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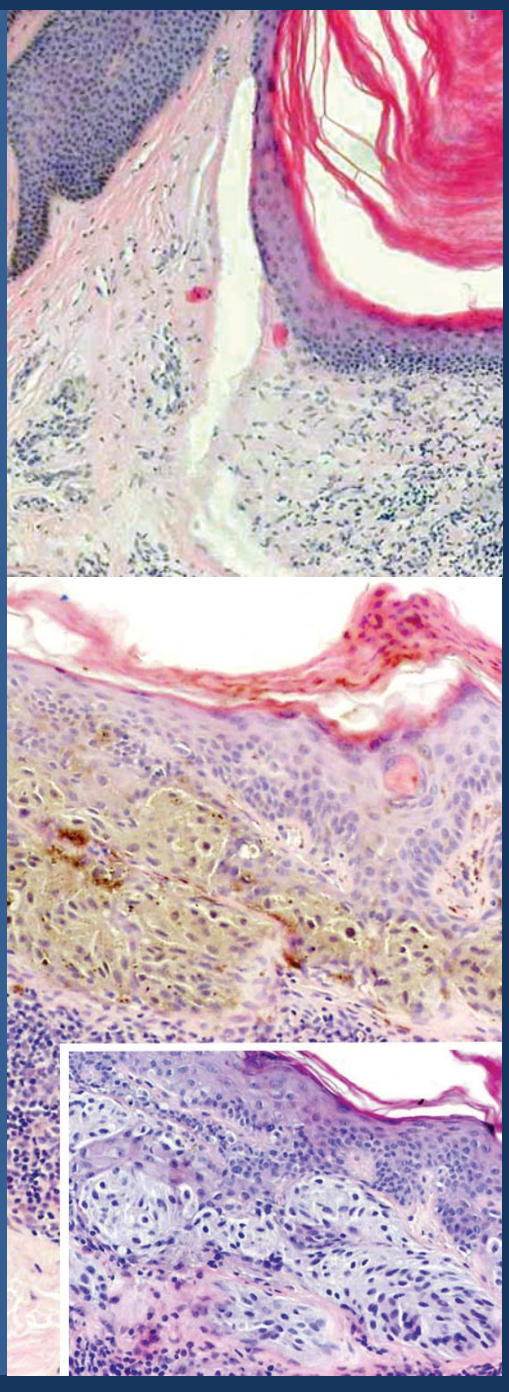

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CONTENTS

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Cutaneous Larva Migrans – Report of 2 new Cases Locally Acquired in Serbia

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Abstract

Cutaneous larva migrans (CLM) is a parasitic skin disease caused by the accidental percutaneous penetration and subsequent intraepidermal migration of larvae of various nematode parasites of the hookworm family. The hookworms responsible for CLM are spread worldwide, but the infection occurs mostly in tropical and subtropical climates. Nowadays, because of ever increasing foreign travel, the disease is no longer confined to these areas. Moreover, a significant increase of autochthonous cases in southern Europe has been observed in recent years. We report two new patients from Serbia who acquired CLM, none of them having traveled abroad. As the recommendations for the treatment of CLM are not uniform, two different treatment modalities were applied in these patients, both with an excellent response.

Key words: Larva Migrans; Skin Diseases, Parasitic; Hookworm Infections; Treatment Outcome; Case Reports; Albendazole; Ivermectin

Introduction

Cutaneous larva migrans (CLM) is a zoonotic infestation of the skin caused by the larvae of various animal nematode parasites of the hookworm family. The most common causes of CLM are: Ancylostoma braziliense, Ancylostoma caninum and Uncinaria stenocephala, but other species have also been reported (1, 2).

In Europe, CLM is usually seen among the travelers returning from subtropical or tropical countries who have visited beaches there. Lesions are typically distributed on the feet, thighs and buttocks, but any part of the body, which has been in the direct contact with the contaminated soil and sand, could be affected (3). Clinically, CLM is characterized by the presence of intensely pruritic, erythematous, serpinginous tracts that keep advancing up to several centimeters a day. The tunnels left behind the migrating parasite desiccate and become dry and crusted (3). Palmar and plantar lesions frequently contain some serous fluid, although vesicular and bullous lesions might also develop everywhere on the skin in 9-15% of cases (4).

Except pruritus, which could be severe and lead to epidermal damage and secondary infections due to the rubbing and scratching, CLM is a benign, self-limiting disease. It is rarely accompanied by peripheral blood eosinophilia, and usually not associated with systemic symptoms (3, 5).

The diagnosis of CLM is clinical, based on the characteristic skin lesions in a patient who has traveled to high-risk areas (4). Biopsy is sometimes performed, but it is not necessary for the diagnosis as the parasite is located 1-2 cm ahead of the leading edge of a tract and could be easily missed (6). Dermoscopy has become a useful, additional diagnostic tool in recent years (7).

The prognosis of CLM is generally favourable, even without treatment. In most cases, the larva dies and the lesions resolve spontaneously within 2–8 weeks. Sometimes untreated disease lasts longer and may persist up to 2 years. With specific therapy, remission is usually observed within a week (8, 9).

Herein, we describe two new autochthonous cases of CLM in Serbia which were

successfully treated with different treatment modalities.

Case Reports

Case 1. A 72-year-old man, from a city in western Serbia, was admitted to our Department in August 2016 because of intensively pruritic, migrating and linear erythema in the presternal area. The skin changes appeared 5 months before admission and they were treated with oral antihistamines and different topical antibiotics, without effect. The patient was otherwise healthy and denied recent travel to endemic regions. However, he reported that his favorite hobby was fishing at the local river, where he might have got in contact with a larva.

On examination, erythematous, serpiginous and raised tract was present over the patient's presternal region (Figure 1). Over the next few days, the lesion progressed toward the upper left side of the thorax. Regional lymphaedenopathy was not present, and there were no other significant findings and systemic symptoms. The routine blood parameters, including complete blood count and total serum IgE, were within normal limits. The diagnosis was made based on the typical clinical picture and the history of contact with potentially contaminated sand around the river.

The patient's response to oral albendazole, given at a dose of 400 mg daily for three days, was excellent. Pruritus improved rapidly in the next few days and the skin lesions resolved completely within 10 days. No side effect was observed during the treatment period. On the follow-up visit after one month, only hypopigmentation at the affected site was present (Figure 2).

Case 2. A 31-year-old man, from a small town in central Serbia, was admitted to our Department in the middle of September 2016 because of intensively pruritic, vesiculobullous and linear lesion on the right hand. The skin changes appeared 15 days before admission and were treated with topical corticosteroids without improvement. Otherwise, the patient was healthy and did not report any other associated symptoms, neither did he travel to endemic regions. However, because of his job, he had to spend a lot of time during that summer in a warm and moist environment (forest), where he may have been exposed to a parasite.

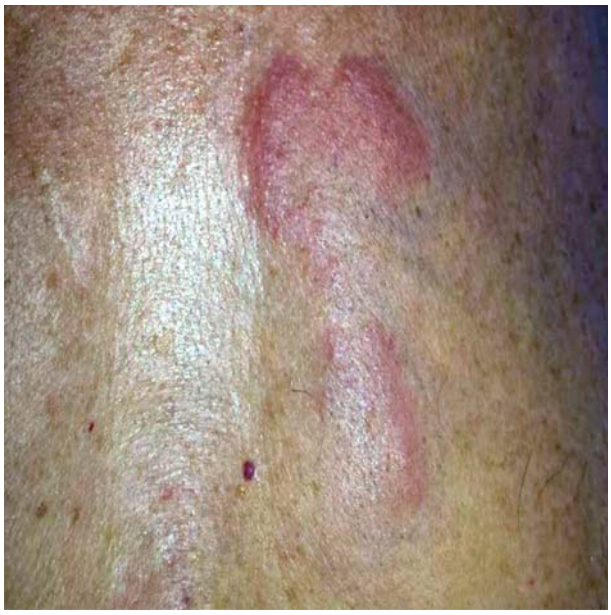

Figure 1. Erythematous, serpiginous, raised

On examination, a raised, erythematous, serpiginous tract, with bullae formation was observed on the patient's right hand (Figure 3). Over the next few days, the lesion advanced progressively. Regional lymphadenopathy was not present, and there were no other significant findings and systemic symptoms. The routine blood tests were within normal ranges. Peripheral blood eosinophilia and total serum IgE elevation were not present. The diagnosis was made based on the skin lesions typical for CLM and the history of contact with possibly contaminated soil in the warm and moist forest.

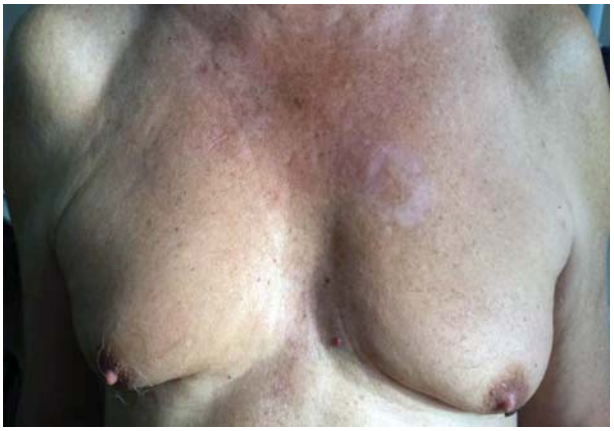

Figure 2. Residual hypopygmentation after tract over the presternal region treatment

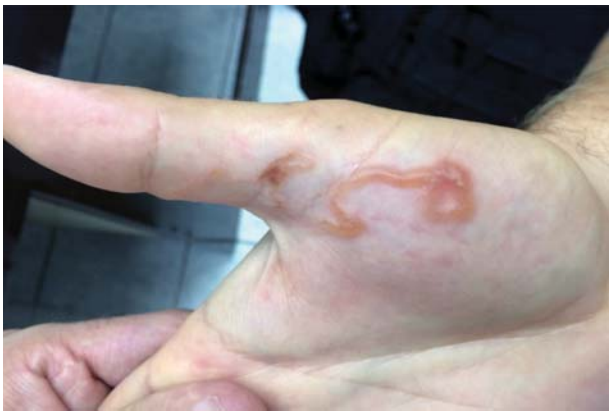

Figure 3. Serpiginous, bullous tract on the right hand

The patient was treated with oral ivermectin, given as a single dose of 200 μg/kg/kg and his response was excellent. The pruritus disappeared almost immediately after the treatment and the lesions resolved completely within the next 15 days (Figure 4). No side effect was observed during the treatment period.

