis, heterosexuals notified their partner/s more frequently than homosexuals, but the difference was not significant (Table 2).

All notified patients were asymptomatic and all of them were adequately treated.

Syphilis was diagnosed by positive serological tests. When it comes to gonorrhea, the diagnosis through inoculation on culture media was technically limited and sexual partners were treated in the same way as contacts.

Discussion

Partner notification is the process of contacting sexual partners of a person with a STI and informing them that they have been exposed to infection. They are then offered screening and treatment if indicated. The aim is to find and treat an undiagnosed, often asymptomatic infection and shorten the average period of infectiousness, thus reducing transmission of the infection. Partner notification should be undertaken for all those with treatable STIs (gonorrhea, chlamydia, syphilis, trichomoniasis, and chancroid) including hepatitis B and HIV (13).

The most commonly used method for partner notification is patient referral, whereby the index case has a responsibility to inform his sex partner/s about their exposure to a STI. Patient referral is the preferred approach, partly because most patients prefer to notify their own partners than to give the physician their names, post and/or email address or telephone numbers, and also be-

Table 2. Number of sexual partners by sexual orientation notified by gonorrhea and syphilis index patients

Sexual orientation	Number of index patients with gonorrhea	Number (%) of notified sexual partners
Heterosexual	52	10 (19.2)
Homosexual	15	7 (46.7)*†
	Number of index patients with syphilis	
Heterosexual	11	5 (45.5)
Homosexual	34	12 (35.3)

* 3 index patients notified one sexual partner and 2 index cases notified 2 partners; † $P < 0.05$ for differences between heterosexual and homosexual men

cause it may be the only option in non-specialist settings (14). The clinician has to discuss the importance of partner notification with index patients, explaining the information confidentiality process, the possibility of partners being infected and asymptomatic, the risks of re-infection and also the consequences of non-treatment. Providing resources such as STI fact sheets and partner notification cards and an individualized approach have been used successfully to enhance partner notification efforts (13).

Gorbach et al. (15) reported that up to 1/3 of patients failed to inform all partners (especially casual and ex-partners) due to embarrassment or fear for personal safety and reputation. However, fear of partner reactions to the possibility of positive test results to a STI is associated with important obstacles for partner notification (16).

In our study, patient referral was the only accepted modality of partner notification. The only data that our index cases gave to the dermatologist were their sexual partners' names or gender and promise to inform or refer them to our Institution. The majority of their sexual partners were anonymous or untraceable. Moreover, some cases were reluctant to identify their partners, despite knowing the importance of informing them.

Patient referral effectiveness relies on index cases being willing or able to identify their sexual contacts, and finally, their notified contacts must be willing and able to access health services and require testing and treatment. According to our results, only 1/3 of partners were notified (25.4% for gonorrhea and 37.8% for syphilis). During an outbreak of early syphilis in Belgrade, 24.4% of cases were referred by their sexual partners (17). In the study by Reynolds et al., 19.9% of cases with syphilis were detected through partner notification (18). Another study has shown that the outcome of patient referral in gonorrhea and chlamydia infections was 20.5% (19). Low et al. (20) reported that in the United Kingdom, patient referral reached 40 - 60% of named sexual partners. One study showed that between 22% and 68% of men with gonorrhea were notified by partners who had an asymptomatic infection (21).

In our study, gonorrhea was more frequent among heterosexual men, and syphilis among homosexual men. This is in line with the fact that at the beginning of the new millennium, the incidence of syphilis has been on rise in Belgrade, occurring primarily among men who have sex with men (17).

In the group of patients with gonorrhea, homosexuals notified their sexual partners significantly more frequently than heterosexuals, while among patients with syphilis, heterosexuals notified their partners more frequently, but not significantly, than homosexuals.

Since 2008, counselling is provided at the Department for Sexually Transmitted Diseases of our Institution, and it is at disposal to patients without referral of their physicians. The Department is friendly to vulnerable population (homosexual men, patients who live with HIV). This fact partly explains better partner notification among gonorrhea cases in homosexual men. At the same time, in Serbia, traditionally, men with genital symptoms and venereal diseases visit dermatologists, while women prefer to visit their gynecologists, and even when our heterosexual patients referred their female partners, the notification failed. Owing to inadequate laboratory facilities (culture for endocervical, rectal and pharyngeal specimens), gynecologists cannot confirm the diagnosis of gonorrhea, and therefore women are not properly treated.

Early syphilis is always treated by a dermatologist. According to the data from the official partner notification form, our heterosexual syphilis cases notified their partners more frequently because they were their regular partners, while a predominant barrier to notification in homosexual men was engagement with anonymous sexual partners.

Over the last decade, several non-traditional methods have been developed to facilitate the notification process. In patient-delivered partner therapy, gonorrhea- and chlamydia-positive patients are provided with prescriptions or medications to be directly given to their sexual partners (22). Other methods involve anonymous notification via email, text messaging or electronic postcards (23).

Conclusion

In summary, under the present study, effectiveness of partner notification for gonorrhea and syphilis cases was only 30.4%, and its contribution to prevention and control of these diseases was lower than expected. Cur-

rently, our country has no national guidelines offering standardized protocols for partner notification service provision which could enhance this process. Provider referral can be more effective, especially for patients who are wary of informing partners themselves. A non-traditional method of patient-delivered partner therapy may improve partner notification. We should also provide more sensitive diagnostic tests for gonorrhea, such as Nucleic Acid Amplification Tests, and change testing policies including testing at multiple anatomical sites (e.g. rectum, pharynx). Coordinated and efficient surveillance, partner services, screening of population at-risk and their education, as well as early diagnosis and treatment could diminish transmission and consequences of these diseases.

Abbreviations

STIs - sexually transmitted infections

VDRL - Venereal Disease Research Laboratory

TPHA - Treponema pallidum hemagglutination assay

Acknowledgement

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Kontaktiranje partnera osoba obolelih od gonoreje i sifilisa u Beogradu

Sažetak

Notifikacija partnera predstavlja identifikaciju seksualnih partnera osoba obolelih od polnih bolesti radi njihovog medicinskog ispitivanja i lečenja. Godinama predstavlja značajnu kariku u kontroli širenja i prevenciji polnih bolesti. Napori zdravstvenih radnika da obezbede tretman i partnerima obolelih od polnih infekcija, mogu sprečiti rizik nastanka reinfekcije i uticati na smanjenje daljeg širenja infekcije u populaciji. Postoje tri načina notifikacije partnera: partnera obaveštava zdravstveni radnik, oboleli pacijent i postoji takozvano ugovorno obaveštavanje. Cilj našeg istraživanja bio je da utvrdimo efikasnost notifikacije partnera pacijenata obolelih od gonoreje i ranog sifilisa koji su registrovani u Gradskom zavodu za kožne i venerične bolesti u Beogradu tokom 2016. godine i doprinos notifikacije u prevenciji i kontroli širenja ovih oboljenja. Analizirani su podaci prikupljeni iz zdravstvenih kartona obolelih, kao i podaci iz notifikacionih lista o njihovoj seksualnoj orijentaciji i izvoru infekcije. U istraživanje je uključeno 112 muškaraca, 67 sa dijagnostikovanom gonorejom i 45 sa dijagnostikovanim sifilisom. Svi oboleli su prihvatili da sami obaveste svoje partnere ali su i oboleli od gonoreje i oboleli od sifilisa notifikovali samo po 17 partnera (25,4%, odnosno 37,8%). Efikasnost notifikacije partnera obolelih od gonoreje i sifilisa bila je ukupno 30,4% i njen doprinos kontroli širenja ovih bolesti je manji nego što smo očekivali. Nacionalni vodiči sa standardizovanim protokolima značajno bi poboljšali proces notifikacije partnera kao i usvajanje novih netradicionalnih metoda notifikacije kao što je podela terapije seksualnim partnerima od strane obolelog pacijenta.

Ključne reči: Kontaktiranje partnera; Seksualni partneri; Gonoreja; Sifilis; Seksualno prenosive bolesti

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Unilateral Laterothoracic Exanthem – Asymmetric Periflexural Exanthem of Childhood – a Case Report and Literature Review

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Abstract

Unilateral laterothoracic exanthem (ULE), or asymmetric periflexural exanthem of childhood (APEC), is an uncommon skin eruption that usually occurs in childhood, with unilateral distribution and self limiting course. The etiology of ULE is unknown, but viral cause is suspected. We report a case of ULE in a 4-year-old girl, that was associated with parvo virus B19 infection, and a brief selected literature review. The patient presented with unilateral maculopapular rash on the left side of the body which was asymptomatic and resolved spontaneously within 5 weeks. The clinical diagnosis of ULE may be precise, ruling out a broad spectrum of differential diagnosis, and prevent unnecessary examinations, whereas the patient is informed about the benign self-limiting nature of ULE.

Key words: Exanthema; Child, Preschool; Diagnosis; Parvovirus B19, Human; Signs and Symptoms; Disease Progression

Introduction

Unilateral laterothoracic exanthem (ULE), also known as asymmetric periflexural exanthem of childhood (APEC), is a distinctive self-limiting skin eruption, with unknown etiology, that most commonly occurs in children (1, 2).

ULE manifests as a macular or papular rash, that typically develops unilaterally on the skin within or around the axilla, less often in the groin area, and spreads along the same side of the trunk and the corresponding arm or leg (1, 2 - 5). Rarely, the rash progresses bilaterally with an asymmetric predominance (1 - 3, 6). The exanthem tends to resolve spontaneosly within 3 - 6 weeks (1 - 3, 5, 6). Most of the affected patients are otherwise healthy. Histopathological features are rather nonspecific, although skin biopsies were not frequently performed. Perivascular lymphocytic infiltrates tend to cluster around the dermal blood vessels or eccrine ducts, but mild exocytosis and spongiosis in the epidermis are noted as well (1, 6). The cause of ULE is unknown, but viral etiology is suspected (1, 2, 4, 6 - 8).

Case report

A four-year-old girl was admitted to our Dermatology Department with a 10-day history of unilateral skin eruptions affecting the left side of her body. The exanthem had begun under her left axilla, and spread centrifugally along the left thoracic wall to the left side of the abdomen and the left arm and leg. The rash was asymptomatic, and there were no constitutional symptoms. Her previous medical hystory was unremarkable. A short course of topical corticosteroid cream (mometasone 0.1%) produced no improvement. Dermatological examination revealed numerous coalescing, small erythematous papules on the left side of the trunk (Figure 1), and on the left

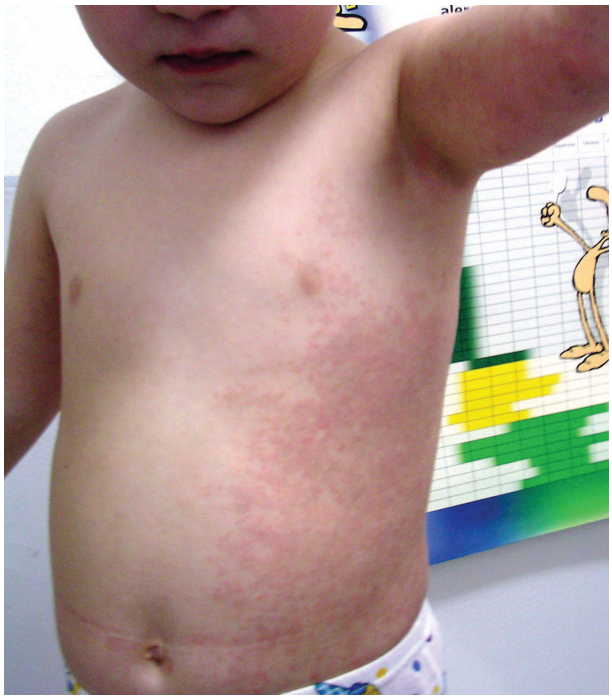

Figure 1. Unilateral laterothoracic exanthem with unilateral distribution (10th day)

arm and leg (Figure 2). Clinical diagnosis of ULE was established.

Basic laboratory results (blood count, liver enzymes, C-reactive protein) were normal. Serological tests for Epstein–Barr virus, cytomegalovirus, hepatitis B and C viruses were negative. However, parvovirus B19 serology showed raised IgM and negative IgG titres, indicating a recent infection. Further follow up of parvovirus B19 titer dynamics was not performed. The girl was treated symptomatically with a topical emolient cream, and the lesions resolved in 5 weeks.

Disscusion

We report a 4-year-old girl with ULE that followed a typical clinical course, associated with parvovirus B19 infection, suggesting that this virus was a possible etiologic factor. ULE is an uncommon disease which mostly affects children between one and five years of age. The eruptions usually start in the axilla, like in our case (1, 2, 5, 6, 8). The clinical course of the rash had two phases. The exanthem first began as a centrifugal periflexural spread during the initial 8 days, followed by more widespread skin eruptions (1). Although both sides

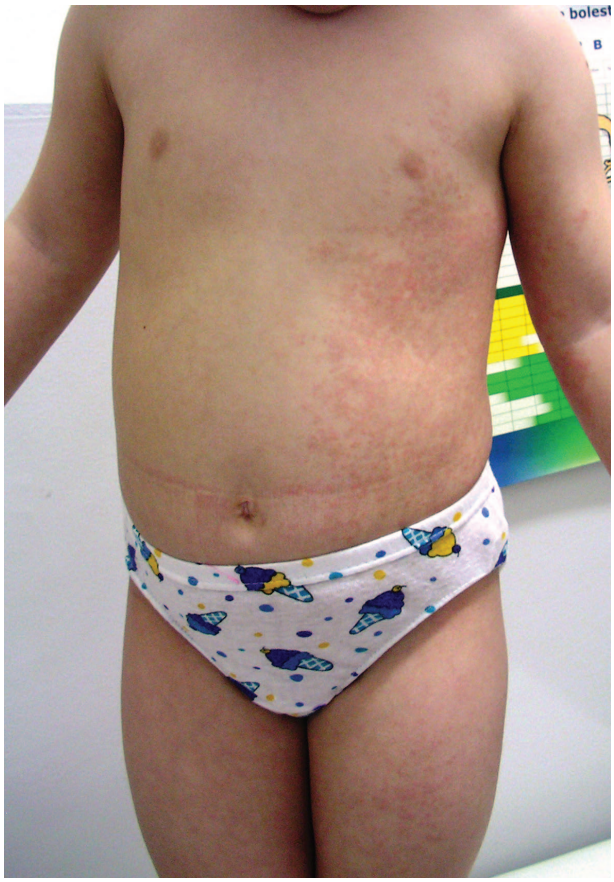

Figure 2. Erythematous papules on the left sides of the chest, abdomen, arm and leg

of the body are affected in 70% of cases, almost all have a unilateral predominance (1, 2, 6, 8). Spontaneous regression of exanthem occurs between the third and sixth week, as in our patient (1, 2, 5, 6). Pruritus and mild local lymphadenopathy is seen in about 50% patients (1, 2, 5, 8).

The etiology of ULE is unknown, although viral cause has been suggested in a number of cases (4, 6 - 13). Association with adenovirus, parainfluenza virus, parvovirus B19, human herpes virus 6 and 7, and Epstein–Barr virus has been reported in ULE (4, 7, 9 - 13). The virus most commonly associated with ULE was parvovirus B19, like in our case (10 - 12). ULE is more frequent in the winter and spring (1, 2, 5 - 8). However, interhuman transmission was not clearly documented (8). In a microbiological case-control study, Coustou et al. were not able to point to a specific virus or bacteria (14).

Several authors recently proposed a term ‘superimposed lateralized exanthem of child-

hood' (SLEC), instead of ULE or APEC. They considered that both terms were innaccurate, as they do not fully match the clinical features of exanthem (4, 15, 16). The exanthem usually presents in childhood, but there are several reports of adult cases of ULE (10, 12, 17 - 19). The skin eruptions do not always remain unilateral, and they are mostly followed by the appearance of less pronounced bilateral lesions or may affect, at least primarily, the groin area and the legs (6, 8, 16). Happle hypothesized that strict lateralized involvement can be explained by a postzygotic mutation at an early stage of embryogenesis that may have changed the cutaneous epitopes on one side of the body, causing an altered responsiveness of the skin to various infectious agents (15). In most cases, the subsequent bilateral involvement reflects a less severe reactivity of the contralateral keratinocytes, with a less pronounced polygenic predisposition to develop an inflammatory rash (4). According to this concept, some authors consider SLEC as the most suitable term for this condition (4, 15, 16).

The proposed mechanism is consistent with the assumption of an infectious etiology of SLEC (4). In our patient, serological findings indicated a recent parvovirus B19 infection, suggesting a causal relation. Many authors have supposed a viral trigger because of the children's age, frequent association of upper respiratory tract or digestive prodromes, serologic findings, spontaneous resolution in a few weeks, and seasonal fluctuations in incidence (1, 6, 8, 11). Duarte et al. considered a relationship to infections with adenovirus, parainfluenza virus 2 or 3, parvovirus B19, human herpes virus 6 or 7, and Epstein–Barr virus (7).

Differential diagnosis of ULE includes contact dermatitis, nonspecific viral exanthems, atypical pityriasis rosea, drug-related eruptions, miliaria, scarlet fever, Gianotti-Crosti syndrome, superficial fungal infections and scabies (2, 5, 6). The diagnosis is clinical, and laboratory investigations and biopsy are generally not required (5).

This uncommon exanthem is self-limiting and usually resolves in three to six weeks with no sequelae (1 - 3, 5, 6, 8). The treatment is symptomatic including emollients and antihistamines for pruritus.

Conclusion

The diagnosis of ULE is based on characteristic clinical findings, and patients should be informed about the benign nature and self-limiting course of this disease. Awareness of these conditions is required in order to prevent unnecessary examinations.

Abbreviations

ULE - Unilateral laterothoracic exanthem

APEC - Asymmetric periflexural exanthem of childhood

SLEC - Superimposed lateralized exanthem of childhood

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Unilateralni laterotorakalni egzantem/asimetrični perifleksuralni egzantem dečjeg doba – prikaz slučaja i kratak pregled literature

Sažetak

Unilateralni laterotorakalni egzantem/asimetrični perifleksuralni egzantem dečjeg doba je egzantem spontano rezolutivnog toka, sa asimetričnom distribucijom promena koji se obično javlja kod male dece. Etiologija unilateralnim laterotorakalnim egzantemom je nepoznata, ali se pretpostavlja da je virusna. Prikazujemo slučaj četvorogodišnje devojčice sa unilateralnim laterotorakalnim egzantemom, udružen sa infekcijom parvo virusom B19, uz kratak pregled izabrane literature. Pacijentkinja je imala asimptomatski unilateralni osip na levoj polovini tela, koji se spontano povukao za pet nedelja. Dijagnoza se postavlja na osnovu karakteristične kliničke slike i toka oboljenja. Pacijente treba informisati o benignoj prirodi i samoograničavajućem toku oboljenja, kako bi se izbegla nepotrebna dodatna ispitivanja.

Ključne reči: Egzantem; Predškolska deca; Dijagnoza; Humani parvovirus B19; Znaci i simptomi; Tok bolesti

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Distinguishing a Rare Variant of Lipidized Dermatofibroma from Nonlipidized Dermatofibromas in a Patient with Hypothyroidism and Alopecia Areata

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Abstract

Introduction. Lipidized dermatofibromas represent rare and often underrecognized variants of dermatofibromas. Histologically, dermatofibromas are composed of fibroblast-like spindle cells, foam cells, giant cells, siderophages, lymphocytes, capillaries, collagen fibers, and hyaline dermal collagen fibers. Lipidized dermatofibromas are characterized by numerous foam cells, Touton giant cells, and hyalinized wiry collagen in the stroma. **Case report.** We present a case of a 31-year-old woman with a history of hypothyroidism and alopecia areata, presenting with an enlarging 8 mm, firm erythematous nodule on her upper-mid back. Biopsy examination showed a cellular proliferation of spindle cells with peripheral collagen trapping and cholesterol clefts with associated foam cells and sclerosis, staining weakly positive for Factor XIIIa and negative for CD34. The diagnosis of a benign lipidized dermatofibroma was rendered. **Conclusion**. Lipidized dermatofibromas are rare histologic variants of dermatofibromas, biologically indolent, and should be distinguished from other cutaneous foamy histiocytic lesions, particularly xanthomas, which may alter patient management.

Key words: Histiocytoma, Benign Fibrous; Skin Neoplasms; Diagnosis; Treatment Outcome; Comorbidity

Introduction

Lipidized dermatofibroma is a rare variant of dermatofibromas. The prevalence of this variant in the general population is unknown, but some evidence suggest that it is as low as 2.1% in different dermatofibroma types (1). Lipidized dermatofibroma was described by Iwata as “ankle-type” dermatofibroma (fibrous histiocytoma) due to its characteristic location on the lower extremities (2). Subsequent evaluation by Wagamon demonstrated no significant difference in location between nonlipidized and lipidized dermatofibromas (3). Lipidized dermatofibromas are histologically characterized by an abundance of foam cells and stromal wiry hyalization (2). A case of a lipidized dermatofibroma is reported herein, and the significance of this rare pathological variant is discussed.

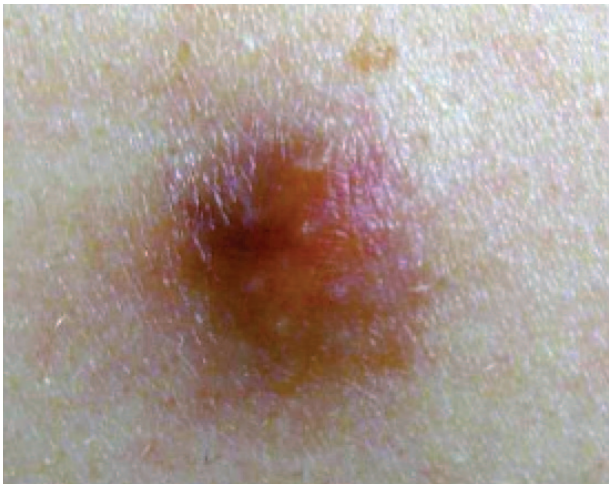

Figure 1. Upper back with 0.8 cm firm, erythematous, dome shaped nodule

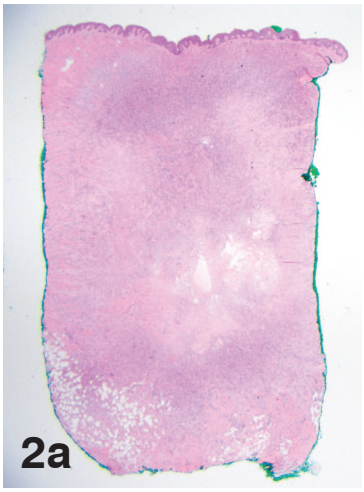

Figure 2a. Punch biopsy at 4 x demonstrating a mildly acanthotic epidermis with a basophilic cellular infiltrate in the dermis extending into subcutis

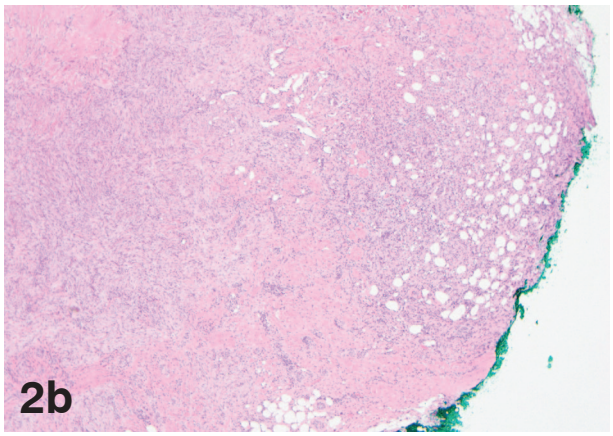

Figure 2b. 10 x demonstrating spindle cells with peripheral collagen trapping. The central aspect of the spindle cell proliferation contained cholesterol clefts with associated foam cells and sclerosis

Case Report

A 31-year-old woman with a history of hypothyroidism and alopecia areata presented with an enlarging 8 mm, firm erythematous nodule on her upper-mid back (Figure 1). The intermittently tender nodule had been present for over ten years. An 8 mm punch biopsy was performed from the central portion of the nodule. Histological evaluation revealed a mild epidermal acanthosis (Figure 2A). Within the dermis and extending into the subcutis, there was a cellular proliferation of spindle cells with peripheral collagen trapping (Figures 2B, C). The central aspect of the spindle cell proliferation contained cholesterol clefts with associated foam cells and sclerosis (Figure 3). No significant cytologic atypia or mitotic activity was identified. The sample stained weakly positive for Factor XIIIA within the spindle cell proliferation (Figure 4). It stained negatively for CD34 in the central aspect of spindle cell proliferation and positively along the periphery (Figure 5). The diagnosis of a benign lipidized dermatofibroma was rendered. Three month follow up showed no recurrence.

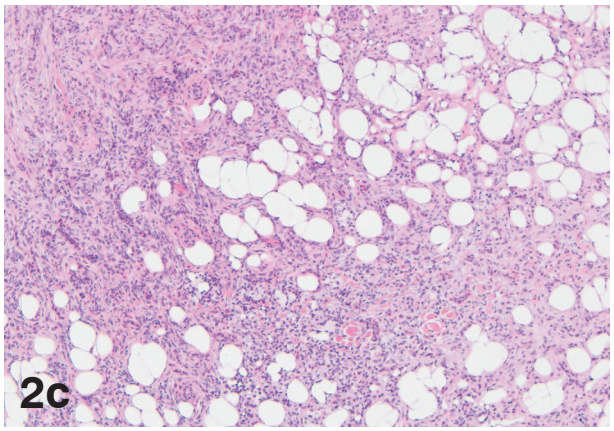

Figure 2c. 40 x no significant cytologic atypia or mitotic activity was identified

Discussion

Lipidized dermatofibromas represent a rare and often underrecognized variant of dermatofibromas. Histologically, dermatofibro-

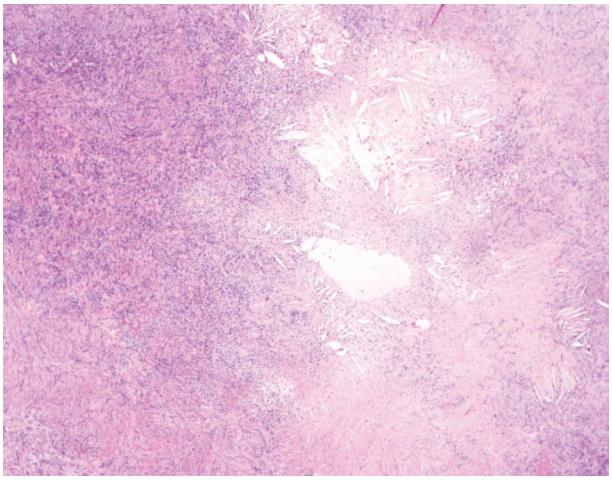

Figure 3. 40 x spindle cell proliferation containing cholesterol clefts

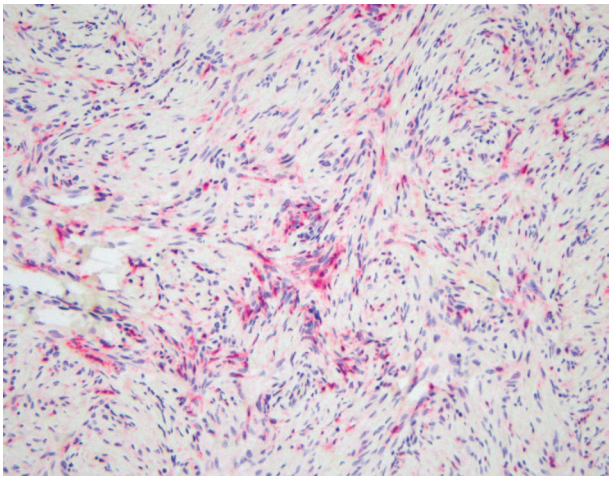

Figure 4. Factor XIIIA stain weakly positive within the spindle cell proliferation

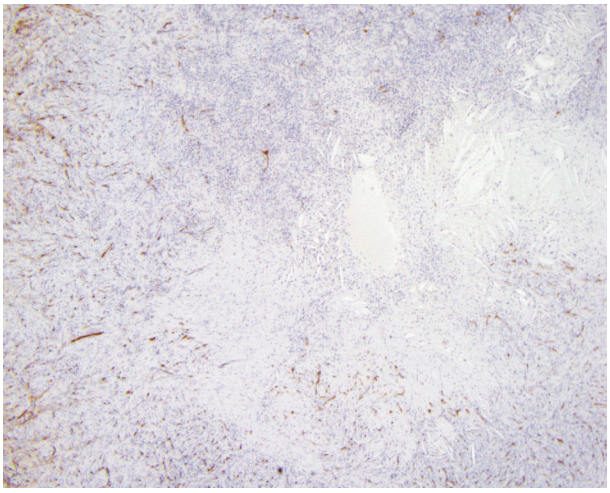

Figure 5. CD34 stain negative in the central aspect of spindle cell proliferation and positive along the periphery

mas are composed of a mixture (in varying proportions) of fibroblast-like spindle cells, as well as foam cells, giant cells, siderophages, lymphocytes, capillaries, collagen fibers, and entrapping hyaline dermal collagen fibers (4). Lipidized dermatofibromas are most remarkable for numerous foam cells and frequent Touton-type giant cells, as well as hyalinized wiry collagen in the stroma, which can sometimes be extensive (5).

Wagamon et al. (3) conducted a retrospective case review to investigate the relationship between lipidized dermatofibromas and patient age, anatomic location, and total serum cholesterol. They determined that patients with lipidized dermatofibromas did not differ significantly from patients with regular dermatofibromas in regard to age, tumor location, or underlying serum lipid levels.

Conclusion

Lipidized dermatofibroma is a rare histological variant of dermatofibromas, biologically indolent, which should be distinguished from other cutaneous foamy histiocytic lesions, particularly xanthomas, which may alter patient management.

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Razlikovanje retke varijante lipidizovanih od nelipidizovanih dermatofibroma kod pacijentkinje sa hipotiroidizmom i alopecijom areata

Sažetak

Uvod. Lipidizovani dermatofibrom predstavlja retku i često nedovoljno prepoznatu varijantu dermatofibroma. Histološki, dermatofibromi se sastoje od fibroblastnih vretenastih ćelija, penastih ćelija, gigantskih ćelija, siderofaga, limfocita, kapilara, kolagenih vlakana i hijalinskih kožnih kolagenih vlakana. Lipidizovane der-

matofibrome karakterišu brojne penaste ćelije, džinovske ćelije tipa *Touton* i hijalinski čvrst kolagen u stromi. **Prikaz slučaja**. Predstavljamo slučaj 31-godišnje žene sa istorijom hipotiroidizma i alopecije areata. Primljena je sa čvrstim eritematoznim nodulom na gornjoj polovini leđa prečnika 8 mm. Biopsija ispitivanog uzorka pokazala je ćelijsku proliferaciju vretenastih ćelija sa perifernom pojavom kolagena, holesterola sa penastim ćelijama, sa slabim pozitivnim bojenjem za faktor XIIIa i negativnim za CD34. Postavljena je dijagnoza benignog lipidizovanog dermatofibroma. **Zaključak.** Lipidizovani dermatofibromi su retke histološke varijante dermatofibroma, biološki indolentni, i treba ih razlikovati od drugih akutnih penastih histiocitnih lezija, posebno ksantoma, što može promeniti lečenje pacijenata.

Ključne reči: Benigni fibrozni histiocitom; Kožne neoplazme; Dijagnoza; Ishod terapije; Komorbiditet

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Primary Cutaneous Diffuse Large B-Cell Lymphoma – a Case Report

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Abstract

In 2005, the World Health Organization - European Organization for Research and Treatment of Cancer (WHO-EORTC) classified cutaneous B-cell lymphomas into 4 categories: primary cutaneous marginal zone B-cell lymphoma (PCMZL), primary cutaneous follicle center lymphoma (PCFCL), primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL-LT), and primary cutaneous diffuse large B-cell lymphoma, other (PCDLBCL-O). The absence of evident extra-cutaneous disease is a necessary condition for the diagnosis of primary cutaneous B-cell lymphomas, because they have a completely different clinical behavior and prognosis from their nodal counterparts. PCDLBCL-O basically represents a morphological variation, lacking the typical features of PCDLBCL-LT, neither confirming the definition of PCFCCL, but on the clinical ground, its behavior seems at least to partially overlap the indolent course of PCFCCL. In fact, the present WHO lymphoma classification from 2008 overcame the previous WHO-EORTC classification, including at least a part of PCDLBCL-O within the spectrum of PCFCCL. However, owing to the rarity and heterogeneity of the PCDLBCL-O, the precise clinicopathological characteristics have not been well characterized and the optimal treatment for this group of lymphomas is yet to be defined. Nevertheless, dermatologists and pathologists should be aware of this entity in order to avoid unnecessary aggressive treatment. We present a case of a 46-year-old Caucasian male with one large round-shaped tumor and a few scattered nodules localized on the back. The histopathological features of the lesion corresponded to PCDLBCL-O. The patient follow-up showed that he was disease-free three months after surgical excision of the lesions and adjuvant local radiotherapy. No additional therapy was introduced, including chemotherapy with rituximab, cyclophosphamide, doxorubicin hydrochloride, oncovin, prednisolone (R-CHOP).

Key words: Lymphoma, Large B-Cell, Diffuse; Skin Neoplasms; Diagnosis; Radiotherapy; Treatment Outcome; Case Reports

Introduction

The issue of primary cutaneous B-cell lymphomas (PCBCLs) other than marginal zone lymphoma (MZL) classification has been a matter of debate. In the previous World Health Organization - European Organization for Research and Treatment of Cancer (WHO-EORTC) classification (2005) (2, 3) cutaneous diffuse large B-cell lymphomas had several variants, including PCDLBCL-LT, cases with peculiar morphology (T-cell/histiocyte rich, plasmablastic) as well as diffuse lymphomas of centroblastic-like cells, intermingled with a mixed inflammatory infiltrate and with variable expression of BCL2, which are named primary cutaneous diffuse large B-cell lymphoma, other (PCDLBCL-O). PCDLBCL-O basically represents a morphological variant lacking the typical features of PCDLBCL-LT, neither confirming the definition of PCFCCL, whereas on the clinical ground, its behavior seems at least to partially overlap the indolent course of PCFCCL. In fact, the present 2008 WHO lymphoma classification overcame the previous WHO-EORTC and included at least a part of PCDLBCL-O within the spectrum of

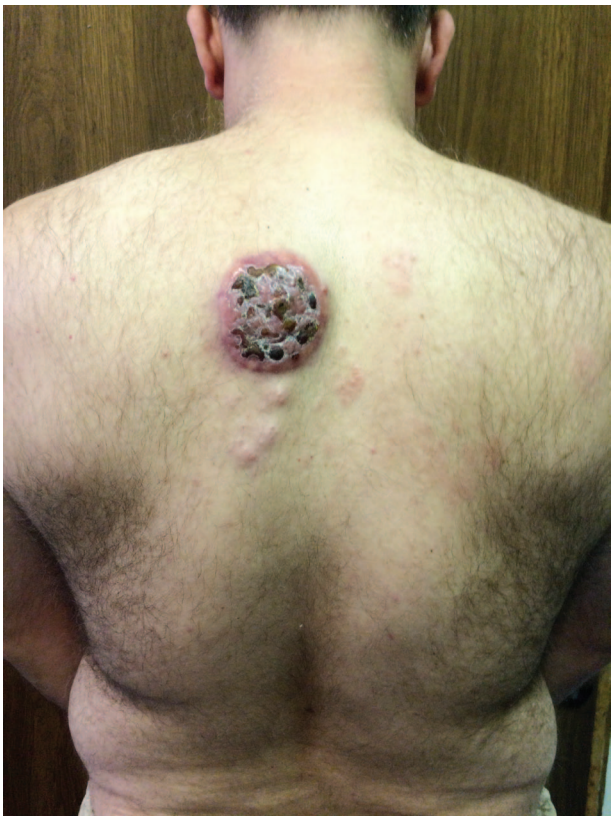

Figure 1. Clinical presentation of tumors and nodules in the left paravertebral region

PCFCCL (4). The absence of evident extracutaneous disease is a necessary condition for the diagnosis of PCBCLs because they have a completely different clinical behavior and prognosis from nodal counterpart (5).

Case Report

A 46-year-old Caucasian male was admitted to our department with an asymptomatic tumor on his back, in the left paravertebral region, that appeared two months earlier. It began growing rapidly, changing color to red and livid with formation of vesicles on the tumor surface, with hemorrhagic crusts upon drying. Also, smaller, new nodules appeared below the lower borderline of the tumor during the following month. Neither systemic symptoms, nor palpable lymphadenopathy were observed. The patient was otherwise healthy. There was no family history of malignancy.

Clinical examination of the patient's back revealed a large, asymptomatic, round shaped and well-demarcated tumor with elevated erythematous border located in the left paravertebral region. It was approximately 6 cm in diameter, and covered with multiple yellowish and black hemorrhagic crusts. In addition, close to the lower border of this tumor, three separate, well-demarcated, skin-colored nodules were noticed (Figure 1 and Figure 2).

Upon admission, tumor biopsy was performed from 2 separate sites. The histopathologic analysis of these two samples showed a diffuse infiltration of large centroblasts with a typical morphology - large nucleus, small basophilic cytoplasm and multiple scattered nucleoli (Figure 3).

On immunohistochemical (IHC) analysis, the infiltrated cells were positively stained with CD20 and Bcl6. There was no evident expression of CD3, CD5, CD10, CD23, MUM-1 and Bcl2. (Figure 4). Fluorescence in situ hybridization (FISH) on skin samples for MYC oncogene was negative, which excluded the possibility of a double-hit lymphoma.

Complete and differential blood cell count, ESR, glucose, urea, serum creatinine, total proteins, albumins, uric acid, total bilirubin, electrolytes, iron, liver enzymes and C-reactive protein were within physiological

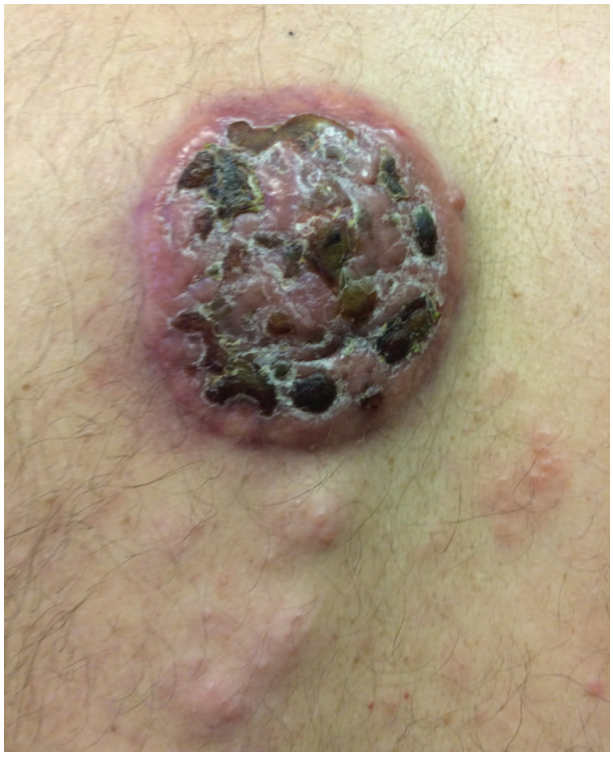

Figure 2. Close-up of tumors and nodules

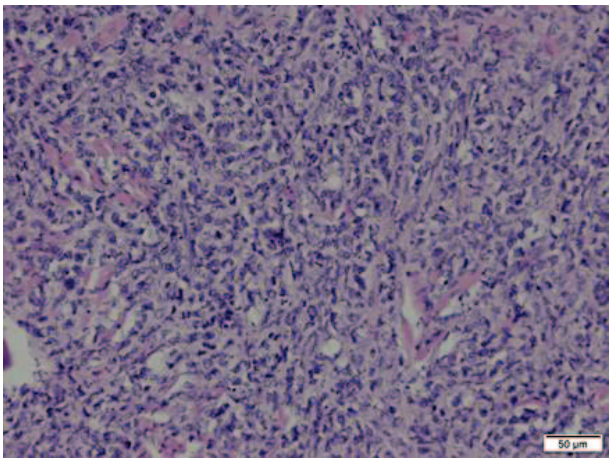

Figure 3. Diffuse infiltration of large centroblasts (hematoxylin and eosin, x 50)

limits. The analysis of B-cell clonality from skin biopsy samples showed monoclonal rearrangement, but bone marrow and blood sample analysis showed polyclonal rearrangement. Bone marrow biopsy was performed and histopathological analysis revealed normal, mature hematopoiesis with no presence of neoplastic cells, both morphologically and immunohistochemically. Peripheral lymph node ultrasound showed no signs of enlarged or pathological lymph nodes. CT scans revealed no signs of central lymphonodopathy or internal organ involvement. PET-CT further excluded extra-cutaneous involvement.