Discussion

CLM is a parasitic dermatosis most commonly found in tropical and subtropical areas like the Caribbean, South and Central America, Southern-East Asia and Africa (3, 5). The parasites live in the small intestines of dogs, cats and wild animals, from where they release their eggs in the feces. Under favorable environmental conditions of temperature and humidity, these eggs hatch and mature into infectious larval form (filariform larvae) in the sand or soil. At this stage, larvae are able to penetrate the intact skin by using their proteases and to infect a new host (1, 10). Once inside the mammalian body, filariform larvae start migrating after an incubation period of about a week (11). Depending on the new host, the parasite migration might eventuate in two different ways. Within the body of their natural hosts, filariform larvae penetrate the basement membrane, invade the dermis, and then travel through the bloodstream or lymphatic system to the lungs, ascend into the trachea to be coughed and swallowed. In the intestine of these animals the larvae molt into adult, sexually mature worms (5). The humans could also be affected, but due to the deficiency of collagenase the parasites are not able to penetrate the basement membrane, invade deeper structures and complete their life cycle in the human skin. Therefore, in the human body, the larvae remain trapped in the outer layers of the skin, they migrate aimlessly a few millimeters to a few centimeters per day, produce the lesions typical for CLM without associated systemic symptoms, until they eventually die (3, 6).

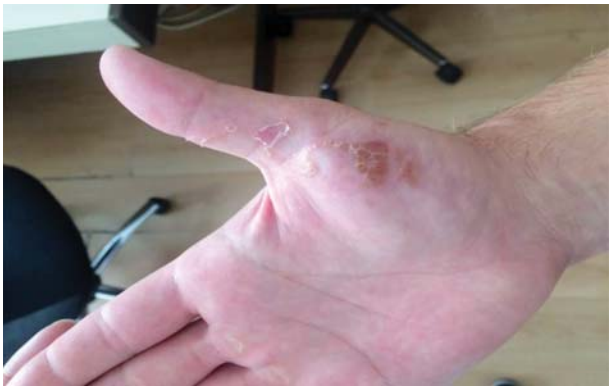

Figure 4. Almost complete resolution of the lesions 15 days after the treatment

The endemic nature of this disease could be explained by the impact of poor sanitary conditions associated with humid and hot climate (5, 12). The infestation is typically acquired through direct contact with sand or soil contaminated with filariform larvae derived from infected animal feces. Frequently, there is the history of walking barefoot or sitting and lying on the wet, sandy beaches, since the warm and humid environment enables nematode larvae to survive and be infective for several weeks or even several months (3, 12).

Until now, CLM has been a rare disease in Europe, usually diagnosed in the tourists arriving from endemic regions, with only sporadic reports of infestations locally developed. In the recent years, the diagnosis of CLM in Europe has become more frequent, probably because of much more frequent foreign travel. Furthermore, the striking rise in numbers of locally acquired cases was noticed, most commonly in southern European countries (10, 11, 13, 14). It is likely that global warming and climate changes with an increase in ambient temperature and humidity, which favor the larva development, are responsible for this phenomenon (10, 11).

Although CLM is a self-limited disease that usually resolves spontaneously within 2-8 weeks, the treatment is advisable because of intense pruritus and high risk for infection (12). Oral ivermectin, given as a single dose of 200 μg/kg, oral albendazole, given at a dose of 400 mg daily for three days, topical ivermectin, or topical thiabendazol are most frequently used drugs (10, 15). A single dose of oral ivermectin is usually considered to be a drug of choice, but the recommendations for the management of cutaneous larva migrans are not uniform, and the recommended methods are not always available neither they are always effective (10, 15).

In conclusion, our personal experience confirms an increase in the incidence of autochthonous cases of CLM in Europe since only 2 cases of infestations locally developed were reported in this country before (1). In addition, based on our results and a literature review, we can make the conclusion that ivermectin given as a single dose of 200 μg/kg/kg, as well as albendazole given at a dose of 400 mg/day for three days are effective and reliable treatment for this condition.

Abbreviations

CLM - cutaneous larva migrans

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Kutana larva migrans – prikaz dva nova slučaja infestacije nastale u Srbiji

Sažetak

Kutana larva migrans je parazitarna dermatoza uzrokovana akcidentalnom perkutanom penetracijom i daljom intraepidermalnom migracijom larvi različitih nematodnih parazita iz familije rudarskih glista. Larve parazita odgovorne za nastanak bolesti rasprostranjene su u čitavom svetu, ali se infekcija najčešće registruje u tropskim i suptropskim regionima. Zbog sve većeg broja putovanja u inostranstvo, bolest u savremenom svetu

više nije ograničena na ova područja. Pored toga, poslednjih godina zabeležen je i porast broja autohtonih slučajeva u južnim delovima Evrope. Prikazujemo dva nova pacijenta iz Srbije kod kojih je postavljena dijagnoza *kutana larva migrans*, a kod kojih nisu postojali anamnestički podaci o prethodnim putovanjima u inostranstvo. S obzirom da preporuke za lečenje ove bolesti nisu uniforme, kod pacijenata su primenjena dva različita terapijska modaliteta, oba sa odličnim terapijskim odgovorom.

Ključne reči: Larva migrans; Kožne parazitske bolesti; Infekcije rudarskom glistom; Ishod terapije; Prikazi slučajeva; Abendazol; Ivermektin

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Fish Tank Granuloma – a Case Report

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Abstract

Swimming-pool granuloma and fish tank granuloma refer to the infections caused by Mycobacterium marinum. After having been discovered in salt water fish in Philadelphia Aquarium and described in 1926, this skin infection was first reported in humans in 1951. It developed in people who had swum in contaminated swimming pools. M. marinum is a non-tuberculous, atypical mycobacterium, which is found on plants, soil and fish in freshwater and salt water worldwide. Humans become infected usually after trauma and contact with an aquatic environment. Infection is limited to the skin and usually occurs in healthy individuals, but in immunocompromised patients the infection may disseminate or spread to the subcutis and bone. The lesions usually appear as solitary nodules or plaques that may lead to suppurative ulcers after 2-3 weeks of incubation. Occasionally, there may be sporotrichoid spread along lymphatics. Its diagnosis is frequently delayed, probably because the infection is very rare and a history of aquatic exposure, which is present in the majority of cases, is often overlooked. Common misdiagnoses include fungal and parasitic infection, cellulitis, verrucous tuberculosis of the skin, gout, rheumatoid arthritis, a foreign body and a skin tumour. We present a case of a 39-year-old Caucasian male with a 12-month history of a single erythematous tender nodule on the right dorsal aspect of the right hand. Histopathological examination revealed longstanding suppurated granulomatous inflammation. The infection was not responsive to several courses of antibiotics until we introduced doxycycline capsules as monotherapy which led to complete remission after 5 months.

Key words: Mycobacterium marinum; Mycobacterium Infections; Skin Diseases, Bacterial; Granuloma; Hand Dermatoses; Doxycycline

Introduction

Mycobacterium marinum is a nontuberculous photochromogenic mycobacterium causing a disease in many fish species from cold or warm, fresh or salted water. Human infection follows the contact with fish or contaminated water. First described as “swimming-pool granuloma”, nowadays M. marinum skin infection often results from inadequate aquarium maintenance and is called “fish tank granuloma”. The infection is commonly limited to the skin of the limbs, but it can spread to deeper structures, resulting in tenosynovitis, arthritis, and osteomyelitis (4, 5). Surgery, antibiotics and cryotherapy have been recommended for the treatment of M. marinum infections, but none of these treatments has proved to be superior. Antibiotic efficacy and its correlation to in vitro susceptibility are unknown because cases were reported separately in the literature, no therapeutic trial has been done, and data on M. marinum susceptibility are scarce (limited number of strains and antibiotics) (6, 7).