The final diagnosis of primary cutaneous large B-cell lymphoma, other (PCLBCL-O) or primary cutaneous large B-cell lymphoma, not otherwise specified (PCLBCL-NOS) was made based on morphology, immunohistochemical and staging evaluations, as well as clonality analysis of the skin, bone marrow and blood samples. The interdisciplinary tumor board decided to perform a surgical excision of the tumor and nodules, and adjuvant radiotherapy after surgery. Recognition of the correct entity led to appropriate therapeutic strategy without relapse on 6-month follow-up (Figure 5).

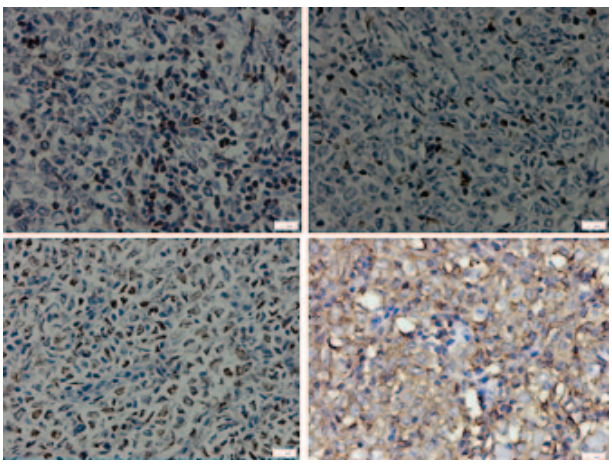

Figure 4. Immunohistochemical staining (a) Bcl2- (b) MUM-1- (c) CD20+ (d) Bcl6+

Discussion

In the light of overlap between histological and immunophenotypic findings, accurate differentiation of cutaneous B-cell lymphoma (CBCL) from infiltrates of nodal or other extranodal B-cell lymphomas is only possible by means of staging examinations: clinical presentation, laboratory tests, radiologic examinations (MSCT and PET-CT), lymph node biopsy (enlarged nodes) and bone marrow biopsy. Ideally, the diagnosis should be made in centers specializing in cutaneous lymphomas and it is usually made by an interdisciplinary team consisting of dermato-oncologists, hematologists and (dermato-) pathologists (6).

Staging is performed according to the tumor-node-metastasis (TNM) system, which was published in 2008 and evaluates cutaneous spread more adequately than other classifications. The T1 stage corresponds to a solitary lesion, while multiple lesions with involvement of one or two neighboring regions (T2) or more body regions (T3) stand for a higher T stage (7). According to TNM staging, our patient had a T2N0M0 stage, since he had multiple lesions limited to one body region without lymph node or systemic involvement.

PCBCL belongs to a distinct group of lymphoproliferative disorders defined by its presentation in the skin without evidence of extracutaneous spread at the time of diagnosis (8). Extranodal involvement occurs in approximately 25% of non–Hodgkin's lymphomas, with the gastrointestinal tract being the most common site of extranodal involvement, followed by the skin (9). The annual incidence of cutaneous lymphomas is approximately 0.5 – 1/100,000 (6). PCBCL group accounts for 20% – 25% of all primary cutaneous lymphomas (10).

A few studies have used the immunohistochemical expression of CD10, bcl-6, or

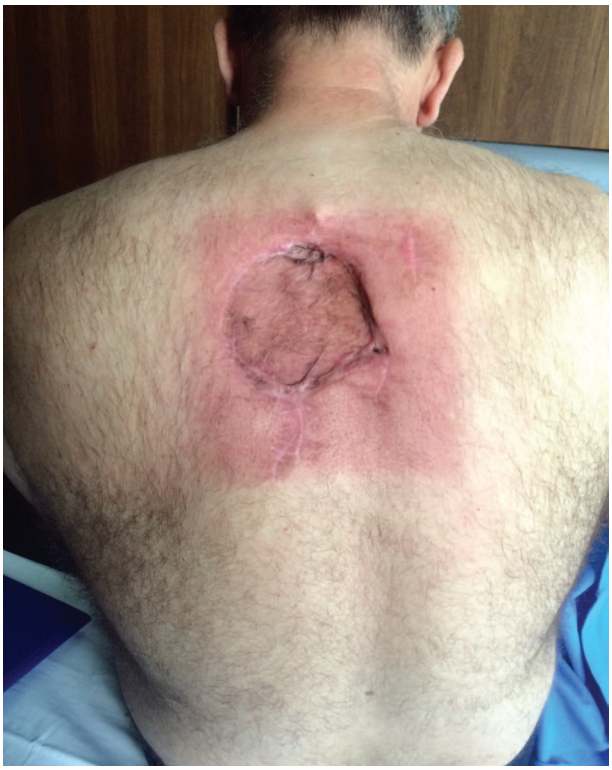

Figure 5. Clinical presentation after treatment

MUM1 to classify cases of DLBCL into GCB (germinal center B-cell) and non-GCB (non-germinal center B-cell) subgroups. Given that bcl-6 and CD10 are markers of germinal center B cells, cases were classified into the GCB group if CD10 alone was positive, or if both bcl-6 and CD10 were positive. If both bcl-6 and CD10 were negative, the case was in the non-GCB subgroup. If bcl-6 was positive and CD10 was negative, the expression of MUM1 determined the group: if MUM1 was negative, the case was in the GCB group; if MUM1 was positive, the case was in the non-GCB group. The 5-year overall survival for the GCB group was 76% compared with only 34% for the non-GCB group (11). When it comes to our patient, immunohistochemically, cells were positively stained with Bcl6 and there was no evident expression of CD10 and MUM-1. All of the above puts our patient to the GCB (germinal center B-cell) subgroup of DLBCL which has much better overall survival compared to other subgroups.

The largest study on the subject of PCBCLs was conducted in Italy, and it was published in September 2016. It was a retrospective, multicentric, consensus-based revision of the clinicopathologic characteristics of 161 cases of PCBCL other than MZL. Upon the histologic features, listed in the WHO classification, 96 cases were classified as PCFCCL and 25 as PCDLBCL-LT; however, 40 cases did not fit in the former subgroups in terms of cytology and/or architecture, so they were classified as PCDLBCL, not otherwise specified (PCDLBCL-NOS), previously known as PCDLBCL, other. This study confirmed that another group, CDLBCL-NOS, exists, which can be recognized through a careful combination of histopathologic criteria coupled with adequate clinical information. Separation of PCDLBCL-NOS upon histogenetic profile documented a worse prognosis for the non-GC subgroup, whereas cases with a GC profile were more similar to PCFCCL. The first-line treatment was mainly radiotherapy in PCFCCL (49%) and in both PCDLBCL-LT (60%) and PCDLBCL-NOS (55%). However, follow-up data of PCDLBCL-NOS were more similar to PCFCCL in regard to complete response, relapse rate, number of patients alive and disease-free, consistently different from PCDLBCL-LT. The 2-year and 5-year overall survival for both PCFCCL and PCDLBCL-NOS was around 95%, while for PCDLBCL-LT it was only around 55%. With the limitations of a retrospective data collection, observations from this study suggest the opportunity of a radiotherapy-privileged first-line treatment for PCDLBCL-NOS, particularly in cases with a GC profile (4).

Sokol et al. proposed a PCBCL treatment algorithm (12). The algorithm was based on the present WHO lymphoma classification, which overcame the previous WHO-EORTC and included at least a part of PCDLBCL-O within the spectrum of PCFCCL. In their opinion, PCMZL and PCFCL (including PCDLBCL-O) are low-grade PCBCLs, with an estimated 5-year disease-specific survival rate greater than 95%. Surgical excision or focal radiation therapy is sufficient to control stages T1 and T2 of the disease. Rituximab monotherapy is frequently used for patients with stage T3 disease. PCDLBCL, LT is an intermediate-grade B-cell lymphoma, with a 5-year disease-specific survival rate of approximately 50%. An anthracycline-based chemotherapy regimen with rituximab is usually required as initial therapy to improve the outcome (12).

We decided to perform a surgical excision and perform local radiotherapy, since our

patient belonged to the germinal center B-cell-like subgroup, with a T2N0M0 stage with multiple lesions limited to one body region without lymph node or extra-cutaneous involvement. So far, he is disease-free after the treatment with regular check-ups planned every three months. Recognition of the correct entity led to appropriate therapeutic strategy with favorable outcome.

Conclusion

In conclusion, primary cutaneous diffuse large B-cell lymphoma, other**,** represents a rare entity which should be acknowledged as a separate diagnostic category in regard to other primary cutaneous B-cell lymphomas. In patients with solitary or multiple lesions limited to one or two neighboring regions and no extra-cutaneous involvement, an indolent clinical course can be expected. Studies published in the last 5 years recommend surgical excision or local radiotherapy, without chemotherapy, as the best treatment option for these patients. Dermatologists and pathologists should be aware of this entity in order to avoid unnecessary aggressive treatment, especially in cases where the lesions on the skin are localized and there are no signs of systemic involvement.

Abbreviations

WHO-EORTC - World Health Organization - European Organization for Research and Treatment of Cancer

CBCL - cutaneous B-cell lymphoma

PCDLBCL-O - primary cutaneous diffuse large B-cell lymphoma, other

PCMZL - primary cutaneous marginal zone B-cell lymphoma

PCFCCL - primary cutaneous follicle center cell lymphoma

PCDLBCL-LT - primary cutaneous diffuse large B-cell lymphoma, leg type

R-CHOP - rituximab + cyclophosphamide, doxorubicin, oncovin and prednisone

IHC - immunohistochemical analysis

MSCT - Multislice Computed Tomography

PET-CT - Positron Emission Tomography - Computed Tomography

TNM - Tumor, Nodes, Metastases

FISH - Fluorescence in situ hybridization

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Primarni kutani difuzni B-krupnoćelijski limfom – prikaz slučaja

Sažetak

Prema zajedničkoj klasifikaciji Svetske zdravstvene organizacije i Evropske organizacije za istraživanje i lečenje kancera iz 2005. godine, B-ćelijski kutani limfomi su klasifikovani u četiri kategorije: primarni kutani limfom marginalne zone (PCMZL), primarni kutani limfom folikularnog centra (PCFCL), primarni kutani difuzni krupnoćelijski B-limfom lokalizovan na nogama (PCDLBCL-LT) i primarni kutani difuzni krupnoćelijski B-limfom, drugi (PCDLBCL-O). Odsustvo ekstrakutane bolesti je neophodan uslov za dijagnozu primarnog kutanog B-ćelijskog limfoma, pošto oni imaju potpuno različito kliničko ponašanje i prognozu u odnosu na njihove ekvivalente koji zahvataju limfne noduse. Primarni kutani difuzni krupnoćelijski B-limfom praktično predstavlja difuznu neoplastičnu proliferaciju krupnih B-limfocita (predominantno centroblasta) u koži koja klinički i histološki ne spada ni u grupu PCFCL niti u grupu PCLBCL, *leg type*. Kliničko ponašanje ovih limfoma se barem parcijalno, ako ne i potpuno, preklapa sa PCFCCL i koji, za razliku od istih limfoma koji zahvataju noduse, imaju odličnu prognozu. Zapravo, trenutna klasifikacija SZO iz 2008. godine prevazišla je prethodnu WHO/EORTC i uvrstila je PCDLBCL-O u spektar PCFCCL. Međutim, uzevši u obzir raritet i heterogenost ovih limfoma, precizne kliničke, histopatološke karakteristike kao i smernice za optimalan terapijski tretman još uvek nisu jasno definisane. Prikaz slučaja. U radu je opisan slučaj četrdesetpetogodišnjeg muškarca sa velikim, asimptomatskim, brzorastućim tumorom i više pojedinačnih nodusa lokalizovanih na koži leđa, paravertebralno levo, čije histopatološke karakteristike odgovaraju primarnom kutanom difuznom krupnoćelijskom B-limfomu (PCDLBCL-O). Dosadašnje praćenje našeg pacijenta je pokazalo da, nakon hiruške ekcizije promena i lokalne radioterapije, nema znakova relapsa bolesti. Nisu korišćene dodatne metode lečenja do danas, ali su neophodne redovne tromesečne kontrole. Zaključak. Dermatolozi i patolozi bi trebalo da budu upoznati sa ovim tipom limfoma kao posebnim entitetom, kako bi se izbegle nepotrebne agresivne metode lečenja, naročito u slučajevima gde su lezije na koži lokalizovane i gde nema znakova postojanja sistemske bolesti. Prepoznavanje pravog entiteta dovodi do svrsishodnog terapijskog plana sa povoljnim terapijskim ishodom.

Ključne reči: Difuzni B-krupnoćelijski limfom; Kožne neoplazme; Dijagnoza; Radioterapija; Ishod terapije; Prikazi slučajeva

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DERMOSCOPY CASE OF THE MONTH
Combined Nevus – a Case Report

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Abstract

Combined nevi are melanocytic lesions composed of two or more distinct types of melanocytic populations within the same lesion. Different types of combined nevi may form bizarrely shaped, multicolored skin lesions, making them one of the greatest melanoma mimickers. We report a 48-year-old female patient with suspicious skin lesion in the left lumbar region. Clinically, there was an oval, slightly asymmetrical lesion measuring 6 x 4 mm, showing multiple colors and shades of brown and black. A dermoscopic examination revealed a brown-bluish coloration in the right part of the lesion, while a fine pigment network with perifollicular halo was found in the left part of the lesion, suggesting the diagnosis of a combined nevus. Histological examination showed a poorly circumscribed proliferation of dendritic melanocytes in the superficial and deep dermis and proliferation of melanocytes in the dermoepidermal junction. A surgical excision of the tumor was performed, in order to confirm the dermoscopic findings. In conclusion, dermoscopy is useful in differentiating combined nevi from other melanocytic lesions.

Key words: Nevus; Skin Neoplasms; Nevus, Blue; Nevus, Pigmented; Dermoscopy; Diagnosis; Melanoma

Introduction

Combined nevi are melanocytic lesions composed of two or more distinct types of melanocytic populations within the same lesion. These are uncommon lesions, accounting for less than 1% of all biopsied nevi (1, 2). Epidemiologically, they are most commonly seen in children and young adults, but they may occur at any age and in both sexes (1).

Different types of nevi may form bizarrely shaped and multicolored skin lesions, making them one of the greatest melanoma mimickers. Accurate clinical diagnosis is made only in 2.4% of all cases, whereas melanoma and dysplastic nevi are most frequent preoperative diagnoses (2).

The clinical presentation of combined nevi varies widely, depending on clinical features of individual components of two nevi cell populations. In addition, presence of trauma, inflammation or regression may modify the lesion, posing a diagnostic challenge even to the experienced dermatologists. Herein we present a case of a combined nevus in a 48-year-old female.

Case Report

A 48-year-old female patient was admitted to our Dermatovenereology Clinic for a regular skin examination. A suspicious skin lesion was detected in the left lumbar region. The patient claimed that as far she knew the lesion has been there for a few years, with no changes in size, color or shape. The patient's personal and family history was negative for any type of skin malignancy. Clinically, it was an oval, slightly asymmetrical lesion measuring 6 x 4 mm, showing multiple colorations and shades of brown and black (Figure 1).

A dermoscopic examination revealed a brown-bluish coloration in the right part of the lesion corresponding to blue nevus, while a fine pigment network with perifollicular halo was found in the left part of the lesion, consistent with a junctional nevus, thus suggesting the diagnosis of combined nevus (Figure 2).

A surgical excision of the tumor was performed in order to confirm the dermoscopic findings. Histological examination revealed the presence of poorly circumscribed prolif-

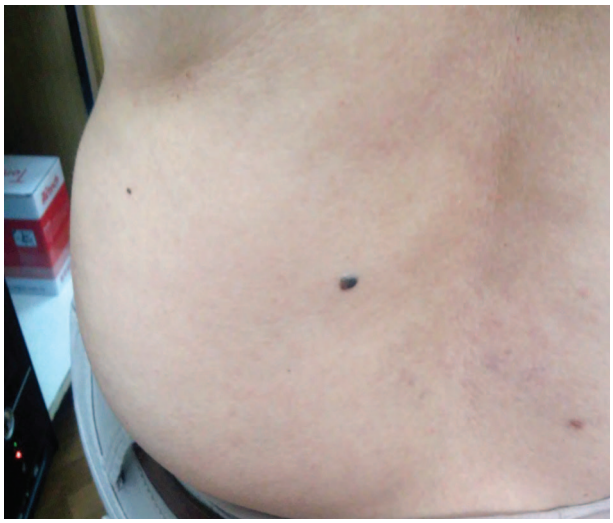

Figure 1. An oval, slightly asymmetrical lesion in the left lumbar region

eration of dendritic melanocytes in the superficial and deep dermis, combined with conspicuous melanophages, corresponding to the blue nevus. In dermoepidermal junction, proliferation of melanocytes was present, as part of junctional nevus (Figure 3).

Discussion

Collision or compound tumors are a coexistence of two different neoplastic lesions within the same biopsy specimen. Seborrheic keratosis, basal cell carcinoma, dermatofibroma are the most commonly found lesions

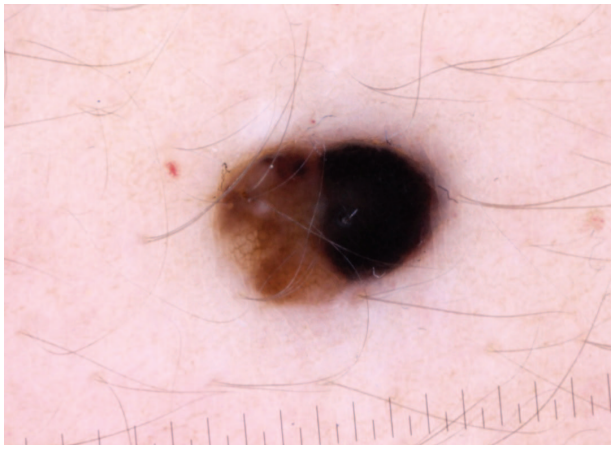

Figure 2. Fine pigmented network on the left and a brown-bluish coloration on right side of the lesion

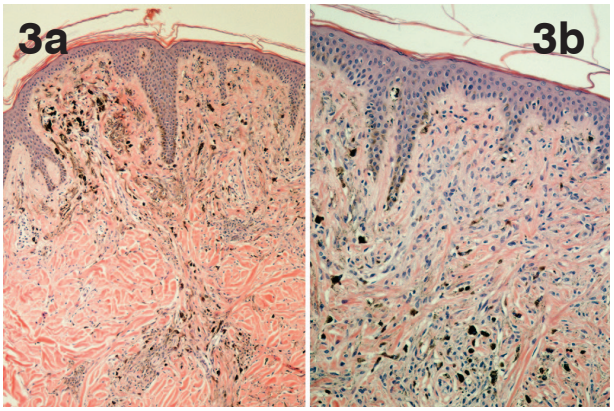

Figure 3. a. Blue nevus: poorly circumscribed proliferation of dendritic melanocytes in the superficial and deep dermis: **b.** Melanocytic proliferation in the dermoepidermal junction as part of the combined nevus

in nonmelanocytic components of collision lesions, while the most frequently found combination is that of basal cell carcinoma and nevi (3, 4). A subtype of collision tumors, where tumor is composed of different forms of melanocytes is called a combined nevus. The origin of two distinctive melanocytic populations in combined nevi may be explained by two hypotheses: divergent terminal differentiation of a single cell population, or coexisting distinctive nevomelanocytes in the same lesion (5).

Patients with combined nevi often report a stabile pigmented lesion which has been present for many years. In other cases, clinical manifestations of combined nevi are rapid growth, changes on pre-existing nevus, or occurrence of symptoms. In both cases, combined nevus often appears as an asymmetrical, multicolored macule, plaque or nodule. One part of lesion may be raised, whereas the other is flat (1, 2).

A large study of 511 identified cases of combined nevi was performed by L. Baran et al. (6). The most common type was the combination of common with blue nevi, commonly found on the trunk and in female patients.

Typical dermatoscopic features of individual components of combined nevi, together with anamnestic information of persistent skin lesions, are usually sufficient for making a diagnosis. In our patient, dermatoscopy revealed fine pigmented network indicating a melanocytic nevus and brown-bluish colora-

tion typical for blue nevi which corresponds to a combined nevus. When presented in combined nevi, blue coloration is usually located in the center of the lesion. Peripheral distribution can also be observed, like in our case, although it is more commonly exhibited in melanoma (7, 8). Since the lesion of our patient presented in the skin area not suitable for daily skin inspection, the patient could not provide reliable information on the possible changes in the size, shape and color of the nevus, indicating the need for surgical excision and histopathological examination.