Case 1

A 39-year-old male patient reported an asymptomatic lesion on the right dorsal third metacarpophalangeal joint with 12 months of evolution. The lesion initially presented as a pustule on the dorsum of the right hand, with progression in the next few months to the plaque with a purulent discharge (Figure 1). Prior to consultations, the patient had received repeated prescriptions for topical corticosteroids, with no evidence of improvement. Skin biopsy was performed and his-

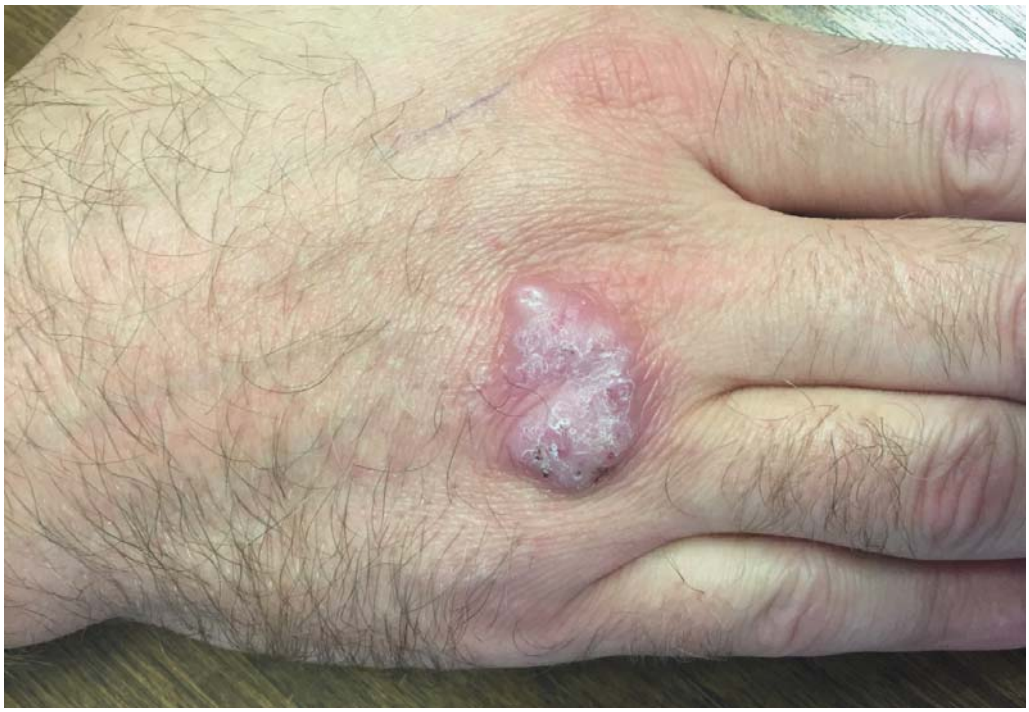

Figure 1. Clinical presentation of tender rough-whitish erythematous nodule on the dorsal side of the right hand

topathological investigation showed suppurative granulomatous inflammation, and he was treated with rifampicin and claritromycin, without improvement. After months of clinical evaluations by different specialists, the patient was admitted to our Department of Dermatology. Clinical examination did not reveal other skin/mucosal lesions, reduced sensitivity, lymphonodopathy, nor any associated systemic manifestations. Having taken the detailed anamnesis (the patient had an aquarium), we performed the second biopsy, along with cultivations of the tissue for typical and atypical mycobacteria that confirmed infection with atypical mycobacteria. Antibiotic treatment with doxycycline caps. 200 mg/daily was introduced and resulted in complete resolution of the lesion after 5 months (Figure 3).

Discussion

M. marinum is a non-tuberculosis mycobacterium living freely in an aquatic environment. It is responsible for the development of a distinctive cutaneous infection that may result in abraded skin, following the contact with the contaminated salt or fresh water or infected aquariums. M. marinum is an uncommon cause of skin infections. Therefore, a substanial delay has been observed between the appearance of the lesions and the correct diagnosis. The disease usually presents as a solitary, red to

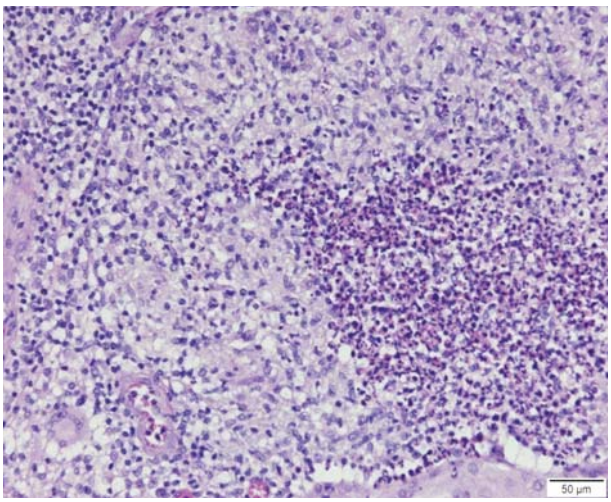

Figure 2. Histopatological examination showed an abscess in the center due to neutrophils and necrosis, with histiocytes, epithelioid cells and multinucleated giant cells, around the abscess (HE x50)

Table 1. Treatment options for fish-tank granuloma*

Type of lesion	Antibiotics	Duration
Superficial (limited 1-3 lesions)	Doxycycline 200mg/day [present case] Clarithromycin 500 mg/day [9] Minocycline 200 mg/day [8,9] Ciprofloxacin 1000 mg/day [8] Trimethoprim-sulfamethoxazole 160/800 mg/day [12] Amikacin 400 mg/day [9]	2-12 months
Numerous lesions (>3), Sporotrichoid spread, deep infection + skin involvement)	Rifampicin 600 mg/day + Ethambutol 15-25 mg/day [11] Rifampicin + Clarithromycin [13] Rifampicin + Minocycline[13] Surgical excision	2-12 months

*modified from Bhatty et al. [14]

violaceous papule and/or nodule evolving to a verrucous plaque that may ulcerate on the areas of trauma. The diagnosis of a skin M. marinum infection requires a high index of suspicion, a detailed exposure history, as well as the knowledge of laboratory growth characteristics of the organism (4, 8, 9). Although the diagnosis was confirmed in our case by isolation and identification of the organism, in practice the diagnosis remains largely presumptive based on clinico-histological features and the response to treatment (10).

There have been many therapeutic modalities used effectively in the treatment of M.

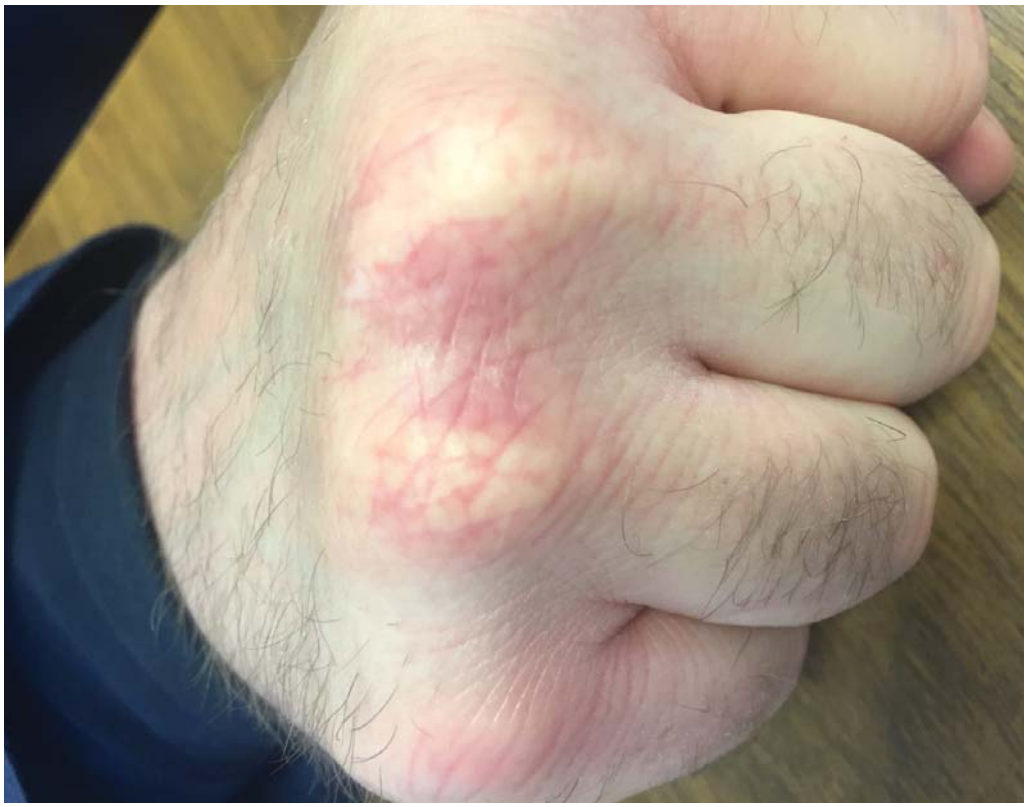

Figure 3. Clinical presentation at the end of antibiotic treatment

marinum infections such as surgery, cryotherapy, and different antibiotic regimens. However, there is no proven treatment of choice because M. marinum is a multidrug resistant species, and treatment is based primarily on personal experience and the preference of the individual researchers. Antibiotic monotherapy is usually, but not always, associated with infections limited to skin and soft tissue, and combinations of two or more antibiotics are used for more severe infections that spread into the local tissue. In superficial skin infections, doxycycline, clarithromicyin, minocycline and trimethoprim-sulfamethoxazole are used as monotherapy. A combined therapy with two or more drugs (e.g. rifampicin associated with ethambutol) might be required due to drug resistance. An isolated combination of rifampicin and ethambutol has been recommended in severe infections, including those with a sporotrichosis-like distribution. (11,12) Treatment should be administered for at least 6 weeks up to 12 months, depending on the clinical evolution of lesion (13). In Table 1 treatment options for fish-tank granuloma are presented.

Conclusion

A detailed exposure history, high index of suspicion, as well as the knowledge of the laboratory growth characteristics of the organism is needed to establish the diagnosis of fish-tank granuloma. Antibiotic therapy should be tailored to the individual patient's reponse, and in resistant cases, surgery should also be considered.

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Fish tank granuloma - prikaz slučaja

Sažetak

Fish tank granuloma je infekcija izazvana atipičnom mikobakterijom (*M. marinum*), koja se može naći kako u slatkoj, tako i u slanoj vodi (najčešće u kontaminiranim akvarijumima i bazenima). Infekciju karakteriše sporastući plak ili nodus, a predilekciona mesta su uglavnom donji ili gornji ekstremiteti, a kod imunokompromitovanih pacijenata, infekcija se može diseminovati ili širiti na supkutano tkivo i kost. Dijagnoza se često kasno postavi, zato što je infekcija ovom bakterijom veoma retka, a česti su i slučajevi kada se infek-

cija pogrešno dijagnostikuje kao gljivična i parazitarna infekcija, celulitis, tuberkuloza kože, giht ili reumatoidni noduli. Prikaz slučaja. Pacijent, starosti 39 godina, koji unazad 12 meseci ima bolno osetljiv, eritematozan nodus na dorzalnoj strani desne šake. Histopatološki je verifikovana supurativna granulomatozna inflamacija. Postejeća infekcija kože nije dala zadovoljavajući terapijski učinak tokom primene dvojne antibiotske terapije klaritromicin i rifampicinom, dok u terapiju nije uveden doksiciklin, kao monoterapija, što je rezultiralo kompletnom remisijom nakon pet meseci lečenja.

Ključne reči: Mycobacterium marinum; Mikobakterijske infekcije; Bakterijske kožne bolesti; Granulom; Dermatoze ruku; Doksiciklin

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Lues Maligna as an Initial Presentation of Underlying HIV Infection in a Homosexual Man

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UDC [616.5-002.6:616.972]:[616.988:578.828]

Abstract

Lues maligna is a rare ulcerative form of secondary syphilis. This clinical entity is predominantly found in patients living with HIV or AIDS. We report a case of a 32-year-old homosexual man with diffuse non-pruritic, papular skin lesions, ulcerated nodules and plaques disseminated on the face, trunk and extremities. The rash was followed by fever, malaise and joint pains. Serological tests for syphilis were positive. The patient was treated with intramuscular penicillin and the lesions resolved completely. Lues maligna was an initial presentation of underlying HIV infection. The HIV seropositivity was confirmed by Western blot analysis. Due to the increased number of syphilis cases and frequent HIV co-infection in Serbia, dermatologists must be able to recognize this condition based on clinical characteristics and risk factors and to diagnose and treat it promptly.

Key words: Syphilis, Cutaneous; HIV Infections; Immunocompetence; Risk Factors; Skin Ulcer; Homosexuality, Male; Case Reports

Introduction

Lues maligna or ulceronodular syphilis is a rare manifestation of secondary syphilis first described by Bazin in 1859 who applied this term based on the grotesque clinical features (1). In the late 1800s, Neisser and Haslund defined the clinical characteristics of this form of secondary syphilis and distinguished it from the necrotizing gummatous disease of tertiary syphilis (2, 3). In the period between 1900 and 1988 only fourteen cases were reported in the English-language literature (4). However, more cases of lues maligna have been described in people with HIV/AIDS since HIV pandemic started (4, 5, 6).

We report a case of lues maligna mimicking Pityriasis lichenoides et varioliformis acuta in a homosexual man. This was the first clinical manifestation revealing a hidden HIV infection.

Case Report

A 32-year-old homosexual man was referred to the Department of Sexually Transmitted Infections for the evaluation of a non-pruritic skin rash. The rash, which had appeared on his face one month earlier and spread to his entire body in the next two weeks, was followed by fever, malaise and joint pains. During the second week of the rash he visited a dermatologist at a walk-in clinic, where he was diagnosed with Pityriasis lichenoides et varioliformis acuta and an oral antibiotic (ciprofloxacine) was prescribed for two weeks. There was no improvement and the patient was referred to the City Institute for Skin and Venereal Diseases.

Physical examination revealed multiple erythematous papules, nodules and oval necrotic ulcerated plaques on the face, trunk and extremities (Figure 1 and 2). Ulcerations were covered with laminated, brown-black rupioid crusts (Figure 3 and 4). His palms and soles, genital area and oral mucosa were unaffected. There were no generalized lymphadenopathies. His personal history showed that he had had five sexual partners in the previous six months. He used a condom only during anal intercourse and practiced unprotected oral-genital and oral-anal sex. It was also found that the patient had had an asymptomatic anal lesion, which

had had appeared two months before skin rash onset but passed spontaneously.

Laboratory findings, including complete blood count and blood chemistry were within normal limits, except for a high sedimentation rate, being 80. Serological tests were performed and Venereal Disease Research Laboratory (VDRL) test was positive with titers 1:512 and *Treponema Pallidum* Hemagglutination Assay (TPHA) test was positive as well. The patient was treated with three consecutive doses of benzathine penicillin G, 2.4 million units intramuscularly at 1-week intervals (total 7.2 million units). A severe Jarish-Herxheimer reaction occurred in our patient. He developed chills, fever and sweating ten hours after the first application of penicillin. He took antipyretics and reaction resolved within 24 hours. Syphilitic lesion healing was fast and serology showed eight-fold decline of VDRL titre (it fell to 1:64) after three months of the treatment. The patient was counselled and tested for HIV. The HIV seropositivity was confirmed by the Western blot analysis.

Discussion

A worldwide syphilis incidence increase was recorded at the beginning of the new millennium, occurring primarily among men who have sex with men – MSM (7). An upsurge of syphilis incidence in Belgrade began in 2010 (8). During the period from 2010 to 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 (9). Men accounted for the most cases of syphilis during an early syphilis outbreak in 2014, with the vast majority of such cases (85.1%) occurring among homosexual men. One third of syphilis cases (all MSM) were co-infected with HIV (10). Patton et al (11) reported the rates of 50-70% of HIV co-infection among MSM infected with primary or secondary syphilis. However, HIV positive patients are presented more often with secondary syphilis and the disease course is more aggressive (12).

Known as the great imitator especially at the secondary stage, syphilis may present itself with a myriad of diverse morphological entities and clinical manifestations (13, 14) which emphasizes the importance of dermatological education of non-experienced physicians, particularly under the current circumstances of syphilis resurgence in Serbia.

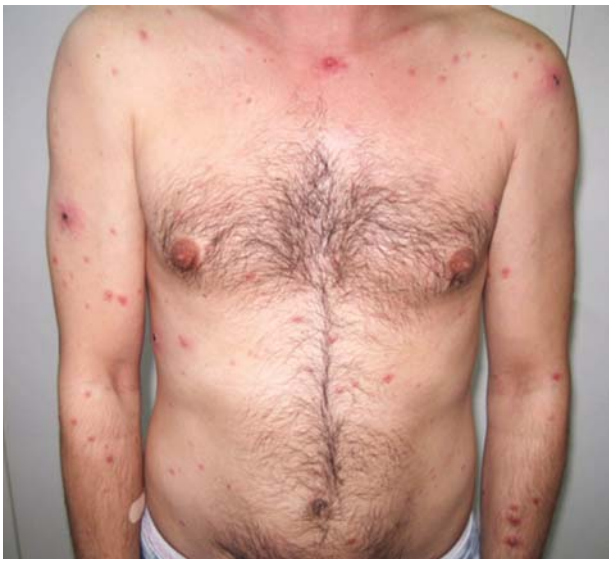

Figure 1. Disseminated papules, nodules and some ulcerated lesions on the trunk and extremities

Lues maligna is a rare ulcerative form of secondary syphilis characterized by papulopustular skin lesions that rapidly enlarge and evolve into round or oval ulcers with sharp borders, centrally covered by a dark, sometimes rupioid crust (as described in our patient) while mucosal surfaces may also be affected (15). The onset of the eruption can be preceded by fevers, chills, anorexia, weight loss and severe headaches.

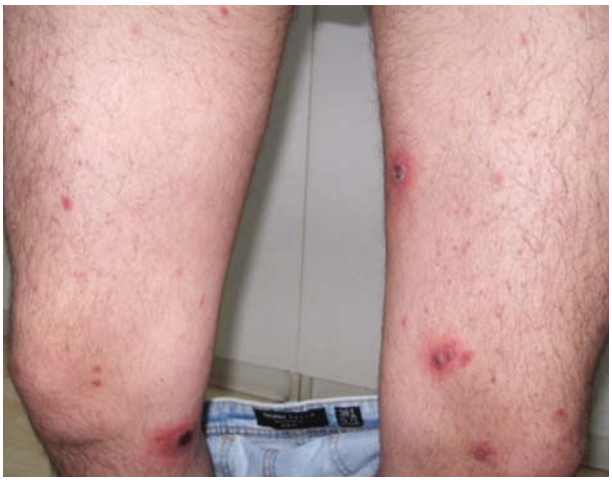

Figure 2. Erythematous papules and ulcerated lesions on the lower limbs

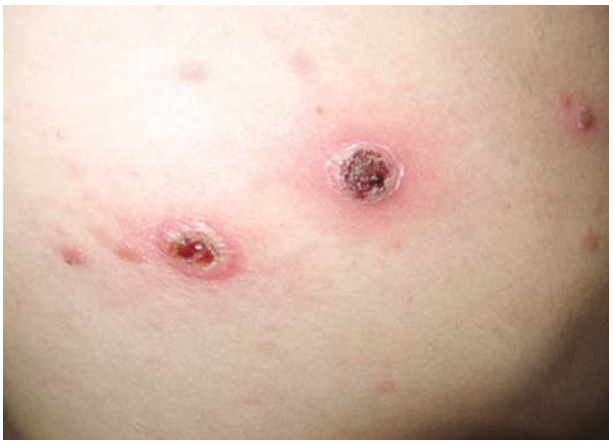

Figure 3. Characteristic ulcerations of lues maligna covered with crusts

Clinical conditions that mimic lues maligna include ecthyma, ecthyma gangrenosum, anthrax, blastomycosis-like pyoderma, pyoderma gangrenosum, atypical mycobacterial infection, deep fungal infection and vasculitis (16). Our patient was misdiagnosed as pityriasis lichenoides et varioliformis acuta.