Histopathological diagnosis is based on distinctive melanocytic population within the same biopsy. Histological features of individual components of combined nevi usually retain typical histological appearance, but sometimes components may be intermingled, making the histopathological diagnosis difficult (1). Richard et all. have examined 180 cases of combined nevi and reported that the most common combination was a common acquired nevus of compound type with a blue nevus (2). In our case, histopathological examination revealed features of junctional nevi at dermoepidermal junction and blue nevi in the dermis, that corresponded to features seen on dermatoscopy. Only 5 cases of common acquired nevus of junctional type associated with blue nevus were observed in the previously reported study (2).

Conclusion

Combined nevi are uncommon melanocytic neoplasms usually misdiagnosed as melanomas. Dermoscopy is useful in differentiating combined nevi from other melanocytic lesions. In order to rule out melanoma, all suspicious lesions should be biopsied.

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Kombinovani nevus – prikaz slučaja

Sažetak

Kombinovani nevusi su melanocitične lezije sastavljene od dve ili više različitih populacija melanocita u jednoj leziji. Kombinacijom različitih nevusa u istoj leziji mogu se formirati lezije neobičnog izgleda i sa više boja, što ih čini jednim od najvećih imitatora melanoma. Prikazujemo 48-godišnju pacijentkinju sa sumnjivom lezijom na levoj slabinskoj regiji. Klinički, uočena je ovalna, blago asimetrična lezija dimenzija 6 x 4 mm, koja je pokazivala više nijansi braon i crne boje. Dermoskopski je uočena smeđeplavičasta koloracija na desnoj strani, dok je u levom delu lezije uočena pigmentna mreža sa perifolikularnim haloom, što je ukazivalo na dijagnozu kombinovanog nevusa. Histološki, uočeno je prisustvo dendritičnih melanocita u površnom i dubokom dermisu, kao i proliferacija melanocita u dermoepidermalnoj spojnici. Hirurška ekcizija je izvršena kako bi se potvrdio dermoskopski nalaz. Može se zaključiti da je dermoskopija korisna dijagnostička metoda u diferentovanju kombinovanih nevusa od drugih melanocitičnih lezija.

Ključne reči: Nevus; Kožne neoplazme; Plavi nevus; Pigmentni nevus; Dermoskopija; Dijagnoza; Melanom

A Report on the 7th Post-Chicago Meeting on Melanoma/Skin Cancer, Munich, 2017

The 7th Post-Chicago Meeting on Melanoma/Skin Cancer was held from June 29 - 30, 2017 in Leonardo Royal Hotel in Munich. Professor Axel Hauschild and Professor Claus Garbe were the congress presidents. The Post-Chicago Meeting on Melanoma/Skin Cancer 2017 attracted 614 participants from 31 countries from the field of dermatology, medical oncology, immunology, radiooncology, and other specialties. The interactive congress offered a comprehensive overview on all new developments in melanoma diagnostics and therapy and a direct communication with the world´s leading experts in these fields. During the 2-day program a wide spectrum of topics in dermato-oncology were covered. Our delegation had two participants. Professor Lidija Kandolf Sekulović presented a topic on "Access to New Drugs in Europe" in the symposium "Burning Questions in the Treatment of Skin Cancer", and Professor Lidija Kandolf Sekulović and Professor Željko Mijušković presented interesting melanoma cases in EADO Forum session.

The next Post-Chicago Meeting will take place in Leonardo Royal Hotel in Munich from June 28 - 29, 2018.

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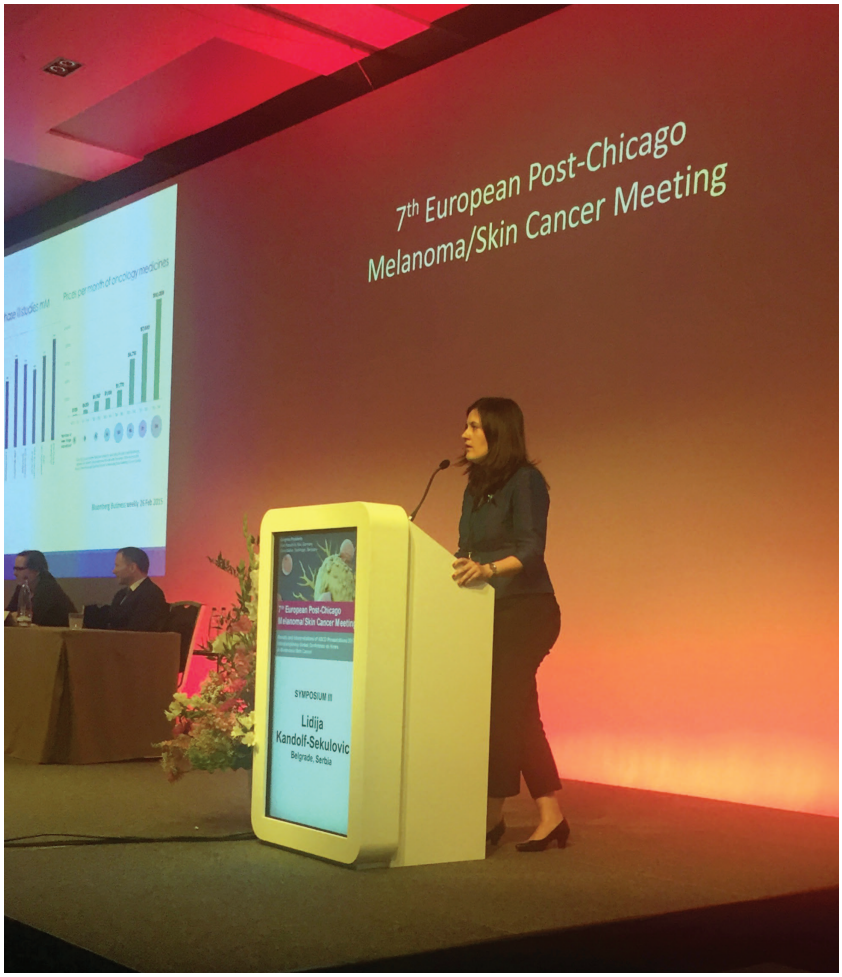

XX CONGRESS

of the Serbian Association of Dermatovenereologists

Belgrade 18–20 May, 2017

- abstracts -

XX KONGRES

Udruženja dermatovenerologa Srbije

Beograd 18–20. maj 2017.

- apstrakti -

P1 Biologic Therapy for Psoriasis – Our Experience

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Abstract

Psoriasis is a chronic inflammatory skin disease that affects around 2% of population. Depending on severity, psoriasis may have devastating functional and emotional consequences. Even though the disease may present with various clinical features, the most common is the vulgar form. It is characterized by erythematous, scaly plaques on the elbows, knees, lumbosacral area, but severe cases may affect even larger body surfaces. Apart from skin lesions, psoriasis patients may suffer from psoriatic arthritis, as well as serious comorbidities. Conventional therapies of psoriasis include topical solutions, phototherapy and photochemotherapy, retinoids, methotrexate or cyclosporine. However, these treatments may fail, may be contraindicated, or associated with severe adverse events. Therefore, novel biologic response modifiers or simply biologic agents are indicated in these cases. They act by targeting the precise elements in immunological cascade. Herein, we present our ten years' experience (2007 - 2017) with biologics used in the treatment of moderate to severe psoriasis, their effectiveness and safety.

P2 Clinicopathological Characteristics of Pemphigus Group

Gjorgji GOCEV

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Abstract

Autoimmune bullous skin diseases represent a heterogeneous group of disorders of skin and/or mucous membranes, characterized by association with circulating autoantibodies (IgG or IgA) against adhesion molecules of the epidermis and dermal-epidermal basement membrane zone. Binding of these autoantibodies to their antigenic targets results in loss of adhesion between epidermal keratinocytes or at the level of the basement membrane zone, which clinically presents with formation of blisters and secondary erosions.

The diagnosis of autoimmune bullous skin diseases is based on correlation between clinical findings, histology and direct immunofluorescence of perilesional skin, and serological detection of autoantibodies by indirect immunofluorescence. Other serological tests (ELISA, immunoblot or immunoprecipitation analysis), may be used to confirm the diagnosis, as well as for immunoserological follow-up.

Pemphigus is a general term for a group of rare autoimmune bullous disorders affecting the skin and mucosa. The disease has a chronic course. The exact cause of pemphigus is unknown. If left untreated, pemphigus is usually fatal.

The loss of adhesion in pemphigus subtypes occurs within the epidermis (intraepidermal blisters). It is characterized histologically by an intraepidermal cleavage and the production of pathogenic antibodies directed against different proteins of the desmosomes, which belong to the cadherin family.

Though not always, pemphigus diseases are characterized by certain clinical and histological features. Some authors consider these disorders similar, yet distinct, autoimmune blistering disorders with different causes and clinical, immunological and histological features.

P3 Characteristics of Primary Mucosal Melanoma - a Web Data Based Review

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Abstract

Primary mucosal melanoma is a very rare type of melanoma. More and more studies on the subject appear every year, but till now there has been no centralized analysis on this subject. In this web data based review and statistical analysis we tried to present a general image regarding the epidemiology, clinical presentation, histology, genomics and prognosis of this malignancy. Mucosal melanoma has a particular development, epidemiology and its genetic characteristics make this pathology a unique and well individualized entity, clearly distinct from its cutaneous counterparts. Our investigation showed that BRAF and NRAS mutations are present in a small percentage of samples from our review, less than 2, respectively 3%, while KIT mutations and increased copy number of KIT genes have a higher prevalence among the evaluated samples. We further discuss the role of main genes involved in mucosal melanomas, biology, and the available therapeutic options.

P4 Allergy Testing in Atopic Dermatitis

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Abstract

IgE-mediated hypersensitivity reactions to aeroallergens play an important role in the pathogenesis of atopic eczema in the majority of patients. Moreover, patients with atopic eczema may be prone to develop allergic contact dermatitis, due to skin barrier impairment and higher exposure to topical treatment. Therefore, both aeroallergen and contact allergen testing should be considered at an early point in individuals with atopic eczema. In general, skin prick tests provide sensitivity and specificity comparable to those of serum specific IgE measurement and a concordance rate of these two classical methods in the diagnosis of IgE-mediated allergy is close to 90 %. Atopy patch tests, although less sensitive, add specificity to allergy diagnosis. Clinical epidemiological studies show comparable prevalence rates of contact hypersensitivity as revealed by patch testing in atopic dermatitis patients and in non-atopics. Allergen testing, part of patch testing with contact allergens, is important in the complex examination of patients with atopic eczema.

P5 Cosmetic Dermatitis

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Clinical Center of Vojvodina, Novi Sad, Republic of Serbia

Abstract

Cosmetic dermatitis is an adverse reaction to cosmetic ingredients that manifests on the skin or visible mucous membranes. Cosmetic preparations are substances which are applied, rubbed or sprayed on the human body for the purpose of cleaning, beautifying, or altering the appearance without compromising its structure and function. The epidemiological data indicate that 10% of adult general population present with mild symptoms (itching, burning, skin dryness) after applying cosmetic preparations. The prevalence is considerably high in population with so-called sensitive skin, accounting for 31 - 57%. From the etiopathogenetic point of view, 90% of published cases are of patients with toxic, irritant, and contact dermatitis. In the eighties of the twentieth century, allergic contact dermatitis caused by cosmetic preparations accounted for 4 - 6%, two decades later for 8 - 15% of all cases of contact dermatitis, and 30% accounted for eyelid dermatitis. When determining the incidence of cosmetic dermatitis caused by certain cosmetic preparation, it is first necessary to determine the following: number of users; presence/absence of previous sensitivity; irritant properties of the preparation; allergenic potential of the preparation. Since cosmetic dermatitis is more common in females, it most often affects the face and persons over 40 years of age, the clinical-epidemiological studies should always include the MOAHLFA index (male sex, occupational dermatitis, atopic dermatitis, hand, leg, face, and age >40 years). For diagnostic purposes, and in order to link a specific cosmetic preparation with the development of dermatitis, it is of importance to examine the existence and role of the following parameters: temporal relationship; exclusion of other diseases and medications; termination of exposure; re-exposure; allergy testing. The most common sensitizers in cosmetics are fragrances and preservatives. At the Department of Allergology and Clinical Immunology of the Clinic of Dermatovenereology Diseases of the Clinical Center of Vojvodina, allergy testing of patients with suspected cosmetic dermatitis is carried out using 58 contact allergens of the standard cosmetic series (Chemotechnique MB Diagnostics AB, Vellinge, Sweden); the series contains chemicals and substances which anyone could be exposed to when using cosmetics and beauty products; these substances are used for fragrances, preservation and vehicles for obtaining optimal formulations. In the period from March 2016 to March 2017, of all the consecutively tested subjects, 11.1% were male, 11.1% had occupational exposure, 22.2% were with atopic constitution, hands were affected in 11.1%, face in 77.7%, legs in 0%, and 77.7% were older than 40 years of age. The highest number of positive reactions was caused by epicutaneous preservatives (57.1%). In 55% of tested subjects no reactivity was established to any allergen of the cosmetic series. It was the best known dermatologist, Alexander A. Fisher, who sought an answer to his own question: “Why do the parabens in topical therapeutic agents sensitize about 1.5% of the population, whereas these identical parabens are “safe” in cosmetics so widely used by millions of individuals?” In conclusion, it should be emphasized that positive allergic (patch) tests to cosmetic agents or their individual ingredients are found in persons whose sensitivity to cosmetic agents may be the only one, but by no means the only factor, or the primary cause of their problems.

Acknowledgement

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P6 Sclerotherapy for Leg Veins - a Practical View

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Abstract

The leg is an important esthetic unit along with the face, neck, decollete and hands. There is an increasing demand from dermatologists to perform interventions that improve both appearance and symptoms of varicose veins. The purpose of varicose veins ablation beyond improvement of esthetic appearance and symptoms is prevention and treatment of complications of chronic venous disorders and restoration of vein functions. Sclerotherapy is a suitable endovenous chemical ablation procedure, perfectly adapted to all types and sizes of varicose veins, performed by intravenous injection of a liquid or foamed sclerosing drug.
Successful sclerotherapy requires thorough planning. After considering absolute and relative contraindications, the treatment starts with large venous trunks, followed by collateral and reticular veins. Telangiectasias should always be treated after detecting and sclerosing feeder vessels. Therefore, a detailed clinical evaluation combined with color duplex ultrasonography for varicose veins and continuous-wave Doppler ultrasonography for telangiectasias and reticular varicose veins, should be performed prior to treatment.
Complications may arise from adverse effects of the used method, such as accidental injection into an artery, septic injection, paravenous injection, poor strategic management, excessive dosage and the speed of injection. Therefore, it is important to follow a strict protocol and guidelines. This includes usage of recommended sclerosant concentration and volume per injection, injection technique and material as well as post interventional management. Anaphylaxis, deep venous thrombosis, superficial thrombophlebitis, local allergy, matting, residual pigmentation, skin necrosis and embolia cutis medicamentosa can be avoided or minimized if sclerotherapy is performed properly.
If the rules are followed, sclerotherapy is an efficient treatment method for varicose veins with a low incidence of complications.

P7 Inadequate Indications, Insufficient Medical History and Complications in Esthetic Dermatology

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Abstract

In the last 20 years, the main problems we have recorded include inadequate indications for cosmetic techniques, application of various types of peels, fillers, botulinum toxins, lasers, minor plastic surgeries and so on. Inaccurate history taking causes problems in diabetic patients, in patients on anticoagulants (there are more and more of them among young people), in patients with neurological problems or other serious mental conditions. Some patients undergo interventions to satisfy their partners or family members, and keep important data from their medical history for themselves (such as repeated herpetic infections). The final effects are not satisfactory, but may also cause mental discomfort. Despite obtaining the informed consent prior to intervention, some cases end up in court, causing great social problems to both sides. The presentation will demonstrate actual cases of complications in esthetic dermatology.

P8 The Role of Biofilms in the Evolution of Chronic Wounds

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Abstract

Antimicrobial resistance of bacteria is a worldwide increasing problem. Bacteria can exist in two different phenotypic types: planktonic form (single, fast-growing cells) and biofilm form (aggregated communities of slow-growing cells). In chronic wounds, a substantial amount of bacteria reside in a biofilm, attached to the biofilm community and the surrounding structures, incorporated in a polymer matrix that is protecting them from neutrophils and macrophages. It may be assumed that all chronic ulcerations have a biofilm. The most commonly reported are Staphyloccocus aureus and Pseudomonas aeruginosa — both well known for biofilm formation.

The exact mechanisms by which biofilm impairs the healing processes of chronic wounds is still not completely clarified. The wound is in a chronic inflammatory stage, which prevents normal wound healing. Delayed healing of chronic wounds is caused by the ability of biofilm to avoid the defence mechanisms of the immune system; tissue destruction due to excessive enzymatic response of the immune system due to the presence of biofilms; high resistance of biofilms to antibiotics.

Detection of biofilm is very hard, and currently there is no gold standard diagnostic test to define the presence of wound biofilm. One should assume that all non-healing, chronic wounds not responding to standard therapeutic measures have a biofilm. Therefore, treatment should be directed toward biofilm eradication.

Management of biofilms is a complex task, with various therapeutic possibilities. The most effective therapeutic options include combination of debridement measures, application of antiseptics and appropriate wound dressings, and systemic antibiotic therapy.

P9 Syphilis and HIV – a Frequent Coinfection

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Abstract

Around 12 million new cases of syphilis and approximately 3 million cases of HIV-infection are registered in the world per year. Syphilis is a disease that manifests with ulcerations, and these patients are at an increased risk for acquiring HIV infection. Syphilitic lesion is a site of local influx of CD4+ cells, the target cells for HIV. On the other hand, serological tests show that HIV-positive people have eight times higher chance to be positive for syphilis than HIV-negative people. Those who are coinfected with syphilis and HIV also have lower levels of CD4 + cells compared to those with HIV infection only, but these values often do not increase in spite of syphilis treatment. Clinical forms of syphilis are often atypical, progression of syphilis is accelerated, and slow healing of ulcus durum is observed. The secondary stage of syphilis progresses faster and it is followed by general difficulties. Malignant syphilis with

prodromal symptoms and necrotic ulcers in such patients is 60 times more common. Skin eruption in the secondary stage of syphilis in HIV-positive patients has larger area of eruption and lasts longer than in HIV-negative persons. The progression of the early syphilis to neurosyphilis is faster. The results of serological tests for syphilis show extremely high titers; it is not infrequent that the serology is negative due to immunosuppression. The treatment protocol for syphilis in HIV-positive patients is the same as in HIV-negative, but it raises the dilemma of whether these patients should be treated immediately according to the protocol for neurosyphilis. It is of great importance to test patients for both infections, because of 246 HIV-positive patients that were treated from 2008 to 2016 at the Clinical Center of Vojvodina approximately 20% were diagnosed with syphilis. The question remains whether the number of people with associated HIV and syphilis infections will continue increasing in the era with more available effective antiretroviral therapeutic modalities.

OP1 Development of an Immune-Associated Molecular Signature Predicting Melanoma Survival

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Abstract

Melanoma patients within AJCC sub-stages exhibit great variability in survival, underscoring the need for more accurate prognostic approaches. Aberrant promoter DNA methylation is a key feature of cancers, including melanoma. Identification of a DNA methylation signature, orCpG island methylator phenotype, has been useful in predicting prognosis, diagnosis and response to treatment in a variety of tumor types. The purpose of this study is to develop a DNA methylation based prognostic tool for melanoma patients, who currently exhibit great variability in survival even within AJCC sub-groups. We used a discovery set of patient-derived melanoma cell lines (n=14) and sub-divided it into two groups, based on overall survival. We examined promoter methylation status of eighty candidate genes using bisulfite modification and Sanger sequencing. Candidate genes exhibiting differential methylation between the two survival groups were used to build a survival prediction score, MethyLive, using a training cohort (n=72) of Stage III melanoma patients. In the independent validation cohort, consisting of melanoma patients from The Cancer Genome Atlas (n=473), a high MethyLive score was associated with a significantly longer recurrence free survival, and longer overall survival in Stage I and II (p=0.0002, HR=7.5), Stage III (p=0.0007, HR=4.8), Stage IIIc (p=0.01, HR=4.4), and melanoma patients of all stages (pcO.OOOl). A high MethyLive score was associated with an immunogenic transcriptional phenotype, activation of interferon signaling, and de-repression of melanoma antigens (pcO.OOl). In this study, we define a methylation based melanoma survival prognostic score, MethyLive, which can significantly improve stratification of patients with favorable and poor outcomes within melanoma AJCC sub-groups. For instance, MethyLive identified Stage IIIc patient sub-groups with 70% and 20% 10-year overall survival, providing significantly more information than the AJCC Stage IIIc 10-year survival of 24%. Improved prognostic accuracy can contribute to improved care of melanoma patients, and provision of most appropriate therapies.