The criteria for diagnosis of lues maligna listed by Fischer et al. (15) include compatible gross morphology, a high titre serologic test for syphilis, a severe Jarisch-Herxheimer reaction and an excellent response to antibiotic therapy. All of these manifestations were present in our patient.

The Jarisch-Herxheimer reaction is a transient immunological phenomenon seen commonly in patients during treatment of secondary syphilis. An increase in the incidence of this reaction has been described in the patients with lues maligna and in HIV infected patients (17). It is manifested with constitutional symptoms such as fever, headache, myalgia, chills and rigours which resolve within 24 hours. Corticosteroids have been used to offset the reaction with no conclusive evidence of their benefit (18).

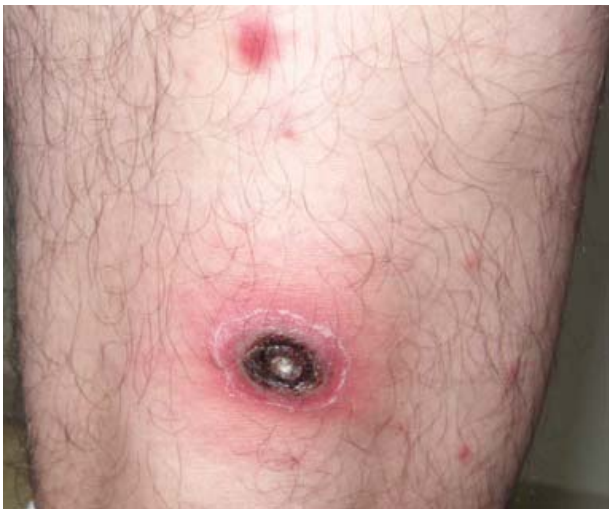

Figure 4. Rupioid crust on the popliteal fossa

Lues maligna was described well before the HIV pandemic and it was associated with severe malnutrition, alcoholism, diabetes mellitus and intravenous drug use (19-21). Following the HIV/AIDS epidemic, the incidence of lues maligna significantly increased; moreover, the patients with HIV were 60 times more likely to present with this form of syphilis (22). At present, it is estimated that up to 7% of syphilis cases found in HIV/AIDS patients meet the criteria for lues maligna (22), and they are frequently the first clinical manifestation revealing a hidden HIV infection, as we described in our patient.

Conclusion

Because of the increased number of syphilis cases and frequent HIV co-infection in Serbia, dermatologists should be well-aware of the possibility of occurrence of lues maligna cases. It is important to recognize and diagnose malignant syphilis early and introduce the appropriate treatment as the complete recovery can be achieved.

Acknowledgement

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Maligna forma sifilisa kao inicijalna prezentacija postojeće HIV infekcije kod homoseksualnog muškarca

Sažetak

Lues maligna je retka ulcerativna forma sekundarnog sifilisa koja se najčešće opisuje kod imunodeficijentnih pacijenata koji žive sa HIV-om. Prikazujemo muškarca homoseksualne orijentacije, starog 32 godine, koji se javio lekaru zbog difuznih nepruriginoznih promena u vidu papula, ulcerisanih nodusa i plakova lokalizovanih na licu, trupu i ekstremitetima. Osip po koži je bio praćen groznicom, malaksalošću i bolovima u zglobovima. Serološki testovi za sifilis bili su pozitivni i pacijent je lečen intramuskularno penicilinom te su se sve promene na koži povukle. S obzirom na to da se maligna forma sifilisa češće javlja kod osoba inficiranih HIV-om, pacijent je upućen na testiranje i seropozitivnost je potvrđena Vestern blot testom. Usled povećane incidencije sifilisa u Srbiji i česte udruženosti ove infekcije sa HIV-om, dermatolozi bi morali da na osnovu karakteristične kliničke slike i faktora rizika posumnjaju, dijagnostikuju i leče ovu retku formu sekundarnog sifilisa.

Ključne reči: Kutani sifilis; HIV infekcije; Imunokompetencija; Faktori rizika; Ulceracije kože; Homoseksualnost kod muškaraca; Prikazi slučajeva

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Squamous Cell Carcinoma Arising from Linear Porokeratosis - a case report and review of the literature

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UDC 616.5-003.87

Abstract

Porokeratosis belongs to a group of disorders of keratinization that are characterized by the histopathological feature of the cornoid lamella, a column of tightly fitted parakeratotic cells. The etiology of porokeratosis is still unclear. Different variants of porokeratosis (PK) have been subsequently recognized, each with its own specific properties in terms of morphology, distribution and clinical course. Linear porokeratosis is one of the variants of porokeratosis, a rare disorder of keratinization that may develop into several epidermal malignancies, squamous cell carcinoma being the most frequent among all of them. Thus, a clinical surveillance for malignancy is an imperative. We present a case of a 54-year-old man with non-healing ulcer of the lower leg caused by squamous cell carcinoma arising on long-standing linear porokeratosis. The treatment included wide excision of tumor with the reconstruction of the area. Acitretin was prescribed for linear porokeratosis treatment. The follow-up of our patient so far has shown that he does not have new malignant lesions after surgical excision.

Key words: Carcinoma, Squamous Cell; Porokeratosis; Skin Neoplasms; Leg Dermatoses; Genes, p53; Dermatologic Surgical Procedures; Case Reports

Introduction

Porokeratosis (PK) belongs to a group of disorders of keratinization that are characterized by the histopathological feature of the cornoid lamella, a column of tightly fitted parakeratotic cells. The etiology of porokeratosis is still unclear. Variants of PK include: linear porokeratosis (LP), disseminated superficial porokeratosis (DSP) disseminated superficial actinic porokeratosis (DSAP), classic porokeratosis of Mibelli (MB), punctate porokeratosis (PP) and porokeratosis plantaris et palmaris disseminata (PPPD) (1). Linear PK is a rare form of porokeratosis that usually presents unilaterally with grouped characteristic lesions following the lines of Blaschko. Although progression to malignancy is rare, it can occur in all types of PK; linear PK is the most common subtype susceptible to malignant degeneration. The diagnosis of PK is typically based on the clinical examination as well as the histopathology analysis (2). A review of cases and case series found in the literature (3) shows that linear PK has approximately 19% chance of malignant transformation compared to approximately 7% to 11% chance (4) in other types of PK. The most common malignancy is squamous cell carcinoma (SCC) (in situ and invasive), followed by basal cell carcinoma (BCC) (2). The exact mechanism by which malignant degeneration develops in PK is not yet completely understood, but the experimental research has suggested that the tumor suppressor gene p53 has a role in the pathogenesis of all types of PK (5, 6).

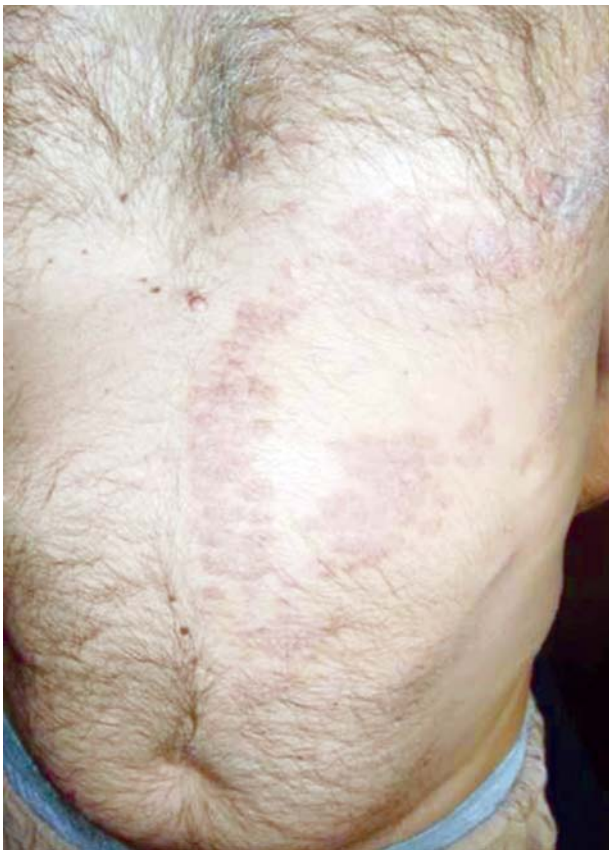

Figure 1. Linear porokeratotic plaques on the left side of the body

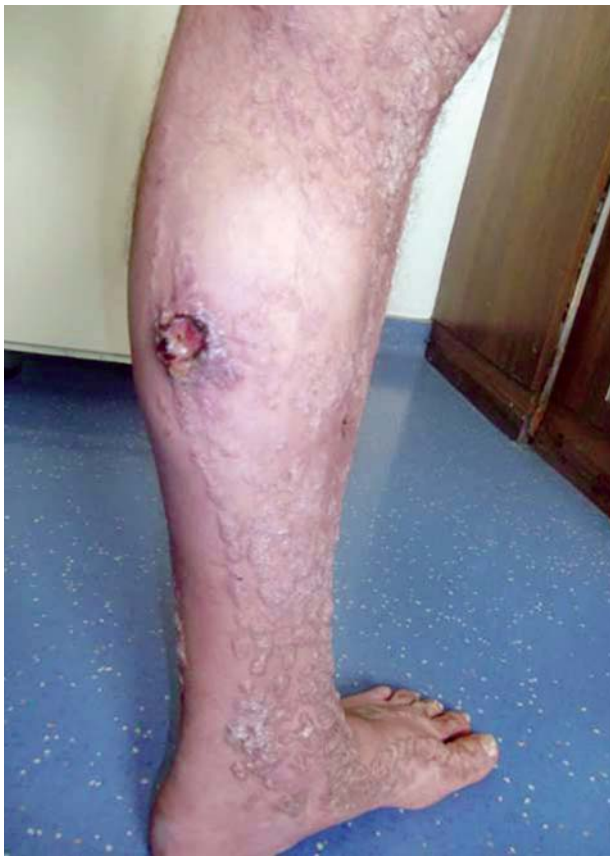

Figure 2. Round-shaped, solitary, well-demarcated ulcer on the posterior side of the lower left leg

Case Report

A 54-year-old man was admitted to our Clinic with painful, non-healing and progressively worsening ulcer on the back side of his lower left leg. It appeared 6 months prior to admission at the site of lesional skin of porokeratosis. He was diagnosed with porokeratosis in his early childhood based on the clinical presentation, without biopsy and histopathological confirmation. He was not regularly followed up by a dermatologist since his condition did not cause any concern. However, six months after gradual development of ulceration he consulted a dermatologist. He was otherwise healthy and there were no chronic skin disorders and skin cancers in his family.

The physical examination of the skin revealed rough, confluent, hyperkeratotic plaques grouped and linearly arranged along the Blaschko lines on the left anterior side of the trunk, anterior and inner side of the left leg and dorsal part of the left foot (Figure 1). In addition, a round-shaped, solitary, well-demarcated ulcer, 7 cm in diameter, was present on the posterior side of the lower left leg (Figure 2).

A skin-biopsy of the lesions clinically resembling porokeratosis was indicated as well as the wide excision of the ulcerated tumor to be performed by a plastic surgeon. The histopathological analysis of skin biopsy confirmed porokeratosis based on the presence of cornoid lamella, which correlated to the raised hyperkeratotic border and was observed at the periphery of the lesion (Figure 3).

Histopathology analysis was performed on excised ulcer as well which showed irregular tumor nests that lead to diagnosis of squamous cell carcinoma, gradus II (Figure 4).

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

physiological limits. X-ray of the chest was performed alongside with ultrasound of the abdomen, pelvis and groins. According to the latest staging manual of the American Joint Committee on Cancer (7) our patient's disease was denominated stage II (T3N0M0). The patient had an uneventful post-excisional recovery with the complete healing of the surgical wounds and successful cosmetic result. Acitretin capsules, 25 mg per day were also prescribed. So far no recurrence has occurred after 2-year follow-up consisting of skin check-up and regular ultrasound surveillance.

Discussion

Porokeratosis (PK) is a group of disorders of keratinization that usually present early in life as well-defined hyperpigmented macules or patches with a distinctive, typically raised, ridge-like hyperkeratotic border histologically characterized by a cornoid lamella. Linear porokeratosis (LP) is a rare form of porokeratosis that usually presents unilaterally with grouped lesions following the lines of Blaschko. Other variants of PK include disseminated superficial actinic porokeratosis - DSAP (the most common type, with the predominance of women in their third to fourth decade of life and involving sun-exposed areas such as the arms, legs, shoulders, and back; it spares the palms and soles); classic porokeratosis of Mibelli - MB (the second most common type, presenting typically in young boys with a large lesion on an extremity and associated with immunosuppression); punctate porokeratosis - PP and porokeratosis plantaris et palmaris disseminata - PPPD (less common type and presenting on the palms and soles) (2). A simultaneous presentation of several types of PK can occur but is seldom reported (4). Although progression to malignancy is rare, it can occur in all types of PK (2). Linear PK is the most common subtype susceptible to malignant degeneration, as is the case with our patient.

The diagnosis of all types of porokeratosis is typically based on the clinical examination. The presence of a flat, discolored, discrete lesion with a well-defined, elevated border suggests this disorder. Histologically, PK is characterized by a column of tightly fitted parakeratotic cells with pyknotic basophilic nuclei (8). This histologic feature (cornoid lamella), which correlates to the raised hyperkeratotic border, is observed at the periphery of the lesion. In our patient, the diagnosis was based on clinical manifestation and typical histopathological features.

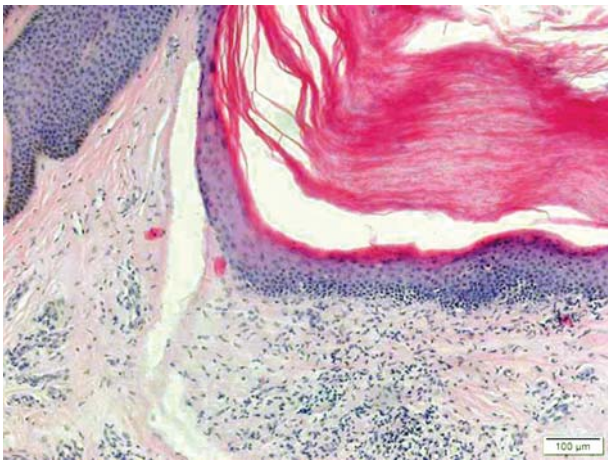

Figure 3. Tightly fitted parakeratotic cells which are well-circumscribed from the rest of the corneocytes extending through stratum corneum – cornoid lamella (hematoxylin and eosin x 100)

A review of cases and case series found in the literature (3) shows that linear PK has approximately 19% chance of malignant transformation compared to approximately 7% to 11% chance (4) in other types of PK. The most common malignancy is squamous cell carcinoma (SCC) (in situ and invasive), followed by basal cell carcinoma (BCC) (2). The exact mechanism by which malignant

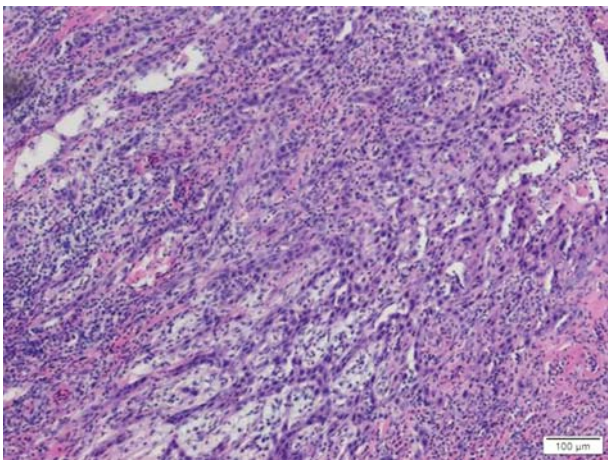

Figure 4. Irregular tumor nests (hematoxylin and eosin x 100)

degeneration develops in PK is not yet completely understood, the experimental research has suggested that the tumor suppressor gene p53 has a role in the pathogenesis of all types of PK because an over-expression of this gene has been demonstrated in these conditions through immunohistochemical studies using immunoperoxidase-stained antibody directed against the p53 protein (5, 6). Malignancy can occur after p53 gene inactivation resulting from the mutation and/or a loss of function.

Unrepaired ultraviolet (UV)-induced DNA lesions are directly responsible for p53 mutations in human BCCs and SCCs in a case review (9). However, PK-derived malignant lesions seem to have an increased occurrence in non-exposed skin, correlating with the results of a study in which no relation was found between UV exposure and the increased expression pattern of p53. Despite this, one of the consistently described risk factors for malignancy in PK is sun exposure. Other predisposing factors include exposure to ionizing radiation, the presence of extensive lesions, long duration of the lesion, and immunosuppression (9).

Similar to cutaneous SCC unrelated to PK, the majority of SCCs developing within the lesions of PK are successfully treated with local therapy – a wide surgical excision. However, several cases of metastatic SCC arising in the setting of PK have been reported (10). Therefore, close monitoring of patients should be conducted so that potential recurrent malignancies could be treated on time (9). In our case, the regular follow-up of our patient has shown that the wide surgical excision proved to be the first line of treatment.

As lymph node involvement by cSCC increases the risk of recurrence and mortality, a lymph node ultrasound is highly recommended. Sentinel lymph node biopsy (SLNB) has been used in the patients with cSCC, but there is no conclusive evidence of its prognostic or therapeutic value. There is no standardized follow-up schedule for the patients with cSCC. A close follow-up plan is recommended based on risk assessment of locoregional recurrences, metastatic spread or development of new lesions (11).

The eighth edition of the staging manual of the American Joint Committee on Cancer from 2017 incorporates important changes in the classification of skin cancers. Staging for squamous cell carcinoma considers head and neck tumors (excluding the eyelid) and does not offer solutions for other sites except the vulva, penis, and perianal region (7). Therefore, when staging our patient we used the previous, seventh edition which puts his disease in T3N0M0 category.

In conclusion, linear PK presents an increased oncogenic potential. Its characteristic cornoid lamella appears to occur from a mutant group of abnormal keratinocytes, and the frequency of p53 mutations increases with the severity of the atypia. Linear PK is diagnosed clinically, but due to the characteristic features of the lesions histology is also used to confirm the diagnosis. Linear PK should be considered a pre-malignant condition that requires continuous observation for early detection of malignant transformation in order to avoid the progression of malignancy or the development of metastatic disease.