OP2 Dermoscopy of Combined Nevi – is there a Clue?

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Abstract

Introduction: The term combined nevus is used for a combination of a blue nevus with another melanocytic nevus. This uncommon nevus type accounts for less than 1% of biopsied nevi. It often shows a multicomponent pattern and may mimic melanoma. The aim of this study was to describe the dermoscopy of combined nevi.
Material and Methods: This retrospective analysis included a series of 16 combined nevi. Results: This series included 16 patients, 6 females and 10 males, mean age 38.5 years (range: 12 - 62 years). The anatomic sites of involvement were the trunk (14 patients) and arms (2 patients). On dermoscopy, 9 lesions (58.25%) had a multicomponent pattern. The arrangement of patterns was symmetrical in 11 cases (68.75%) and asymmetrical in 5 (31.25%) cases. Blue or grey structureless area was noted in all cases. In 12 lesions, (75%) the structureless area was eccentric and in four lesions (25%) centrally located. In 14 (87.5%) lesions the structureless blue-grey area did not touch the edge of the lesion and in 13 (81.25%) the blue-grey area was well circumscribed. White lines were absent in all but one case.
Conclusion: It is important to describe dermoscopic patterns of this rare and specific types of nevi to improve the diagnostic accuracy of dermatologists when distinguishing combined nevi and other types of nevi, and even more significant to differentiate them from melanomas with similar dermatoscopy features. The absence of white lines, good circumscription of the blue-grey area, and the fact that the blue-grey area does not touch the edge of the lesion may help to differentiate combined nevi from melanomas with similar features using dermatoscopy.

OP3 Ex Vivo Dermoscopy of Melanocytic Lesions: How not to Miss a Melanoma

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Abstract

Background: Correlation with in vivo digital dermoscopy (IVD) can help dermatopathologists to diagnose equivocal skin tumors and turn their attention to the suspicious area in melanocytic lesions.
Objective: We wanted to assess whether the use of ex vivo dermoscopy (EVD) could be a useful adjunct to histopathological diagnosis of melanocytic tumors in cases where complete clinical information is lacking.
Material and Methods: EVD was performed on surgically excised, formalin-fixed, pigmented skin tumors at the Institute of Pathology of the School of Medicine, University of Belgrade.
Results: Out of 195 examined lesions, 104 melanocytic lesions were included in this study arm. Only 53 specimens had a clinical diagnosis of ”nevus“ or “melanoma”. The rest of the specimens had a diagnosis of “pigmented skin tumor”. There were 10 melanomas: 3 in situ, 7 invasive with average Breslow thickness of 1.35 mm. All structures typical for melanocytic

lesions were observed. No blood vessels were present. Receiver operating characteristic curves for diagnostic accuracy was achieved without dermoscopy (only clinical diagnosis – naked eye) and with combined clinical and EVD were designed. The combined diagnostics provided sensitivity increase by 30% while specificity remained 89%. Four characteristics (asymmetry, blue color, pigment network and at least 3 colors) were more frequently found in melanoma. At least two characteristics were necessary for EVD melanoma diagnostics.
Conclusion: In the pathology settings, EVD increases sensitivity for melanoma diagnosis when clinical information is missing. The pathologist does not need to be an expert in dermoscopy to perform a simple EVD algorithm in order not to a miss melanoma.

OP4 Quality of Life in Patients with Psoriasis of the Palms and Soles

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Abstract

Data on quality of life (QoL) in patients with psoriasis of the palms and soles are rarely published. The aim of this study was to compare QoL in four groups: psoriasis patients with both palms and soles involvement (PPS), psoriasis patients with involvement of palms (PP), psoriasis patients with involvement of soles (PS), and patients with psoriasis without palms and soles involvement (PO). The Psoriasis Area and Severity Index (PASI) was used for the assessment of disease severity. For the purpose of QoL evaluation, the Dermatology Life Quality Index (DLQI) was used. There were no significant differences in PASI scores between PPS patients (n = 21), PP patients (n = 9), PS patients (n = 10) and PO patients (n = 60). On the other hand, there were significant differences in DLQI scores between the four groups of patients. This study revealed a lower QoL in PPS patients than in PP and PO patients. Also, QoL in PS patients was lower than in PP patients.

OP5 Psoriasis and Diabetes Mellitus

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Abstract

Introduction: Psoriasis is a chronic inflammatory recurrent disease. In those affected by it, occurrence of other diseases is possible. One of such is diabetes mellitus.
Aim: To determine to frequency of diabetes mellitus in those affected by psoriasis and effects of psoriasis severity on the occurrence of diabetes mellitus.

Material and Methods: A prospective research included 70 respondents affected by psoriasis, with average age of 47.14 (SD =/± 15,41), average duration of psoriasis 15,52 (SD =/± 12,54), 51.43% were men, and 48.57% women. The estimatation of psoriasis severity PASI score was used. Reference values of glucose level for the diagnosis of diabetes mellitus were >5,6 mmol/l.
Results: The incidence of diabetes mellitus was 32.85%, average age of those affected was 51,33 years (SD =/± 11,72). There was no correlation between the severity of psoriasis and occurrence of diabetes mellitus; PASI didn't correlate positively with diabetes mellitus (r = 0,16; p = 0,07).
Conclusion: Psoriasis is a chronic disease often related to the occurrence of diabetes mellitus, and there is no correlation between the severity of psoriasis and the occurrence of diabetes mellitus.

OP6 Biologics in Psoriasis - our Experience

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Abstract

Psoriasis is a common, chronic inflammatory disease characterized by a series of linked cellular changes in the skin: hyperplasia of epidermal keratinocytes, vascular hyperplasia and ectasia, and infiltration of T lymphocytes, neutrophils, and other types of leukocytes in the affected skin. Therapy of psoriasis patients varies depending on the disease severity. Limited and mild conditions are treated by topical treatment modalities. Patients with more severe disease are often treated with photochemotherapy, methotrexate, acitretin or biologic agents, such as tumor necrosis factor antagonists, and interleukin 12/23 inhibitors.
During the last 3 years, we followed 7 patients treated by biologics (adalimumab and ustekinumab). We presented our experience in regard to patient selection (eligibility criteria) for biologic therapy, therapeutic response, safety and patients' follow up.

OP7 Human Leukocyte Antigen Class II Alleles in Patients with Pemphigus in Serbia

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Abstract

Introduction: Pemphigus vulgaris (PV) is a severe blistering autoimmune disorder. Pathogenic autoantibodies are directed against keratinocyte adhesion molecules. The disease is more prevalent in some ethnic groups. The etiology is multifactorial. Genetic background is believed to be the most predisposing factor for the development of PV. Among genetic factors,

it has been shown that certain human leukocyte antigen (HLA) class II alleles confer susceptibility for the development of PV.
Aims: The purpose of this study was to determine HLA-DR and HLA-DQ allelic frequencies in patients with PV in Serbia.
Material and Methods: The study was conducted in patients with the diagnosis of PV. The allelic groups were determined with low/intermediate resolution tests. Alleles were determined with high resolution tests using polymerase chain reaction sequence-specific primers. The allelic frequencies were compared with healthy volunteers donors registered in the National Registry of Bone Marrow Donors of Serbia. Also, the results were compared with other results obtained in different population groups.
Results: We demonstrated, for the first time, that certain HLA-DR and HLA-DQ allelic groups and alleles were significantly increased in PV patients in Serbia.
Conclusion: Our findings supplement current knowledge on the significance of HLA II gene polymorphism in the development of pemphigus.

OP8 Pemphigus Biomarkers in Serbian Population

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Abstract

Pemphigus group is a subset of rare autoimmune blistering diseases with a presumed T-cell–dependent pathology. In pemphigus vulgaris (PV) autoreactive antibodies are directed against Dsg3, whereas in pemphigus foliaceus (PF) the target antigen is Dsg1. Production of autoreactive antibodies by B cells is controlled by their interaction with T cells. Activation of naïve T cells is dependent on antigen recognition, subsequent signaling through the T-cell receptor complex and various other interactions of T cells with antigen presenting cells. In general, CD28 molecule provides activation signals, and cytotoxic T-lymphocyte–associated antigen 4 (CTLA-4) is conferring inhibition. IL-10 and TNF may have important role in pemphigus, so altered function of genes encoding TNF and IL-10 may influence disease susceptibility. Single nucleotide polymorphisms (SNPs) within genes encoding those molecules may alter the signaling process. SNPs are also biomarkers for disease susceptibility. In this study we analyzed functional single nucleotide polymorphisms within genes encoding molecules important in pemphigus development. Also, we analyzed these molecules in pemphigus patients and healthy controls, and compared results in Serbian pemphigus patients and healthy controls with results obtained in different populations groups. We demonstrated, for the first time, SNPs within genes encoding molecules important for pemphigus development in healthy Serbian control group and in Serbian pemphigus patients.

OP9 Tumor Associated Breast Skin Lesions - a Report of a Case Series

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Abstract

Breast cancer is the most common form of cancer in women worldwide, with the estimated incidence of 70,8/100,000 in Serbia in 2009. But although so frequent, breast cancer is rarely subject for dermatologic assessment, because less than 5% of primary breast cancers are involving the skin, in the form of Paget's disease. Advanced breast cancers tend to give skin metastases in around 30% of cases, most often in the chest and abdominal region, but such patients are usually regularly followed up by the oncologists, therefore getting appropriate and timely treatment. We presented a case series of tumor associated breast skin lesions. Clinical and dermoscopic features of Paget's disease, syringocystadenoma papilliferum, radiotherapy-induced angiosarcoma, and distant intravascular metastases of melanoma in the breast skin are discussed. Due to the rarity of aforementioned medical conditions, they may easily be misdiagnosed, leading to a delay of proper treatment.

OP10 Dermatofibrosarcoma Protuberans – a Case Series

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Abstract

Background: Dermatofibrosarcoma protuberans (DFSP) is a rare malignant cutaneous tumor with often delayed diagnosis, due to the lack of early clinical clues. The objective of this study was to present the main clinical and dermoscopic features of DFSP.
Material and Methods: We performed a clinical and dermoscopic examination in 3 consecutive cases of biopsy-proven DFSP. Firstly, we identified individual clinical and dermoscopic features; secondly, all cases were reviewed separately by four experienced dermoscopists. In the end, features recognized only by all dermoscopists were taken into account.
Results: The mean number of dermoscopic features was four per lesion. The following dermoscopic features were found: delicate pigmented network, vessels, structureless light brown areas, shiny white streaks, and structureless hypo- or hyper-pigmented areas. We did not find pink background coloration described as one of the features of DFSP by some authors, but on the other hand our sample is minute.

Conclusion: The study of clinical and dermoscopic features of DFSP identified three different clinical presentations and five dermoscopic features, always showing a multicomponent pattern. Whether dermoscopy can help to identify a suspected DFSP remains to be established by further studies. For now, in DFSP, both dermoscopic and clinical features are inconclusive. We wish to stress that biopsy should be performed as soon as possible, in all lesions where diagnosis is unclear.

OP11 Infections and Occurrence of Premalignant and Malignant Lesions of the Lower Female Genital Tract

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Abstract

Introduction: Lower female genital tract infections are a significant factor in the occurrence of pathological changes of varying intensity, especially if they are not appropriately and timely treated. Human papillomavirus (HPV) infections frequently cause premalignant and malignant lesions. It is believed that other infectious agents, to a smaller or greater extent, contribute to the development of pathological lesions.
Aims: To investigate the incidence of uterine cervix premalignant lesions in patients with HPV infection, the stage of pathological changes, Pap cytology tests, microbiological agents of cervico-vaginal infections, as well as epidemiological parameters (age, place of living) during a four-year period.
Materials and Methods: A retrospective analysis included patients of the Outpatient Gynecology Clinic of the Clinical Center of Priština, currently relocated to Gračanica and the Health Center in Kosovska Mitrovica; Institute of Pathology, Faculty of Medicine in Priština and Outpatient Microbiology Institute of Public Health in Kosovska Mitrovica, and statistical analysis of the obtained data.
Results: In the four-year period, from January 1, 2013 to December 31, 2016, there were 187 female patients (in 2013: 78, in 2014: 56, in 2015: 32 and in 2016: 21) with cervico-vaginal infections and histo-pathologically verified genital warts of the lower genital tract. The patients were between 21 and 77 years old, average age of 43.79 years.
Different pathological findings indicated a biopsy of the cervix and/or vulvar Condylomata acuminata and histopathological examination, as well as Papanicolaou test. A biopsy of uterine cervix was performed in every second (51.9%) female patient due to chronic cervicitis; in every third (34.8%) patient due to suspected findings on the portiovaginalis uteri, as well as suspected LSIL (low-grade squamous intraepithelial lesion) and HSIL (high-grade squamous intraepithelial lesion). Due to suspected carcinoma, the biopsy of uterine cervix was performed in 6 (3.2%) patients, and due to vulvar flat condylomas and uterine cervicitis in a small number of patients (3 patients - 1.6%). The patients were divided into groups according to the histopathological findings (chronic cervicitis was diagnosed in all patients): chronic cervicitis and cervical papillary condylomas/vulvar and vaginal condylomas; chronic cervicitis and endophytic condylomas; flat condylomas; LSIL; HSIL; uterine cervix carcinoma. Every fourth female aged 41 to 60 years (24.66%) was histopathologically diagnosed with flat condylomas. HSIL was found in a total of 30 patients (16%). Chronic cervicitis was histopathologically verified in 10 patients (5.3%).
The majority of patients (160 patients - 85.6%; mean age 44.2) presented with Papanicolaou test group II (Pap II), in 17 (9.1%) patients it was Pap IIIa ASCUS/ASCH, LSIL/IIIb in 7 (3.7%)

patients Pap IV (HSIL) and Pap V (invasive cancer) in 3 (1.6%, average age 39.7) patients. We obtained statistically significantly different results of Pap smears compared to the histopathologic findings ($p < 0.01$).
In most of the patients, the isolated infectious agent was Candida albicans, alone or with a bacterial infection (in 65 patients - 34.8%), and in a small number of patients - 10 (5.3%) Mycoplasma hominis.
Conclusion: This four-year retrospective study showed that in 187 women, aged from 21 to 77 years (mean age 43.79 years), with chronic cervico-vaginal infections, human papillomavirus infection was cytologically and histopathologically confirmed. Every sixth patient had HSIL changes, and every twentieth patient had an invasive uterine cervix carcinoma. Considering that the human papillomavirus infection is the most significant cause of cervical cancer, in order to prevent the development of premalignant and malignant cervical pathology, it is very important to examine and treat all the cervico-vaginal infections, especially HPV infections.

OP12 Herpes Zoster in Childhood

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Abstract

Herpes zoster (HZ), a painful vesicular dermatomal eruption, is the result of reactivation of the varicella-zoster virus (VZV) from infected sensory ganglia. Generally, HZ is a disease of adults, in contrast to primary infection with VZV, which tends to occur mainly in children. In the absence of risk factors for complicated courses, HZ is usually a self-limiting disease.
HZ is rare in children. The incidence rates of HZ are lowest in the group 0 to 14 years old, and highest among persons aged 75 years and older. In the pediatric population, the incidence is lowest in the group of 0 to 5 years old. Pediatric HZ usually occurs in immunocompromised children, and in immunocompetent children who had a primary intrauterine infection with VZV or varicella in the first year of life.
Generally, HZ is much better tolerated by children than adults; the disease is usually mild and lasts from 1 to 3 weeks. In contrast to adults, HZ is usually painless in children. Otherwise healthy children usually have a benign course of HZ and exellent outcome.
The diagnosis of HZ is often clinical. The diagnosis can be confirmed by Tzanck smear, direct fluorescent antibody tests, VZV PCR evaluation and by culture of the VZV virus. The most common differential diagnosis is impetigo.
European Dermatology Forum (EDF) in cooperation with the European Academy of Dermatology and Venereology (EADV), recommended the treatment of patients with HZ (antiviral medication, pain management, local therapy), considering various clinical situations, in the Guidelines on the Management of HZ (JEADV 2017). In cases without risks of complications, the expert panel suggested no antiviral therapy in immunocompetent children. On the other hand, antiviral therapy is suggested in the presence of risk factors for complicated courses of the disease, if potential benefits outweigh the potential risks. Treatment of HZ should be initiated within 72 hours of exanthem onset, or at a later time in the presence of any of the conditions listed in the Recommendations of the Guidelines on the Management of HZ. Although many antivirals are available, acyclovir, given orally or intravenously, remains the first line-agent for VZV infections in children. Analgesics and appropriate skin care provide relief and reduce the risk of secondary infections. The application of topical antiviral preparations for cutaneous HZ is not recommended.
In this paper we reviewed the risk factors, clinical manifestations, epidemiologic data, treatment and outcome of HZ in children.

OP13 A Study of Onychomycosis in Patients of the Institute of Dermatovenereology

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Abstract

Aim: Fungal nail infections account for around 50% of all nail disorders. The aim of this study was to determine the incidence of fungal fingernail and toenail infections, to identify the fungus, determine morphological patterns of onychomycosis, and the most frequently affected age and sex groups in patients of the Institute of Dermatovenereology in Belgrade.
Material and Methods: All data were obtained from the mycological laboratory protocol containing samples of all patients who visited the Institute of Dermatovenereology in Belgrade during 2016 with clinically suspected fungal nail infection, who were examined by potassium hydroxide (KOH) preparation, and fungal cultures.
Results: This study included 1.896 patients with clinically suspected onychomycosis. Fungal fingernail infection was diagnosed in 332 patients (17.51%; 34.6% males and 65.4% females), out of which 327 patients (98.5%) had a positive KOH preparation, while fungal culture was positive in 156 patients (46.99%). Candida spp. (91.03%) was the most frequently isolated species, followed by Aspergillus spp. (4.48%), Trichophyton interdigitale (1.92%), Trichophyton rubrum (1.28%) and Trichophyton species (1.28%). Fungal toenail infections were confirmed in 974 patients (51.37%; 33.1% males and 66.9% females), out of which 971 patients (99.7%) had positive toenail KOH preparation, and 407 patients (41.8%) had positive fungal toenail culture. Candida spp. (79.36%) was the most frequent cause of toenail fungal infections, followed by Trichophyton interdigitale (8.59%), Trichophyton rubrum (7.86%), Trichophyton species (1.97%), Aspergillus spp. (1.97%), and Trichophyton violaceum (0.25%). KOH preparation and fungal cultures of fingernail or toenail were the most frequently positive in patients aged 60 - 69 years (30.6%, 31.4%, 29.4% and 28.5%, respectively). The most common clinical type was distal lateral onychomycosis (32.4%). Positive KOH preparation in both fingernails and toenails, was found in 124 patients (6.5%; 34.7% males and 65.3% females), while positive fungal culture was found in 49 patients (2.6%; 40.8% males and 59.2% females). In all these patients the cause of infection was the same in both fingernails and toenails (Candida spp. – 89.8%, Aspergillus spp. – 6.12%, Trichophyton interdigitale – 4.08%).
Conclusion: These results showed that 17.51% of examined patients of the Institute of Dermatovenereology in Belgrade, with clinically suspected onychomycosis, had fungal fingernail infection, and 51.37% had fungal toenail infection. Females and persons aged 60 to 69 years were more frequently affected, and the most common cause of fingernail and/or toenail fungal infection was Candida spp.

OP14 Geriatric Dermatology - Multimorbidity and Geriatric Syndromes in the Elderly Patients with Acquired Blistering Diseases

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Abstract

Introduction: As the population is getting older, dermatology is facing demands for adaptation of diagnostic and therapeutic frameworks to satisfy specific needs of old patients. Geriatric dermatology focuses on disorders that are more prevalent in older population, and need to understand all consequences of the aging process, in order to set proper treatment goals and options. It is necessary for dermatologists to be familiar with geriatric functional assessment and the estimation of risks for specific geriatric syndromes or their aggravation during dermatological treatment.
Material and Methods: Patients diagnosed with acquired blistering disease, in the period 2012 - 2017 at the Clinical Center of Vojvodina, were divided into two groups: with intraepidermal blistering (97 patients, average age at diagnosis 60.9 years, 37% of patients were older than 65 years) and with subepidermal blistering (94 patients, 71.6 years, 75% respectively). The retrospective study analyzed medical records of patients older than 65 years at diagnosis, in the period 2012 - 2017, for the presence of geriatric syndromes and comorbidities.
Results: 18 patients with intraepidermal blistering (pemphigus group) and 44 with subepidermal blistering (pemphigoid group) were included the in study. Cardiovascular diseases were the most prevalent (89% in pemphigus, 78% in pemphigoid group); neurological impairment caused by Parkinson disease or previous stroke was more prevalent in pemphigus (17%) than in pemphigoid group (7%). The incidence of diabetes, incontinence, gait disturbances, and functional decline was similar in both groups. Acute confusion – delirium upon hospital admission was more frequent in pemphigus (11%) than in pemphigoid group (7%), being a strong predictive factor for mortality in upcoming 6 months than the presence of concomitant malignancy (17% in pemphigus, 7% in pemphigoid group).
Conclusion: Cases of aged patients with acquired blistering diseases are complex; the comprehensive picture with multiple comorbidities and geriatric domains has to be realized, hence it affects the success of dermatological treatment. It is necessary for dermatologists to know how to manage this complexity to minimize functional decline.