Abbreviations

PK - Porokeratosis
LP - linear porokeratosis
DSP - disseminated superficial porokeratosis
DSAP - disseminated superficial actinic porokeratosis
MB- classic porokeratosis of Mibelli
PP - punctate porokeratosis
PPPD - porokeratosis plantaris et palmaris disseminata
SCC - squamous cell carcinoma
BCC - basal cell carcinoma
UV - ultraviolet
SLNB - Sentinel lymph node biopsy

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Skvamocelularni karcinom nastao od linearne porokeratoze

Sažetak

Porokeratoza predstavlja poremećaj keratinizacije epiderma za koji su histopatološki karakteristične kornoidne lamele, kao i kolumne tesno poređanih parakeratotičnih ćelija. Etiologija porokeratoze još uvek je nejasna. Opisani su različiti oblici porokeratoze, svaki sa svojom specifičnim svojstvima u smislu morfologije, distribucije i kliničkog toka. Jedan od oblika porokeratoze je linearna porokeratoza, redak poremećaj keratinizacije koja se može razviti u nekoliko vrsta maligniteta epiderma, a najčešći od njih je skvamocelularni karcinom. Prikaz slučaja. U radu je opisan slučaj 54-godišnjeg muškarca sa bezbolnom ulceracijom na levoj potkolenici uzrokovanom skvamocelularnim karcinomom nastalim na terenu dugogodišnje linearne porokeratoze. Lečenje je uključivalo široku eksciziju tumora sa rekonstrukcijom zahvaćenog regiona. Takođe, propisan je acitretin za terapiju porokeratoze. Dosadašnjim praćenjem našeg pacijenta nije pokazan nastanak novih malignih lezija nakon hirurške ekscizije. Zaključak. Uzevši u obzir da linearna porokeratoza pokazuje onkogeni potencijal i da se u velikom broju slučajeva može razviti neki od oblika maligniteta, najčešće skvamocelularni karcinom, redovno detaljno praćenje pacijenata radi ranog otkrivanja maligne transformacije, a samim tim i spečavanje dalje progresije bolesti, jeste imperativ.

Ključne reči: Skvamocelularni karcinom kože; Porokeratoza; Kožne neoplazme; Dermatoze nogu; Geni, p53; Dermatološke hirurške metode; Prikazi slučajeva

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DERMOSCOPY OF THE MONTH
Nevi with Site-Related Atypia

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Abstract

The term "nevi of special sites" refers to melanocytic nevi of specific anatomic locations including the breast, axillae, umbilicus, genitalia, flexural areas, acral surfaces, ear, scalp and the conjunctiva. Nevi from these anatomic sites display sometimes dermoscopic and histological features of melanoma, resulting in unnecessarily high rates of excisions and re-excisions. Some authors have categorized nevi excised in the axillary, breast, umbilical and perineal areas as the nevi of the milk line. Two patients, a 32-year-old female and 23-year-old male with breast and periumbilical pigmented lesions, presented to our Department during 2017. Dermoscopy revealed features that were highly specific for melanoma. Excisional biopsies were done and histopathology revealed benign nevi with present site-related atypia. Irregular blotches, non-uniform radial streaks, blue-gray veil, and regression are the most specific features of melanoma of the breast and flexural areas. Excision is always recommended in pigmented lesions on the breast and flexural areas, which exhibit these features. However, larger studies are needed to define specific criteria required to distinguish special-site nevi from melanoma.

Key words: Nevus, Pigmented; Skin Neoplasms; Breast; Umbilicus; Dermoscopy; Melanoma; Case Reports; Histology

Introduction

The term "nevi of special sites" refers to melanocytic nevi of specific anatomic locations including the breast, axillae, umbilicus, genitalia, flexural areas, acral surfaces, ear, scalp and the conjunctiva. Nevi from these anatomic sites display sometimes dermoscopic and histological features of melanoma, resulting in unnecessarily high rates of excisions and re-excisions (1). Breast nevi have been reported to have significantly higher levels of histologic atypia than nevi from other sites (2). Excision of such lesions from the breast and chest area in women can lead to poor cosmetic or functional results (3). Umbilical nevi have been described as a form of flexural nevi, which have been reported to have more significant atypia and prominent fibrosis (4). Some authors have categorized nevi excised in the axillary, breast, umbilical and perineal areas as the nevi of the milk line (5). Dermoscopy is the most useful diagnostic

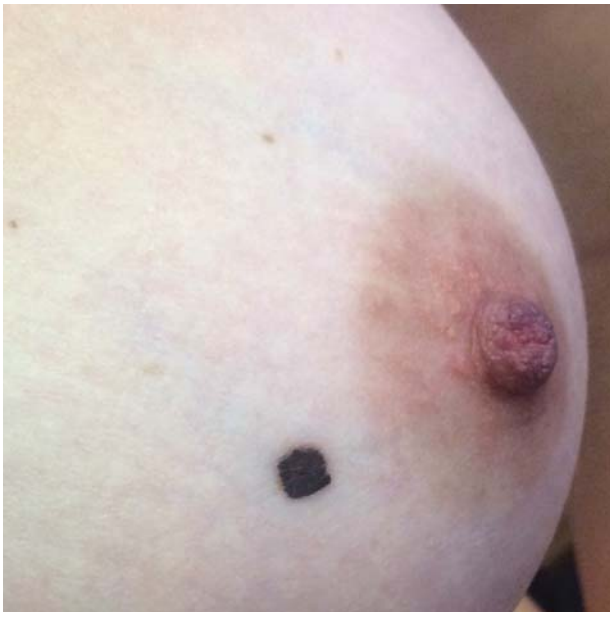

Figure 1. Slightly elevated brownish papule with irregular border on the breast

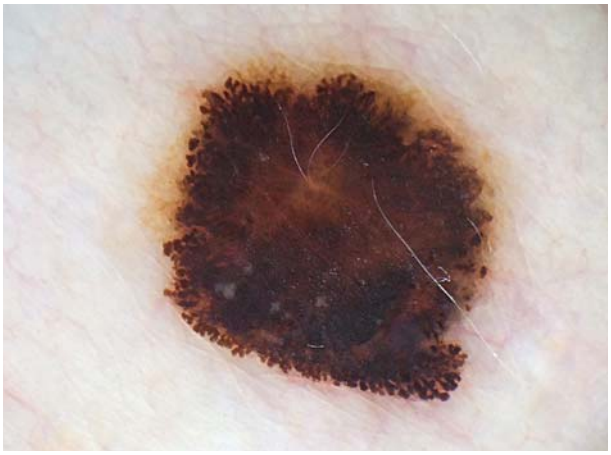

Figure 2. Dermoscopy of the pigmented lesion on the breast: atypical pigment network with irregular globules, pseudopods and radial streaming and multiple blue-gray dots at the periphery of the lesion

method for visualizing morphologic structures beyond the epidermis (3).

Case Reports

Case 1

A 32-year-old woman presented to our Department in May 2017 with a pigmented lesion on her left breast. She had noticed an asymptomatic small brownish-black papule 9x4 mm in diameter that did not change in the size or color over the previous period of more than 5 years. The patient reported negative family history of skin cancer. The physical examination revealed a round, slightly elevated brownish papule with irregular border which was homogenous in color to the naked eye (Figure 1). The regional lymph nodes were not palpable. Dermoscopy revealed atypical pigment network with irregular globules, pseudopods and radial streaming and multiple blue-gray dots at the periphery of the lesion (Figure 2). The excision of the lesion was recommended because of high suspicion for superficial spreading melanoma. The histological examination of the excisional biopsy showed large, rounded, coalescing, pigmented junctional melanocytic nests, melanocytes without nuclear polymorphism and with no mitotic activity (6). The histologic finding was specific for junctional nevus with the present site-related atypia (Figure 3).

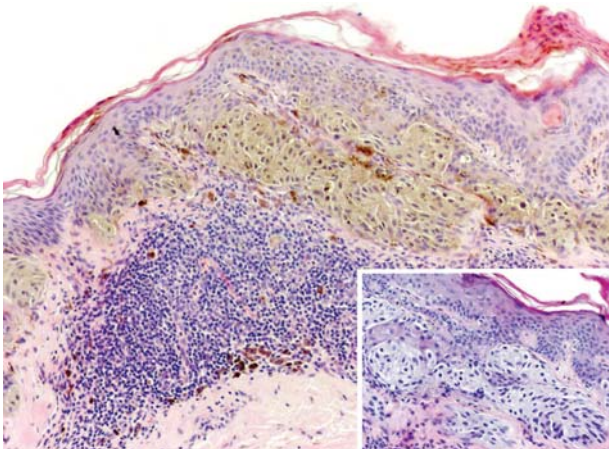

Figure 3. Site-related atypia in junctional nevus with large, confluent pigmented nests and band-like lymphocytic infiltrate; no increase in nuclear cytoplasmic ratio, no prominent nucleoli and no mitotic figures are evident at higher power magnification (inset) (hematoxylin-eosin, original magnification 100x, hematoxylin-eosin with melanin bleaching, 200x (inset)

Case 2

A 23 year old man presented to our Department in June 2017 with a periumbilical pigmented lesion. He had noticed an asymptomatic small brown papule about 4 years before. The papule enlarged rapidly during the first year after it had appeared. The patient reported that his father had melanoma. The physical

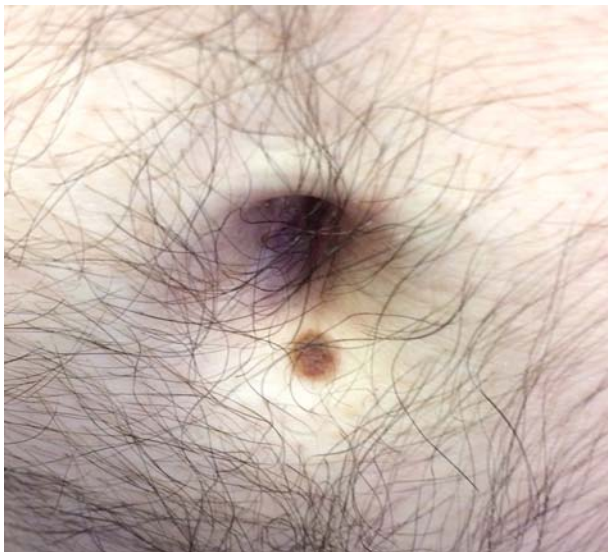

Figure 4. Periumbilical pigmented lesion

examination revealed round, slightly elevated brown papule, 13 x 5 mm in size (Figure 4). Dermoscopy showed an atypical pigment network with irregular globules and pseudopods at the periphery of the lesion (Figure 5). The leading diagnosis was dysplastic nevus, the possibility of melanoma was considered because of the patient's positive family history and the lesion was excised. Histopathology revealed a compound nevus with larger, slightly irregular and focally confluent junctional nests, and lamellar fibrosis extending into dermis, entrapping some small dermal nests (7) (Figure 6).