OP15 Cutaneous Tuberculosis - our Ten-Year Experience

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Abstract

Introduction: Tuberculosis (TB) is one of the oldest infectious diseases. According to World Health Organization, there are about 9 million new cases per year, including 1, 5 million patients with lethal outcome. Cutaneous tuberculosis accounts for 1 – 1.5% of all non-pulmonary forms of TB. This form of the disease has a wide variety of clinical presentations. Lesions can be due to direct inoculation of M. tuberculosis from exogenous source, skin involvement due

to endogenous infection, or from immune reaction to M. tuberculosis. The aim of this study was to analyze demographic, clinical features, as well as diagnostic procedures and therapeutic modalities for all forms of cutaneous tuberculosis in the Clinic of Dermatovenereology (CDV), Clinical Center of Serbia (CCS), during a 10-year period, from 2007 to 2017.
Results: During the time of observation, 16 patients were diagnosed with cutaneous tuberculosis, 12 (75%) females and 4 (25%) males. The average age of female patients was 62 years (range 27 - 87), and 71 years (range 66 - 83) in male patients. Five patients (31.25%) had lesions on head and neck, four patients (25%) on upper extremities, and seven patients (43, 75%) had lesions on lower extremities. Lupus vulgaris was diagnosed in 7 (43.75%) patients, Erythema induratum of Bazin in 5 (31.25%) patients, Papulonecrotic tuberculid in 2 (12.5%) patients, Tuberculosis verrucosa cutis in 1 (6.25%) patient, and Scrofuloderma in 1 (6.25%) patient. Diagnosis of cutaneous tuberculosis was made based on clinical presentations, histopathology analysis and in certain number of patients with additional diagnostic procedures (PPD, Quantiferon Gold test, Mycobacteria Growth Indicator Tube). Before the diagnosis was confirmed, the skin lesions were present between 2 months and 15 years. Two of our patients had previous history of cutaneous TB earlier in their lifetime.
Conclusion: According to literature data, the incidence of TB is growing. The possible cause of the significant rise is increase of HIV infection and massive migration of people. Furthermore, the increase may be explained by more objective diagnostic procedures, which include more precise diagnostic tests. Small number of patients in our study confirmed the fact that cutaneous TB is a rare form of extra-pulmonary TB. For a more accurate incidence trend and detection of the total number of affected population, it is necessary to conduct multicentric studies which would include a higher number of patients.

OP16 Systemic Lupus Erythematosus in Childhood – Clinical and Immunoserological Characteristics

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Abstract

Introduction: Juvenile systemic lupus erythematosus (JSLE) is a chronic, multisystemic autoimmune disease of unpredictable course. It is estimated that 15 - 20% of systemic lupus erythematosus (SLE) patients develop signs and symptoms during childhood and adolescence.
Aim: To determine the number of patients with SLE under the age of 18 diagnosed and treated at the Department of Dermatovenereology, Clinical Center of Serbia in the last 30 years (1987 - 2016), to summarize their clinical and immunoserological characteristics and the course of the disease.
Material and Methods: Our retrospective study included 26 patients under the age of 18, who were diagnosed and treated in a 30-year period at the Division of Pediatric Dermatology. The SLE patients were diagnosed according to the ACR (ARA) criteria. The activity and prognosis of the disease at the time of diagnosis were assessed based on the values of SLEDAI-2K (Systemic Lupus Erythematosus Disease Activity Index).
Results: Girls accounted for 88.5% (23/26) of the affected children. The mean age of patients at the time of onset was 13.2±3.6 years. In the same period, 32 children with only cutaneous lupus were diagnosed (28 discoid lupus erythematosus and 5 subacute cutaneous lupus

erythematosus). All SLE patients had skin lesions, most commonly malar erythema (96.2%,). Signs of vasculopathy on the palms and soles were present in 38.5%, purpura in 34.6%, livedo reticularis in 19.2%, and urticaria-like vasculitis was observed in 11.5% of our patients. Hematologic abnormalities were found in 73.1%, renal manifestations in 26.9%, and neuropsychiatric disorders in 19.2% of JSLE patients. Average SLEDAI-2K score was 8 (range 2 - 14). Moderate to severe SLEDAI-2K (≥7) had 62%, and mild SLEDAI-2K (<7) 38% of patients. All patients were positive for ANA, Anti-dsDNA antibodies were found in 75% of patients, Anti-Sm in 81.3%, anti-cardiolipin antibodies in 39% of JSLE patients.
There was no statistically significant difference between the onset of the disease at a younger age (<12 years) and severity of JSLE. We did not find statistically significant correlation between lupus nephritis and other clinical manifestations, as well as between lupus nephritis and the immunoserological parameters (anti-dsDNA, anti-ENA, and low C3 and C4 components of complement).
The average follow-up period in our patients was 8.8±5.9 years. A lethal outcome occurred in 5 patients due to CNS lupus, lupus nephritis, pulmonary hypertension, severe agranulocytosis and autoimmune hepatitis. Seven patients were lost to follow-up.
Conclusion: Clinical presentation of SLE in children is frequently more severe than in adults, with multi-organ involvement and a worse prognosis. Although JSLE may have a serious prognosis, with adequate treatment and disease control, length of survival and quality of life have been significantly improved.

OP17 Alexithymia as a Risk Factor for Alopecia Areata

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Abstract

Introduction: Psychosomatic factors, such as emotional stress and personality traits, have been suggested to play a role in triggering alopecia areata (AA). Although an association between stressful life events and the onset of AA has been investigated in many studies, most of them neglected other factors potentially modulating susceptibility to disease, such as social support, attachment style and alexithymia. Alexithymia is a personality trait characterized by reduced symbolic thinking and limited ability to understand and verbally define emotions. Inadequate mechanisms of coping with stress and difficulty to overcome stressful situations, which are present in alexithymic persons, may alter the functioning of autonomic, pituitary-adrenal and immune system and to induce the onset of AA in genetically predisposed individuals. The aim of this study was to examine the role and significance of alexithymia in the onset of AA.
Material and Methods: The research was conducted in the Clinic of Dermatovenereology, Clinical Center of Serbia in Belgrade. In order to evaluate the role of alexithymia in triggering AA, a hospital-based, case-control study was designed. The study included 32 consecutive AA patients and 47 control subjects from the general population. The presence of alexithymic traits was assessed with the 20-item Toronto Alexithymia Scale (TAS-20). A Serbian version of a self-report questionnaire was used with previously established reliability and validity.
Results: Comparing the mean values of total alexithimia score and the mean scores of TAS-20 subscales, a significantly higher level of alexithimia as well as all alexithymic traits were found in AA patients, in comparison with the control subjects.
Conclusion: The results of this study suggest that personality characteristics, such as alexithimia, may play an important role in the pathogenesis of AA and indicate the need for further investigation in this area.

PP1 Cannabis Arteritis

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Abstract

Introduction: Cannabis arteritis (CA) is a major and underdiagnosed cause of peripheral arterial disease in young patients. It resembles thromboangiitis obliterans (TAO) (aka Buerger's disease) and both should be considered in young adults under the age of 40 years presenting with peripheral vascular disease. Over 20% of lower extremity arteriopathy in young adults is due to TAO and/or CA. The clinical and arteriographic findings of TAO and CA are nearly identical. Both cause a non-atheromatous peripheral arteriopathy with segmental and multifocal involvement of the small and medium-sized arteries distal to the elbow and knee. Superficial venous thrombosis has also been reported. Both diseases predominantly affect young males and can cause gangrene of the digits. Laboratory evaluation is frequently unremarkable, including normal acute phase reactants.
Results: Five cases of arteritis associated with the use of cannabis and two additional case series of TAO, in which some patients also used cannabis, have been reported. Clinical and pathological features of cannabis-associated arteritis do not differ from TAO, and the major risk factor for TAO use was present in most, if not in all of these cases. The proposed pathophysiological mechanisms for the development of arteritis by cannabis use are not substantiated. Tetrahydrocannabinol (THC) and some other substances may have direct toxic effects on blood vessels. In addition, activation of cannabinoid (CB1) and non-cannabinoid receptors on endothelial cells can cause increased production of reactive oxygen species and decreased nitric oxide production. This may potentially lead to endothelial cell injury, vasoconstriction, and thrombosis. Cannabis users may also abuse other illicit drugs with vascular effects (methamphetamines, cocaine, etc.), thus, this possibility must also be considered.
Conclusion: A legitimate but unanswerable question, given the high frequency of marijuana use, is why are there so few cases of CA or TAO? Clearly more research needs to be done. In the meantime, it is important for dermatologists to consider cannabis use in all patients presenting with a distal peripheral arteriopathy resembling TAO whether or not the patient smokes or chews cannabis.

PP2 Orofacial Granulomatosis in a 12-Year-Old Girl Successfully Treated with Intravenous Pulse Corticosteroid Therapy and Chloroquine

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Abstract

Introduction: Orofacial granulomatosis (OFG) is defined as orofacial swelling without a systemic disease. OFG is also a monosymptomatic Melkersson-Rosenthal Syndrome.
Case Report: We present a 12-year-old girl with asymptomatic erythematous swelling of the upper lip, cheeks and chin persisting for more than two years. She was previously treated

with systemic antibiotics and topical corticosteroids, with no improvement. A biopsy of the upper lip confirmed the diagnosis of OFG. Other systemic granulomatous diseases have been excluded. Given the vast area that was affected, intralesional corticosteroids were not administered, but a 3-day intravenous pulse corticosteroid therapy (dexamethasone at 1.5 mg/kg). The pulse treatment was repeated once in 4 weeks, and she received a total of 6 cycles. Our patient also received chloroquine 250 mg/day, with topical emollient creams. At the end of the 6th pulse cycle the infiltration had completely regressed, leaving a slight residual erythema. **Conclusion:** Orofacial granulomatosis is very rare in childhood. There are different therapeutical approaches in treating OFG, with intralesional corticosteroids being the first treatment option. To the best of our knowledge, our patient is the first case of OFG treated with pulse corticosteroid therapy combined with chloroquine, which we found an effective and safe treatment option.

PP3 Generalized Pustular Psoriasis as a Paraneoplastic Dermatosis

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Abstract

Case Report

Generalized pustular psoriasis (GPP) is a rare form of psoriasis manifested with widespread pustules on an erythematous ground localized on the whole body surface. Psoriasis, especially GPP, is uncommon as a paraneoplastic dermatosis, but there are reports which suggest that psoriasis may develop at an onset of a tumor, improve after tumor treatment, or exacerbate during tumor relapse or metastasis. In this report we describe a case of GPP associated with advanced, inoperable, metastatic squamous cell carcinoma of the hypopharynx.

A 46-year-old male with no personal and/or family history of psoriasis was referred to the Department of Dermatology. He was febrile, with malaise, distress and dehydrated. Clinically, generalized bright erythema was present with individual and coalescent pustules localized on the whole body surface. The face and scalp were deep red in color and covered by thick yellowish scales, while a lamellar thick scale was observed on palms and soles. No mucosal involvement was present. Physical examination revealed a tumorous formation fixed to skin and underlying structures on the right side of the neck. The patient appeared undernourished, with poor personal appearance. He claimed that the skin redness began ten days before he was referred to see a dermatologist. He denied taking any drugs or medications, but admitted that he was a heavy cigarette smoker and alcohol abuser. Complete blood count showed mild anemia and leukocytosis with predominance of neutrophils. The sedimentation rate was elevated, as well as C-reactive protein, while procalcitonin was within normal values. The peripheral smear showed no abnormalities. The biochemical analysis showed elevated urea and creatinine levels, hypoproteinemia and hypoalbuminemia, elevated hepatic enzymes, and decreased iron serum levels. Other biochemical parameters as well as urine analysis were normal. Fecal occult blood tests were negative. His blood cultures were negative. Cultures for bacteria and fungi from the pustules were also negative. Carcinoembryonic antigen (CEA) and CA 19-9 were within normal levels. The abdominal ultrasound and chest radiography showed no abnormalities. Otorhinolaryngologic examination revealed infiltrating tumorous outgrowth of the right lateral wall of the hypopharynx which also invaded the tongue and the base of the

oral cavity. Ultrasound of the neck showed metastatic lymph nodes on both sides of the neck and solid hypo and hyperechoic formation on the right side, which was in continuity with the endopharynx. Biopsies were obtained from the tumorous tissue and the skin. Skin biopsy showed epidermal hyperkeratosis, parakeratosis, elongation of the rete ridges and subcorneal macropustula with numerous neutrophils, dilated capillaries and perivascular mononuclear infiltrates in the edematous superficial dermis. Histopathological examination of the hypopharyngeal tumor showed an invasive squamous cell carcinoma, moderately differentiated, with incomplete keratinization. After admission, the patient was treated with antibiotics (consecutively amoxicillin, garamycin and amoxicillin/clavulanic acid), corticosteroids (methylprednisolone and prednisolone), supportive therapy (antipyretics, gastro-protective agents, prevention of alcohol withdrawal syndrome, intravenous fluid infusion), topical emollients. Ten days after admission, the patient's clinical state improved and retinoid therapy (40mg of acitretin daily) was initiated. Three weeks later, he was transferred from our department to the Oncology Department in order to start cancer treatment (radical radiotherapy, 66 Gy in 33 fractions and cisplatin chemotherapy). Dermatological checkup, two weeks later, showed generalized erythema with less prominent scales than on admission and no pustule flares. He was released from the Oncology Department with advice to continue radiotherapy and chemotherapy at the Outpatient Oncology Center. However, he never visited the oncologist, otolaryngologist or dermatologist again. His outcome remained unknown to all specialists involved in his treatment. We presented this case in order to emphasize that appearance and behavior of psoriasis and pustular psoriasis may be linked to malignancy, so dermatologists should perform clinical evaluation for possible neoplastic diseases.

PP4 Collision Lesions of Seborrheic Keratosis and Non-Melanoma Skin Cancer – a Report of Two Cases

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Abstract

The coexistence of two or more neoplasms in a single cutaneous specimen is relatively uncommon and has been defined as collision or compound tumors. The collision lesions may be composed of a benign and a malignant part, and the malignant neoplasm determines the therapeutic approach. Malignant neoplasms associated with seborrheic keratosis have been described not only in case reports, but also in studies of histological specimens of seborrheic keratoses. The studies that analyzed histopathologic features of seborrheic keratoses found their collision with other tumors in 0.001% to 5%. It is important to keep in mind the possibility of such collisions, especially with malignant tumors, since cryosurgery is often used for treatment of seborrheic keratosis, and if the collision is left unrecognized, it may remain untreated.

Case 1

A 65-year-old retired male clerk was referred for follow up after previous surgery of basal cell carcinoma on the left arm. Pigmented lesions on his face, in the left infra-auricular region, 8 mm in diameter, without any evidence of collision, were examined by dermoscopy. Dermoscopy showed that the pigmented part had a cerebriform pattern, which corresponded clearly to seborrheic keratosis, but also a discrete reddish part with arborizing vessels in the lateral part, which pointed to basal cell carcinoma. The lesion was excised and histopathology revealed a collision tumor consisting of a seborrheic keratosis and a basal cell carcinoma.

Case 2

A 71-year-old retired male farmer presented with pigmented lesion on his parietal region. As usual, total skin examination was performed with dermoscopy without clinical preselection.

The pigmented lesion was suspected to be a seborrheic keratosis. We also noticed a lesion in the right frontal part of his face which was clinically partly pigmented, and partly ulcerated. Dermoscopy showed that the pigmented part corresponded to seborrheic keratosis, while the lateral part had microerosions/ulcerations, white structureless areas, centrally located, amorphous, yellow-white areas without any recognizable structure. The lateral part was suspicious for malignancy, primarily for squamous cell carcinoma. The lesion was excised and histopathology revealed a collision tumor consisting of seborrheic keratosis and squamous cell carcinoma. The lesion about which the patient was concerned was also excised and histopathologic finding was seborrheic keratosis.
These cases, especially the first one, were about clinically "silent" lesions, showed that dermoscopy can "make a difference", and help in making a definitive diagnosis, or at least raise the level of suspicion and detect malignant lesions in cases of collision lesions.

PP5 Dermatomyositis with Calcinosis Cutis in an Adult – a Case Report

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Abstract

Introduction: Dermatomyositis (DM) is an idiopathic autoimmune-mediated inflammatory process with characteristic muscular and cutaneous manifestations. It is characterized by violaceous (heliotrope) discoloration of the eyelids, flat-topped, violaceous papules over the knuckles (Gottron's papules), periungual telangiectasias, proximal muscle weakness, and occasionally interstitial pneumonitis, vasculitis, or myocardial involvement. Calcinosis of the skin or muscles is unusual in adults, but it accounts for about 40% of juvenile DM. Calcinosis is characterized by the deposition of hydroxyapatite crystals and amorphous calcium phosphates in soft tissues, muscles, or tendons and skin. Calcinosis in DM is usually of dystrophic type with normal serum levels of calcium and phosphate.
Case Report: We present a 61-year-old female patient who was referred to our Clinic because of a painful heel fissure. If we had not checked the whole body, we would have missed this peculiar case of DM.
The patient's medical history showed a 28-year-old condition that started with progressive weakness of her extremities, followed with pain, heliothrope periorbital violaceous erythema, and Gottron's papules on her dorsal proximal and distal interphalangeal and metacarpophalangeal joints. A few moths later, she noticed difficulties when climbing stairs, generalized fatigue, and a few years later she presented with "bumps" and "hard places" on the abdomen and thighs, elbows and many other places. She was treated at the Rheumatology Department with corticosteroids, for long periods of time, with brakes, all these years.
On physical examinations the patient had normal vital signs and normal laboratory, CPK and Ca were also in normal range. She had a well regulated HTA and diabetes mellitus. In general, the skin was taut with firm non-mobile, tender mass-calcinosis (25 x 18 cm) in her abdomen and flanks areas. The same but smaller masses were present on her back, elbows, on both thighs and all over the skin. There were ulcerations on some of them. On examination, she couldn't raise her arms above the head without assistance, as well as when sitting down and standing up.
The fissure was treated with an antibiotic cream and she was referred for a CT of the abdomen and thorax to see if there were calcifications in the internal organs. However, the patient did not have a CT because she died a few months later from a heart attack.

Discussion: We present a rare, 28-year-long case of calcinosis in an adult with DM. Unfortunately we couldn't do anything to help this patient. On the other hand, she helped us by allowing us to make pictures and present them to other colleagues. She was very well informed about her illness, and very cooperative.
According to the literature, the therapy should include high-doses of steroids, immunosuppressant and cytotoxic agents, in the early stage, in order to wean off steroids. Methotrexate, azathioprine, and mycophenolate mofetil are common agents used in dermatomyositis. If this combination of drugs is unsuccessful, intravenous immunoglobulins have shown promise for short-term treatment.
Conclusion: Calcinosis is a difficult complication to treat. Some studies have shown success with diltiazem, aluminum hydroxide, and even alendronate in children. However, refractory cases of calcinosis that cause pain or interfere with function may need to be referred for surgical excision.

PP6 Skin Toxicity Associated with Cetuximab Treatment during Radiotherapy of Head and Neck Cancer

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Abstract

New therapeutic modalities in the treatment of cancer patients such as radiotherapy in combination with target therapy have led to an extended life expectancy of patients. Target therapy (e.g., monoclonal antibodies) works by inhibiting specific target molecules. Using targeted therapy with radiotherapy can improve the response to radiation, radiotherapy is therefore more effective. An example of a combination treatment is cetuximab, which is indicated in the treatment of patients with squamous head and neck carcinoma with platinum-based chemotherapy as the first line treatment for relapse and/or metastatic disease in combination with radiotherapy in locally advanced disease. Complications that occur during radiotherapy using cetuximab most commonly affect the skin in the form of acneiform eruptions, skin dryness, pruritus, paronychia, hair damage, mucositis, and increased facial malformations. Complications on the skin during epidermal growth factor receptor (EGFR) target therapy should be classified according to the scale of the National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0 and the Radiation Therapy Oncology Group (RTOG) scale based on which the degree of adverse effects is assessed. According to these scales, there are four grades of complications based on which a dermatological treatment is determined. New therapeutic modalities in the treatment of cancer patients such as radiotherapy in combination with target therapy have led to an extended life expectancy of patients, however, the comorbidities and complications arising from this treatment are significant and long-term issues in oncology. Target therapy (e.g., monoclonal antibodies) works by inhibiting specific target molecules. Using targeted therapy with radiotherapy can improve the response to radiation, and radiotherapy is therefore more effective.
We present several cases of patients who underwent treatment at the Clinic of Radiological Therapy at the Institute of Oncology of Vojvodina and during the course of treatment developed different degrees of skin toxicity during concomitant aerial and biological therapy with cetuximab. Combined treatment with radiotherapy and target therapy should be reduced to an effective, patient-friendly treatment strategy. New guidelines for detection and risk management are needed in order to avoid possible complications on the skin that are characteristic after administration of this drug.

PP7 Papuloerythroderma of Ofuji – a Case Report

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Abstract

We present a case of a 55-year-old patient with skin papules that appeared three months earlier. The papules were localized on the gluteus, abdominal fold, around axillary folds, and were followed by pronounced itching. The patient was unsuccessfully treated with antihistamines and corticosteroids, and after discontinuation of treatment, the lesions reappeared. A few days before hospitalization, they deteriorated and flowed together forming skin erythema on the trunk and extremities. The history of earlier skin disease was negative.
At the time of admission, the patient presented with flow together unclear limited erythema saving the folds. Excoriated papules were present on the upper leg and the abdominal wall on the erythematous background. Single erythematous plaques, about 15 cm in diameter, were present on the upper extremities. The facial erythema was also present, but saving the central part.
The necessary tests were performed and relevant findings were as follows: erythrocyte sedimentation rate and complete blood count within normal ranges with eosinophilia 25%; C-reactive protein: 3,3..61,7...11,7 mg/l; LDH: 621...631...737...597...472 U/l; tumor markers: CEA: 5,7...5,5...5,9...3,5 ng/ml; AFP: 7,3...7,7...7,6...4...6,5 IU/ml; IgE: 4846…….4343 IU/mL; b 2 microglobulin: 3,05 ...5,33 mg/l; ANA on the aggregate substrate: positive, homogeneus, with moderate intensity; anti-mitochondrial antibodies: negative; antiparietal antibodies: negative; anti-smooth muscle antibodies: negative; ANA on HeP-2 cells: positive; nucleoplasm: positive, homogeneous type, with moderate intensity; nucleolus: negative; cytoplasm: negative; centromere: negative. A skin biopsy was performed a few times and histopathological diagnosis was chronic spongiotic dermatitis and erythema annulare centrifugum. Enlargement of axillary lymph nodes was detected by thoracic CT. The abdominal and pelvic CT showed enlargement of pelvic and inguinal lymph nodes. Histopathology and immunohistochemistry examinations of lymph node extirpation indicated dermatopathic lymphadenopathy. Histopathological and cytological evaluation of bone marrow showed that there were no clear morphologic signs of lymphoproliferative and myeloproliferative disorders. Morphologic findings corresponded to mild reactive hyperplasia of granulocyte lineage. The symptomatic systemic and topical treatment with emollients and corticosteroids was initiated. The diagnosis was based on laboratory, immunological, and pathological findings, and immunohistochemistry; immunoproliferative disorder was ruled out, and regression of lesions was achieved by a topical corticosteroid. The patient needs continued monitoring by a dermatologist and a hematologist.

PP8 Pyoderma Gangrenosum on the Face and Leg Successfully Treated with Biologic Therapy - a Case Report

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Abstract

Pyoderma gangrenosum is a rare neutrophilic dermatosis associated with systemic diseases in about half of the cases. Inflammatory bowel disease is one of the conditions most commonly seen with pyoderma gangrenosum, usually occurring on the extensor surfaces of the legs and trunk. The face is rarely affected.
We present a case of a 55-year-old female patient with a 3-month history of skin lesions appearing first on her left thigh and then on the face. Clinical examination showed two painful ulcers with a hemo-purulent exudate. Histopathological examination showed an inflammatory infiltrate throughout the sample with edema of the walls of blood vessel; immunohistochemistry showed focal remnants of hair follicles and eccrine ducts within the infiltrate, consistent with the diagnosis of pyoderma gangrenosum. This was followed by systemic exploration leading to the diagnosis of ulcerative colitis.
Treatment with systemic corticosteroids was initiated and it lasted for three months, alongside Azathioprine for two months. Thereafter, Adalimumab was introduced, showing almost complete epithelization of both ulcers after 3 months of therapy.
We report this case for the atypical localization of this rare condition and its successful treatment with systemic corticosteroids followed by biological therapy.

PP9 Punctate Palmoplantar Keratoderma Type 1 - a Case Report

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Abstract

Punctate palmoplantar keratoderma type 1 (PPKP1), also known as Brauer-Buschke-Fischer syndrome is an autosomal dominant genodermatosis, characterized by multiple hyperkeratotic papules on the palms and soles. Molecular genetic studies showed loss of function due to mutations in AAGAB gene. The estimated prevalence of PPKP1 is 1.17/100.000. The lesions usually develop in early adolescence but may also occur later in life. Important characteristic is the association of PPKP1 with an increased risk for several types of cancer (pancreatic, colonic, breast, renal, etc.). The diagnosis of PPKP1 is based on positive family history, presence of multiple tiny hard rounded bumps of skin on the hands and feet, and certain cell histology (marked hyperkeratosis, parakeratosis and mild acanthosis, without changes in the dermis). Treatment options include keratolytic agents such as topical salicylic acid, urea, lactic acid or vitamin A, as well as systemic therapy with retinoids. Surgery has been used in lesions resistant to medical treatment.

We described a 78-year-old male with hyperkeratotic lesions on the palms and soles. Similar skin lesions were reported in his father and his son. He had a surgery of a malignant colonic tumor, 9 years before. The laboratory test results were within normal limits. Clinical findings and histology proved the diagnosis of this rare hereditary disease. Monitoring of such patients and their affected and non- (clinically) affected family members may have an important impact on the society, because they may be at higher risk for malignancies and prevention may be achieved in this way.

PP10 Unusual Clinical Presentation of Piloleiomyoma – a Case Report

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Abstract

Introduction: Multiple cutaneous piloleiomyomas (PLMs) are uncommon, often painful, benign tumors of the skin arising from the arrector pili muscle of the hair follicles, characterized by reddish-brown and skin-colored papules or nodules of firm consistency, predominantly located on the trunk and limbs.

Materials and Methods: A 42-year-old Caucasian woman with an eight year history of painless lesions on the cheeks, neck and the back, which gradually multiplied, was referred to our Clinic. The lesions were previously diagnosed as viral warts (verrucae virales) and unsuccessfully treated with liquid nitrogen; she also self-administered antifungal creams. Four years earlier, the patient underwent uterine myomectomy. Apart from having tortuous elongations of blood vessels and headaches occasionally treated with nonsteroidal anti-inflammatory drugs, the patient was otherwise healthy and not receiving any medications.

Results: Clinical examination showed numerous densely grouped and individual, painless dermal papules, mildly erythematous, yellowish and skin-colored on the forehead and the cheeks, on the back side of the neck and gluteal area, elastic upon palpation. Regional lymph nodes were not enlarged. Complete blood count, sedimentation rate, C-reactive protein, lipid status, renal and liver biochemistry, as well as urinalysis were all within the limits. Serum protein electrophoresis and immunoelectrophoresis were normal. Antinuclear antibodies had a fine speckled pattern, with a titer 1:80. Anti-thyroglobulin antibodies were slightly elevated. Thyroid stimulating hormone, triiodothyronine, thyroxine, anti-thyroid peroxidase antibodies and calcitonin were within limits. The serological screening for human immunodeficiency virus, hepatitis B and C were all negative. Histopathological examination of two biopsy specimens, taken from the cheek and from the back, revealed the diagnosis of piloleiomyoma. A gynecologic examination confirmed multiple myomas of the uterus and hysterectomy was indicated. Mammography showed no abnormalities. Abdominal ultrasound revealed a renal cortical cyst. Serum tumor markers were within normal limits. The patient was advised to see an esthetic surgeon for further treatment.

Conclusion: Multiple cutaneous PLM is a very rare entity. Physicians need to be aware of its association with uterine leiomyoma, renal cell tumors and visceral involvement, because early recognition is highly important. The treatment of multiple lesions remains a challenge.

PP11 Mondor's Disease of the Penis

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Abstract

Introduction: Mondor's disease is a rare, self-limiting, benign process with acute presentation characterized by subcutaneous bands in several parts of the body. Penile Mondor's disease is considered to be thrombophlebitis of the superficial dorsal vein of the penis. Some findings suggest that it might be of lymphatic origin. Braun–Falco first reported this entity on the penis in 1955. Fifty years later, in the "Dermatology" by Braun–Falco, this disease is described as non-venereal sclerosing lymphangitis. External compression may trigger its development. This disease is almost always self-limited. Patients usually feel the superficial vein of the penis like a hard cord and complain about the pain around this hardness, especially when in erection.
Case report: We present a young football player who developed a hard cord on the dorsum of his penis a few hours after vigorous sexual intercourse. He had a sensation of discomfort and slight pain when in erection. After two weeks, without therapy, the symptoms resolved spontaneously.
Discussion: Mondor's disease of the penis is a benign, self-limited condition. We presented this case as a relatively rare condition of the penis.

PP12 Fox-Fordyce Disease

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Abstract

Introduction: Fox-Fordyce disease is a rare skin disorder that primarily affects women and it is accompanied by intense itching especially in the underarm area, the pubic area and around the nipples. It is supposed that in Fox-Fordyce disease, abnormalities affecting the apocrine sweat glands, cause inflammation and enlargement of the glands. Skin near the affected area may become darkened and dry and multiple, small, raised bumps (papules) may develop. Hair follicles in the affected area may become secondarily damaged, resulting in hair loss. The exact cause of Fox-Fordyce disease is unknown.
Case report: We report a young woman 19 years of age, with multiple skin colored and yellowish papules about 2 mm in diameter localized in the underarm zones. She presented with a sensation of slight pruritus, especially under stressful conditions. We prescribed topical Clindamycin gel which alleviated itching, but had no influence on skin lesions that remained unchanged.
Conclusion: We reported a relatively rare skin condition and our attempts to resolve it.

PP13 Cutaneous Metastasis from an Ovarian Carcinoma – a Case Report

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Abstract

Sister Mary Joseph nodule (SMJN) is a metastatic umbilical lesion commonly associated with advanced intra-abdominal tumors, gastrointenstinal mostly in men, and ovarian in women. Here we report a case of a 54-year-old female patient with an 8-week history of several umbilical nodules resistant to local treatment, who was referred to the Dermatology Department, Clinical Center of the University of Sarajevo. The patient was diagnosed with SMJN and suspected underlying malignancy. A necessary diagnostic workup was performed using computerised tomography of abdominal cavity and pelvis, showing an expansive tumorous formation covering uterus with a carcinomatosis of peritoneum. The histopathological examination of the skin biopsy revealed metastatic deposits of intradermal tumor cells. The morphology and immunohistohemical profile suggested adenocarcinoma of ovarian origin. The patient was then refferd to the Oncology Consilier of Gynecology Department and further continued follow-up by the oncology team. Seven weeks after the initial admission to the Dermatology Department, the patient started chemotherapy treatment prior to possible surgical tumor excision. In the meantime, skin metastases have grown larger and spread with multiple smaller, ulcerated nodules over the abdominal area. However, the patient is still stable.

PP14 Multiple Neoplasms Due to Vemurafenib Treatment of Metastatic Papillary Thyroid Carcinoma

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Abstract

Vemurafenib is a B-Raf enzyme inhibitor used in the treatment of BRAF V600E or V600K mutation-positive late stage melanoma. It inhibits B-Raf/MEK/ERK pathway and causes programmed cell death. It is also used in the treatment of BRAF V600E positive inoperable or metastatic papillary thyroid carcinoma refractor to radioactive iodine treatment. Skin neoplasms have been reported as common side effects of the drug, but if the mutation of the BRAF is not present in melanocytes stimulation can occur, and paradoxically new melanomas may develop.
We report a 71-year-old patient receiving vemurafenib treatment due to papillary thyroid carcinoma for 2 years. Twenty four years ago, total thyroidectomy and radioactive iodine ablation (120mCi) were performed. Nineteen years ago, a hypoechoic nodule was found ultrasonically in the jugular region and dissected. Two years ago, a slight increase of thyroglobulin was found, although levothyroxine sodium substitution treatment was used. An additional work-up was done and lung metastases were found and PET-CT, fiber endoscopy and surgery

were performed. Treatment was started with vemurafenib at a dose of 960 mg. Three months later, she reported a neoplasm on her forehead that was excised and SCC was verified. Six months later, on regular check-up, an abdominal neoplasm was found, excised, and keratoacanthoma was verified. Regular dermoscopy check-ups were performed every three months. At the end of November 2016, she reported new lesions on her left thigh and the lower leg that were suspected to be keratoacanthomas, but on the check-up a new atypical pigmented lesion was seen suspected to be a melanoma. All of the lesions were excised and squamous cell carcinoma and melanoma pT1a were verified. The patient refused to stop taking vemurafenib, so it was continued, although she was warned about all possible side effects and possible occurrence of new neoplasms. Regular dermoscopy check-ups and ultrasound of the regional lymphatic nodes were also recommended.
Vemurafenib is used as a study drug for BRAF V600E positive papillary thyroid carcinoma that has metastasized or is not responding to radioactive iodine treatment. Recent studies have shown that it limits the disease activity and the prognosis is very good, but it is associated with side effects such as melanoma and other skin tumors.

PP15 A Case of Paraneoplastic Atrophoderma of Pasini and Pierini

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Abstract

Atrophoderma of Pasini and Pierini is a benign, asymptomatic disease with no reported association with any complication or mortality. Here, we present a case of atrophoderma of Pasini and Pierini associated with a rare malignant neoplasm with unusual localization.
A 34-year-old male patient, with a three-month history of well-defined symmetric lesions localized in axillae and both sides of the trunk, was admitted to the Department of Dermatovenereology. Asymptomatic lesions were hyperpigmented, non-indurated, slightly depressed plaques with distinct margins which gave the characteristic appearance of “cliff-drop” borders. A routine laboratory test showed that sedimentation rate and C-reactive protein were elevated, while complete blood count, biochemical analysis and urine analysis were within reference values. Serological examination of Borrelia burgdorferi was negative. Virological analysis (hepatitis C and B virus, HIV) was negative. Chest X-ray and abdominal ultrasound did not reveal any abnormalities. Histopathological examination of skin lesion showed normal epidermis while mild perivascular infiltrate and homogenization of collagen fibers were present in the dermis. Adnexal structures were not affected. The treatment included oral doxycycline 200 mg/day, for 14 days and topical potent corticosteroid ointment, but no clinical improvement was observed.
Three months after the dermatological examination, the patient presented with dyspepsia, so gastroduodenoscopy was performed, which did not show any abnormalities, but retroperitoneal lymphadenopathy was suspected on abdominal ultrasound and confirmed with computed tomography of the abdomen; increased lymphatic nodes (diameter 57 mm) were present in the retroperitoneum. Laparotomy of retroperitoneal lymph nodes and affected part of colon was performed. A diagnosis of extramedullary plasmacytoma was postulated, based on clinical examination (painless, firm and solitary tumorous formation, 10 centimeters in diameter, was present in epigastrium), histopathological (tissue biopsy showed presence of plasma cells) and immunohistochemical examinations were characteristic for plasmacytoma. Bone

marrow biopsy showed 30 - 35% plasma cells. The laboratory test showed that sedimentation rate and C-reactive protein were elevated, as well as total serum protein and globulins. Serum albumin and β2 microglobulin were 33 g/l and 3.19 mg/l, respectively. Immunological examination showed an increase in IgG antibodies titer, while other antibody levels were within reference range. Skeletal x-ray showed no abnormalities.
Chemotherapy, *thalidomide, adriablastin, dexamethasone* (TAD) protocol was commenced: adriablastin and dexamethasone as a monthly pulse therapy, with thalidomide at a daily dose of 100 mg every cycle day, and radiation therapy (patient received 40 Gy over 20 sessions). After four cycles of chemotherapy, stem cells were harvested, frozen and stored. After six cycles, chemotherapy was completed and autologous stem cell transplantation was performed. After the first cycle of chemotherapy complete regression of skin lesions was observed.
Atrophoderma, a superficial form of morphea, differs from other types of morphea with absence of sclerosis in dermis. Etiology is unknown and association with Borrelia burgdorferi infection was confirmed in small number of patients.
Atrophoderma in our case was associated with extramedullary plasmacytoma. Plasmacytomas present rare malignant plasma cell neoplasms which in majority of cases arise in bone marrow. In 3% of all plasma cells neoplasms, it has soft tissue involvement as extramedullary plasmacytoma. About 80% of lesions are localized in the head and neck region, especially in the upper respiratory tract. In our case, extramedullary plasmacytoma was found in the abdomen which is a rare involvement.
In our case, atrophoderma appeared few months before and extramedullary plasmacytoma was diagnosed. Interestingly, it completely faded after the first anti-neoplastic cycle was commenced. Since atrophoderma in our case behaved as a paraneoplastic dermatosis, we believe that detailed patient screening and follow up is highly recommended in every case of idiopathic atrophoderma.

PP16 Generalized Eruptive Xanthomas – a Case Report

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Abstract

Eruptive xanthomas are skin lesions associated with diabetic dyslipidemia in the majority of reported cases. Here we present a 39-year-old male with generalized, pruritic, small, yellowish papules with erythematous base distributed almost over the whole body surface. Koebner phenomenon was observed as a skin reaction to scratching.
According to the patient, first skin lesions began appearing a few years ago on the extensor side of the elbows and shoulders. His general practitioner asked him to check triglyceride (TAG) and cholesterol (tChol) levels, as well as serum glucose level, but he refused it, since skin lesions did not cause him any trouble. Two months before dermatologic examination, new skin lesions began appearing in crops on the trunk and extremities with a tendency to generalization. The patient's medical history was unremarkable, except for obesity with a body mass index of 41.3 kg/m2, while family history revealed presence of cardiovascular diseases and diabetes mellitus.
The diagnosis of eruptive xanthoma was based on typical clinical presentation, confirmed with histopathological examination (foamy macrophages in the dermis and characteristic presence of extracellular lipid between collagen bundles), while detailed endocrinology examination revealed metabolic syndrome with increased serum glucose levels (147.6 mg/dl), and extremely increased tChol (1055.68 mg/dl) and TAG (4844.99 mg/dl). Chylomicrons were present in serum incubated

overnight. Furthermore, oral glucose tolerance test showed diabetes with compensatory hyperinsulinemia as a consequence of insulin resistance. Hormone testing (parathyroid hormone, thyroid-stimulating hormone, free thyroxin, anti-thyroid antibodies, calcitonin, serum cortisol and prolactin) showed no abnormalities. Abdominal ultrasound showed hepatic steatosis.
After two months of strict diet and physical exercise with administration of metformin (3000 mg/day) and fenofibrate (320 mg/day), led to weight loss and significant reduction of serum lipids (tChol 324.83 mg/dl and TAG 682.01 mg/dl) and serum glucose (102.6 mg/dl) levels.
Dyslipidemia can be a result of endogenous factors (such as deficiency of lipoprotein lipase activity, dysfunction of apolipoprotein C-II, impaired insulin activity or increased hepatic production) and exogenous factors (such as administration of oral retinoid therapy, alcohol abuse, and obesity or diabetes de novo). Differential diagnosis includes a wide spectrum of diseases (molluscum contagiosum, folliculitis, generalized eruptive histiocytoma, papular sarcoidosis, multicentric reticulohistiocytosis, etc), but clinical presentation (sudden eruption of small, yellow, dome shaped papules with erythematous base) and specific histological findings are most helpful in making the correct diagnosis.
We presented an interesting case of a rare skin disease, generalized eruptive xanthoma with Koebner phenomenon, which has been reported only in a small number of cases of eruptive xanthomas associated with metabolic syndrome. In our case, cutaneous manifestations preceded the diagnosis of metabolic syndrome. Since uncontrolled diabetes and dyslipidemia could lead to life threatening conditions (pancreatitis, cerebral and myocardial infarctions etc.), the patient was advised to continue regular clinical and laboratory monitoring.

PP17 Pyoderma Gangrenosum, Acne and Suppurative Hidradenitis – a Case Report

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Abstract

Introduction: In the spectrum of autoinflammatory syndromes, the clinical triad of pyoderma gangrenosum (PG), acne conglobata (A) and suppurative hidradenitis (SH) was identified as a new entity, named PASH syndrome. Some similarities to previously described PAPA (pyogenic sterile arthritis, PG and A) and PAPASH syndrome (pyogenic arthritis, PG, A, and SH) exist, but in PASH syndrome there is no arthritis, visceral involvement or associated mutation of the proline-serine-threonine phosphatase interacting protein 1 gene (PSTPIP1).
Case Report: We report a 32-year-old obese Caucasian woman with PASH syndrome. She had severe nodular acne since puberty and SH since the age of 25 years. She reported rapidly expanding ulcerations on her lower extremities, which started 7 months before admission. The patient was diagnosed with polycystic ovary syndrome (PCOS) at the age of 30.
On admission, the patient presented with inflammatory, suppurating and scarring nodules with draining sinuses and abscesses in the large skin folds (Hurley stage III). There were numerous scars resulting from nodular acne on her face and neck. Also, an ulcerated plaque, 15 cm in diameter, with violaceous, polycyclic margins, as well as multiple cribriform atrophic scars were present on her lower legs.
She had elevated androstenedione, C-reactive protein, and erythrocyte sedimentation rate. Genetic testing of the PSTPIP1 gene showed no mutations. A skin biopsy specimen from the

edge of the ulcerated plaque was consistent with PG. The patient received oral prednisone, dapsone and antibiotics.
Conclusion: We have already published this case report. Similarities in the inflammatory response of PCOS and PASH syndrome may mean that they could be etiologically related as we referred previously. Further cases are required to establish the association.

PP18 Brooke-Spiegler Syndrome – a Case Report

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Abstract

Brooke-Spiegler syndrome is rare autosomal dominant hereditary disease with variable penetration. The syndrome is manifested by the appearance of three types of tumors: multiple cylindromas, trichoepitheliomas and spiradenomas. We presented a patient with a typical clinical picture of Brooke-Spiegler syndrome, with a positive family history (mother, two sisters, brother and niece). She refused a surgical treatment, because she was afraid of losing her hair.

PP19 Cutaneous and Subcutaneous Metastatic Melanoma Treated with 2 Lines of Immunotherapy

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Abstract

In the era of new, revolutionary therapies for melanoma, we present a patient with disseminated melanoma who was successfully treated with 2 lines of immunotherapy.
A male patient, V. F. was admitted to our department in October 2009 with primary melanoma on his left foot. After excision, histopathological results showed a deep, ulcerated nodular melanoma (Breslow 9 mm). Sentinel lymph node biopsy and reexcision were performed later and they were clear, without tumor cells.
In November 2010, new cutaneous and subcutaneous melanoma metastases appeared. Multiple surgical excisions were performed, as well as local radiotherapy to relieve painful and ulcerated melanoma lesions. BRAF V600 testing (Cobas test) showed no mutation in V600E locus. Due to the treatment standards at that time in Croatia, our patient received 2 cycles of dacarbazine without any clinical benefits. In March 2013, the patient was enrolled in expanded access programme with anti CTLA-4 inhibitor ipilimumab. After four applications, there were tremendous clinical and radiological effects on melanoma regression. Later on, during follow up in May 2015, our patient presented with new cutaneous, lymphatic and even one visceral (lung) metastases. After inclusion criteria for new expanded access programme with PD-inhibitor pembrolizumab were met, we began a second line treatment with a new type of immunotherapy. Once again, the patient experienced great metastatic melanoma shrinkage with almost complete radiological response. Nowadays, further applications of pembrolizumab are ongoing without any clinically significant side effects.

PP20 Genital Mycoplasma Infections – a Retrospective Analysis

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Abstract

Introduction: Ureaplasma urealyticum and Mycoplasma hominis are causative agents of genital infections. Clinical manifestations are various (urethritis, vaginitis, cervicitis and others), as well as their complications. It is still unclear whether genital mycoplasmas or commensals cause urogenital infections. The aim of this study was to determine the incidence of genital mycoplasma infections, sex and age distribution, clinical indications for microbiological tests (vaginal discharge, cervical swab and a urethral swab), and the sensitivity of isolated pathogens to antibiotics.

Material and Methods: We performed a retrospective analysis of patients of the Outpatient Institute of Public Health in Kosovska Mitrovica and the Department of Gynecology and Obstetrics of the Health Center in Kosovska Mitrovica, and then statistically analyzed the obtained data.

Results: In the period from January 1, 2013 to December 31, 2016, a total of 2.027 genital mycoplasma samples were examined in the Outpatient Institute of Public Health in Kosovska Mitrovica, of which 741 were positive. Genital mycoplasmas were more frequently isolated in women, (16 to 64 years of age; average age 30.68 years), while men were from 20 to 63 years of age (average 35.47 years). In 2014, every third female patient (237 - 32.2%) had a positive finding. We noticed a reducing trend in the number of microbiological examinations in female patients in the reported period (in 2013 there were 178 and in 2016 - 156 examinations), while in males the number of examinations increased from 6 examinations in 2013 to 12 in 2015. Most of the examined patients with isolated genital mycoplasmas were from Kosovska Mitrovica and Zvečan, 468 female patients (63.7%) and 27 males (79.4%).

A total of 573 (77.3%) female patients had a positive Ureaplasma urealyticum finding: Mycoplasma hominis in 32 (4.3%) females, and a mixed infection of Ureaplasma urealyticum and Mycoplasma hominis in 136 (18.4%) female patients. Sex distribution analysis showed that Ureaplasma urealyticum infection was isolated in 550 (77.7%) females, mixed infection in 128 (18.1%) females, and Mycoplasma hominis infection was isolated only in 30 (4.2%) females. Ureaplasma urealyticum infection was found in 23 men (69.7%), mixed infection in 8 (24.0%), and Mycoplasma hominis infection only in 2 (6.3%) patients. The incidence of mixed infection in sex distribution showed a highly statistically significant difference ($p < 0.01$).

The most common clinical indications in female patients with genital mycoplasma infection were vulvovaginitis and chronic cervicitis (74.8%), followed by vulvovaginitis (17.4%). Ureaplasma urealyticum - 550 (74.8%) was isolated in nearly three quarters of female patients with genital mycoplasmas, and mixed infection of genital mycoplasmas (Mycoplasma hominis and Ureaplasma urealyticum infection) was isolated in almost every fifth (17.4%) female patient, which represented a highly statistically significant difference ($p < 0.01$). Forty-two (5.9%) Mycoplasma hominis samples were resistant to four antibiotics, and 40 samples (5.6%) were resistant to three antibiotics. In 40 samples of female patients with vulvovaginitis, Mycoplasma hominis was resistant to four antibiotics, with a high statistically significant difference ($p < 0.01$). Ureaplasma urealyticum was most frequently isolated from female patients with the diagnosis of vulvovaginitis and chronic cervicitis, in 74.8% (548) of cases. The isolated Ureaplasma urealyticum was most often resistant to one antibiotic (in 418 - 57% of samples), then

to two antibiotics - in 134 (18.3%) samples. Ureaplasma urealyticum resistance to antibiotics showed a statistically highly significant difference ($p < 0.01$) in relation to the clinical diagnosis.
Conclusion: In the four-year period, 741 samples were positive for genital mycoplasmas. Female patients were more often examined and proved positive to these agents, with a decreasing trend during the study period. Female patients were on average slightly younger than males and the most common indication for microbiological analysis was vulvovaginitis and chronic cervicitis. Mixed genital mycoplasmas were also microbiologically confirmed, while Mycoplasma hominis was isolated in a small number of patients. The isolated mycoplasmas showed varying degrees of resistance to the tested antibiotics.

PP21 Granuloma Faciale - a Case Report

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Abstract

Granuloma faciale (GF) is an uncommon benign, chronic, inflammatory skin disease of unknown etiology. It mostly affects healthy, middle aged, white males. GF is characterized by solitary, red-brown or violaceous papules, nodules and plaques, localized on the face which may be multiple and disseminated. Extrafacial lesions are possible, but rare. The diagnosis is based on clinical features, histopathological findings of leukocytoclastic vasculitis; recently dermoscopy is also applied.
Case Report: A 58-year-old man was admitted with a lesion on the forehead, in the form of a small, solitary, oval brown-red plaque, with soft consistency, smooth surface, and visible follicular structures. In the left temporal area there were several small papules in annular arrangement, and in the area of the nose there were several erythematous papules with smooth surfaces and rare telangiectasias. The personal history showed that the lesions in the left temporal area and on the nose were present in the past 10 years, and those on the forehead appeared a year before. Dermoscopic examination revealed a pink-brown background and prominent follicular orifices.
Histopathological examination of the sample taken from the plaque on the forehead showed slight hyperkeratosis of the epidermis, without changes in the basal layer, below which Grenz zone was observed. Perivascular focal infiltrates were also found of mixed composition including lymphocytes, histiocytes, neutrophils and eosinophils, without clearly formed granulomas. Groups of granulocytes with signs of leukocytoclastic vasculitis were also observed.
Except for mild eosinophilia in peripheral blood, other laboratory test results were in normal limits. The patient received dapsone (50 mg/day, during seven days, then 100 mg/day for three months, and 50 mg/day for one month),.C vitamin tablets of 1000 mg/day, as well as topical corticosteroid ointments and pimecrolimus 1%. Clinically, a significant improvement was achieved after four months of treatment.
Conclusion: This case substantiates the therapeutic use and efficiency of dapsone in the treatment of GF. Definitive diagnosis of GF is histopathological, but recently, there is a growing interest in dermoscopic analysis of inflammatory diseases, and it was very helpful in this case.

PP22 Non-Bullous Congenital Ichthyosiform Erythroderma – a Case Report

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Abstract

Introduction: Non-bullous congenital ichthyosiform erythroderma (NBCIE) is a chronic, inherited genodermatosis, a very rare autosomal recessive inflammatory ichthyosis characterized by fine, whitish scales on a background of erythematous skin over the body.
The disorder affects 1 in 300,000 individuals of all races. It is associated with an inherited abnormality that affects normal skin shedding. The genes involved in mutation are TGM1, ALOX12B, ALOXE3 and ichthyin. It is not contagious and not associated with any internal abnormalities.
Case Report: A boy, first child from healthy parents, was admitted in the Dermatology Department of the Clinical Center of the University of Sarajevo, presenting with fine white scales and red patches on the face, and palmar and plantar surfaces. Fine white scales and red patches on his body appeared when he was 1.5 month old. Previously, there were only red patches on his neck area and then spread out to the feet and face (sometimes the parents observed the baby was scratching).
There was no history of any blister formation at any time, at birth or later. A detailed history did not reveal presence of any plastic-like membrane at birth. The mucous membranes of the mouth and anus were unaffected and hair was sparse. There was no ectropion or eclabium. There were no contractures and no restriction of joint mobility. The external genitalia were normal.
Conclusion: Histological findings showed a thick, laminated orthokeratotic horn with parakeratosis, focal hypogranulosis, irregular psoriasiform hyperplasia of epidermis, a sparse perivascular lymphohistiocytic infiltrate around the vessels of superficial plexus and increased mitosis in epidermis.
Chromosomal studies revealed a male karyotype (46, XY). The genetic analysis revealed a homozygous mutation in transglutaminase-1 (TGM1 gene p.Val330MetfsX12 [c.984+1G>A]) located on chromosome 14q12.
The treatment included emollient all over the body and 5% urea. Prevention of sunburn and sunstroke is very important.

PP23 Changes in Quality of Life of Patients with Psoriasis after Hospitalization

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Abstract

The aim of this study was to assess the effects of inpatient management of psoriasis on patients quality of life. A total of 28 patients completed the Dermatology Life Quality Index (DLQI) questionnaire on admission and four weeks after discharge. The mean DLQI score improved from 1.8 ± 1.0 to 0.4 ± 0.6 ($p<0.001$). The improvement observed in work or school and leisure sub-scale scores was greater than in other four sub-scales. In conclusion, inpatient management has an appreciable impact on improvement of quality of life, and may positively affect the treatment outcome in psoriasis patients.

FORTHCOMING EVENTS

Dermatology and Venereology Events 2017/2018

DATE	MEETINGS, CONGRESSES, SYMPOSIA	ABSTRACT SUBMISSION DEADLINE	MORE INFORMATION AT
25 - 29 July, 2017	5th International Summer Academy of Practical Dermatology Munich, Germany	No abstract submission	www.isa2017.com
13 - 17 September, 2017	26th EADV Congress Geneva, Switzerland	16 March, 2017	www.eadvgeneva2017.org
27 - 30 September, 2017	6th Congress of Dermatovenereologists of Macedonia with International Participation Ohrid, Macedonia	20 June, 2017	www.unet.com.mk/dermatology
27 - 30 September, 2017	47th Annual Meeting of European Society for Dermatological Research Salzburg, Austria	31 May, 2017	www.esdr2017.org
13 October, 2017	Meeting of the Serbian Medical Society's Section of Dermatology and Venereology, Clinical Center of Vojvodina Novi Sad, Serbia	No abstract submission	www.sld.org.rs
13 - 15 October, 2017	ISD Regional Meeting, Sarajevo, Bosnia and Herzegovina	31 August, 2017	www.pso-simpozij.com
15 - 17 October 2017	9th World Congress on Itch Wroclaw, Poland	31 May, 2017	www.itch2017.syskonf.pl
30 November – 2 December, 2017	8th International Congress on Psoriasis from Gene to Clinic, 2017 London, United Kingdom	1 August, 2017	www.psoriasisg2c.com
01 - 03 March, 2018	17th European Dermatology Congress Paris, France	No deadline information	www.dermatology.conferenceseries.com/europe/
14 - 18 March, 2018	3rd INDERCOS Congress Istanbul, Turkey	26 January, 2018	www.indercos.org
03 - 06 May, 2018	15th EADV Spring Symposium Budva, Montenegro	14 November, 2017	www.eadvbudva2018.org
14 - 16 June, 2018	5th World Congress of Dermoscopy Thessaloniki, Greece	20 January, 2018	www.dermoscopy-congress2018.com
27 - 30 June, 2018	5th World Psoriasis & Psoriatic Arthritis Conference Stockholm, Sweden	No deadline information	www.ifpa-pso.com
28 June - 01 July, 2018	13th World Congress of Cosmetic Dermatology, Dubrovnik, Croatia	15 February, 2018	www.wcocddubrovnik2018.org
12 - 16 September, 2018	27th EADV Congress Paris, France	13 March, 2018	www.eadvparis2018.org

Tatjana Roš, MD, PhD, Clinic of Dermatovenereology Diseases, Clinical Center of Vojvodina, and Dragana Ilinčić Šušnjar, MD, Department of Dermatovenereology, Health Care Centre of Novi Sad, Novi Sad; E-mail: tanjahana40@gmail.com; draganela.dis@gmail.com

AUTHOR GUIDELINES

Serbian Journal of Dermatology and Venereology is a journal of the *Serbian Association of Dermatologists and Venereologists*. The journal is published in English, but abstracts will also be published in Serbian language. The journal is published quarterly, and intended to provide rapid publication of papers in the field of dermatology and venereology. Manuscripts are welcome from all countries in the following categories: editorials, original studies, review articles, professional articles, case reports, and history of medicine.

Categories of Manuscripts

1. Editorials (limited to 5 pages) generally provide commentary and analyses concerning topics of current interest in the field of dermatology and venereology. Editorials are commonly written by one author, by invitation.

2. Original studies (limited to 12 pages) should contain innovative research, supported by randomized trials, diagnostic tests, outcome studies, cost-effectiveness analysis and surveys with high response rate.

3. Review articles (limited to 10 pages) should provide systemic critical assessment ofliterature and other data sources.

4. Professional articles (limited to 8 pages) should provide a link between the theory and practice, as well as detailed discussion or medical research and practice.

5. Case reports (limited to 6 pages) should be new, interesting and rare cases with clinical significance.

6. History of medicine (limited to 10 pages) articles should be concerned with all aspects of health, illness and medical treatment in the past.

7. Short Communications (limited to 3 pages) should disseminate most current results and developments in the shortest possible time. They will be reviewed by expert reviewers and evaluated by the Editor.

The journal also publishes book reviews, congress reports, as well as reports on local and international activities, editorial board announcements, letters to the editor, novelties in medicine, questions and answers, and “In Memoriam”. All submitted manuscripts will undergo review by the editor-in-chief, blind review by members of the manuscript review panel or members of the Editorial Board. Manuscripts submitted to this journal must not be under simultaneous consideration by any other publisher. Any materials submitted will NOT BE RETURNED to the author/s.

All manuscripts are to be submitted to the **Editor in Chief: Prof. Dr. Lidija Kandolf Sekulović,** Clinic of Dermatovenereology, School of Medicine, Military Medical Academy, Crnotravska 17, Belgrade, Republic of Serbia, by mail to: serbjdermatol@gmail.com

Manuscripts for submission must be prepared according to the guidelines adopted by the International Committee of Medical Journal Editors (www.icmje. org). Please consult the latest version of the Uniform Requirements for Manuscripts Submitted to Biomedical Journals.

1. Manuscript Preparation Guidelines

The manuscript should be written in English, typed in double spacing throughout on A4 paper, on one side only; Use Times New Roman, font size 12, with 30 lines and 60 characters per line. Articles must be written clearly, concisely and in correct English. Accepted manuscripts in need of editing will be returned after editing to the corresponding author for approval. When preparing their manuscripts, authors should follow the instructions given in the *Categories of Manuscript:* the number of pages is limited (including tables, figures, graphs, pictures and so on to 4 (four)), and all the pages must be numbered at the bottom center of the page.

For manuscript preparation, please follow these instructions:

1.1. Title page

The title page should include the following information:

– The title ofthe article, which shouldbe informative, without abbreviations and as short as possible;

– A running title (limited to 30 characters);

– Authors’ names and institutional affiliations;

– The name, mailing address, telephone and fax numbers, and email of the corresponding author responsible for correspondence about the manuscript. Furthermore, authors may use a footnote for acknowledgements, information and so on.

1.2. Abstracts

A structured abstract in English (limited to 150 words) should follow the title page. The abstract should provide the context or background for the study, as well as the purpose, basic procedures, main findings and principal conclusions. Authors should avoid using abbreviations.

– An **abstract in Serbian language,** (limited to 150 words) should follow the second page. It should contain a briefing on the purpose of the study, methods, results and conclusions, and should not contain abbreviations.

1.3. A list of abbreviations

Use only standard abbreviations, because use of nonstandard abbreviations can be confusing to readers. Avoid abbreviations in the title, abstract and in the conclusion. A list of abbreviations and full terms for which they stand for should be provided on a separate page. All measurements of length, height, weight, and volume should be reported in the metric units of the International System of Units — SI, available at *http:// w*ww. bipm.fr/en/si/.

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Manuscripts must be accompanied by a cover letter, which should include a date of submission, statement that the manuscript has been read and approved by all the authors and that the authorship requirements have been met. It should also include the name, address, and telephone number of the corresponding author, who is responsible for communicating with other authors about revisions and final approval of the proofs. The original copy of the cover letter, signed by all authors, should be enclosed with the manuscript.

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Tables should capture information concisely and precisely. Including data in tables, rather than in the text, reduces the length of the article itself.

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3. References

References in the text, tables and legends should be identified by Arabic numerals in parentheses. Number references consecutively in the order in which they are first mentioned in the text. The Vancouver System of referencing should be used. List each author's last name and initials; full first names are not included. List all authors, but if the number exceeds six, give the first six followed by „et al." National journals, which are not indexed in Index Medicus, should be abbreviated according to the style in the List of Abbreviated Titles of Yugoslav Serial Publications available on http:// vbsw.vbs.rs. For further information please visit www. ICMJE.org.

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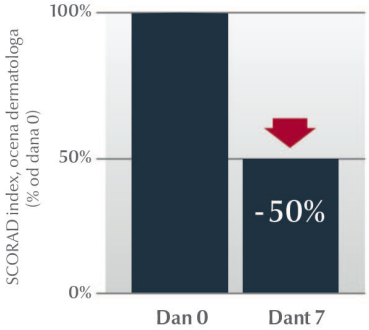

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