Discussion

Nevi of special sites have distinct dermoscopic and histological features that may raise concern for melanoma (8).

The breast nevus in our first case exhibited an atypical pigment network with irregular globules, pseudopods and radial streaming with multiple regression structures (blue-gray dots) at the periphery of the lesion. Dermoscopy of the periumbilical lesion in the second case showed an atypical pigment network with irregular globules and pseudopods at the periphery of the lesion.

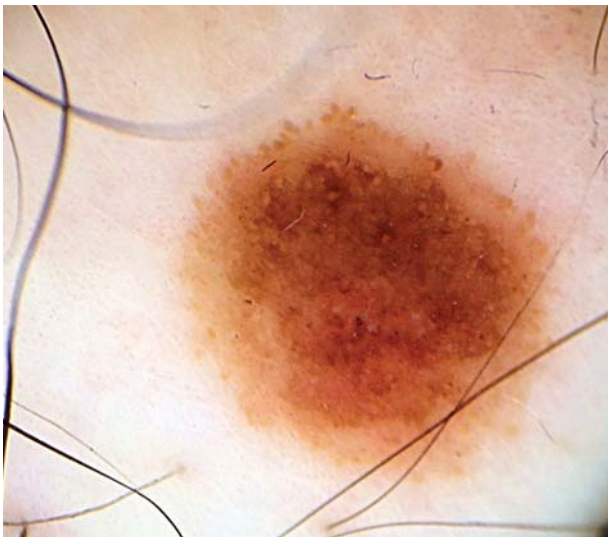

Figure 5. Dermoscopy of the periumbilical pigmented lesion: atypical pigment network with irregular globules and pseudopods at the periphery of the lesion

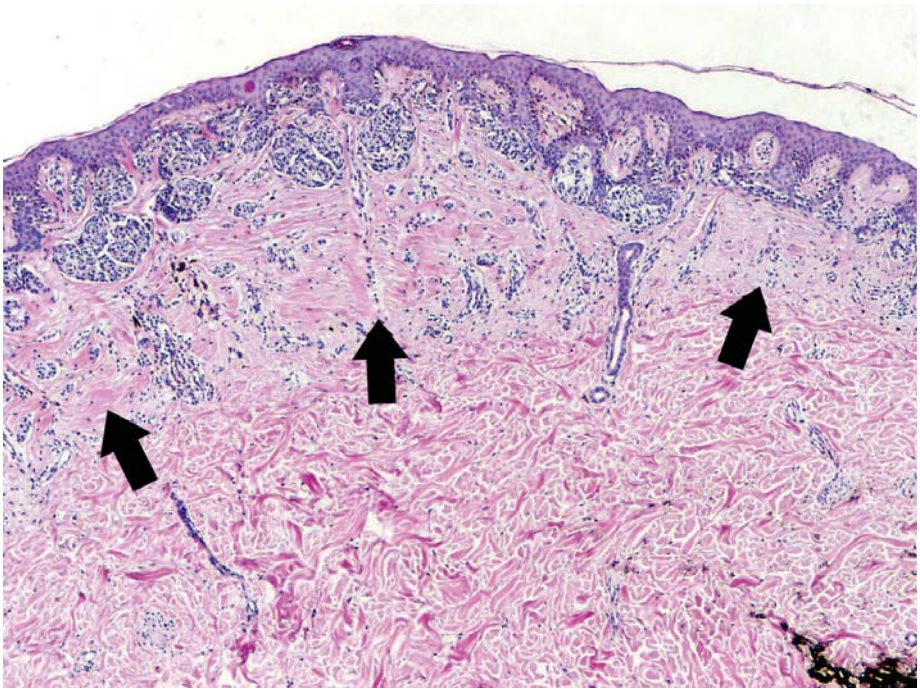

Figure 6. Site-related atypia in umbilical nevus - compound nevus with larger, slightly irregular and focally confluent juntional nests, and lamellar fibrosis extending into dermis (arrows), entrapping some small dermal nests (hematoxylin-eosin, original magnification 40x)

There are only a few case reports describing dermoscopic features of flexural nevi, including the nevi form the umbilical area. Some authors have categorized nevi in the axillary, breast, umbilical and perineal areas as the nevi of the milk line. The only published retrospective study of the dermoscopic features of 104 nevi and 13 melanomas from the breast and chest, reported by Merkel et al., found that the atypical pigment network and irregular dots and globules were more common than regular distributions of these features, although there was no statistically significant association between these patterns and diagnosis (3). This is in contrast to studies that did not take into consideration specific anatomic locations, in which atypical pigment network and irregular dots and globules were highly specific for melanoma (9, 10). Dermoscopic criteria that were highly specific for melanoma of the breast included asymmetric blotches, non-uniform radial streaks, blue-white veil, and regression-like structures, which was not the case in our patient with the breast nevus. Melanomas were significantly larger (median 7 mm,) than nevi (median 5 mm). The majority of women have not reported any evolution in the lesion which is in accordance with our first case (3).

Histologically, breast nevi often have large coalescing junctional melanocytic nests, scattered, irregular intra-epidermal melanocytes above the basal layer, larger melanocytes with some atypia and dermal fibroplasia (1, 2). Rongioletti et al. have reported that breast nevi exhibit more atypical features than nevi from other sites. In particular, breast nevi showed higher tendency to have intra-epidermal melanocytes above the basal layer, atypical cytologic features, and papillary fibroplasia (2).

Rongioletti et al. who had examined 40 flexural nevi including 13 cases taken from the umbilicus, found that more than a half of these flexural nevi displayed a nested and dyshesive pattern, which was also the case with our patient (4).

Conclusion

Irregular blotches, non-uniform radial streaks, blue-gray veil, and regression are the most specific features of melanoma of the breast and flexural areas. Excision is always recommended in pigmented lesions on the breast and flexural areas, which exhibit these features. However, larger studies are needed to define specific criteria required to distinguish special-site nevi from melanoma. It is important to achieve the balance between the careful surveillance of lesions for any clinical or dermoscopic atypia and the prevention of unnecessary excisions.

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Dermoskopske i histološke karakteristike nevusa sa „*site related atypia*”

Sažetak

Uvod. Nevusi posebnih anatomskih lokalizacija predstavljaju melanocitne nevuse koji se nalaze na grudima, aksilama, pregibima, genitalijama, umbilikusu, ušima, poglavini i konjuktivi. U određenim slučajevima, ovakvi nevusi pokazuju dermoskopske i histološke karakteristike melanoma, što rezultuje nepotrebnim ekscizijama i reekscizijama. **Prikazi slučaja**. Prikazujemo dva slučaja: žena od 32 godine sa pigmentnom lezijom na levoj dojci i muškarac od 23 godine, sa pigmentnom lezijom priumbilikalne regije koji su ambulantno pregledani u Klinici za dermatovenerologiju VMA tokom 2017. godine. Učinjena je dermoskopija obe pigmentne promene koja je pokazala karakteristike visokospecifične za melanom. Učinjena je ekscizija ovih promena i uzorci su poslati na patohistološku analizu. Patohistološki nalaz ovih pigmentnih promena je odgovarao benignim melanocitnim nevusima sa *site related atypia*-om. **Diskusija**. Nevusi posebnih anatomskih lokalizacija pokazuju dermoskopske i histopatološke karakteristike koje mogu biti visokospecifične za melanom. U jedinoj do sada objavljenoj retrospektivnoj studiji (Merkel et al.) koja se bavila dermoskopskim karakteristikama melanocitnih nevusa i melanoma mamarne regije, utvrđeno je mnogo češće prisustvo dermoskopskih karakteristika specifičnih za melanom kod benignih melanocitnih nevusa ove regije. Takođe, nevusi posebnih anatomskih lokalizacija mnogo češće imaju atipične patohistološke odlike u odnosu na nevuse drugih lokalizacija. **Zaključak.** U slučaju pigmentnih promena sa posebnom anatomskom lokalizacijom (dojke, pregibi), koje pokazuju dermoskopske karakteristike visokospecifične za melanom, uvek je indikovana ekscizija. Neophodne su veće studije koje bi utvrdile jasne dermoskopske kriterijume za razlikovanje melanocitnih nevusa posebnih lokalizacija od melanoma, kako bi se sprečile nepotrebne ekscizije.

Ključne reči: Pigmentni nevus; Kožne neoplazme; Dojka; Umbilikus; Dermoskopija; Melanom; Prikazi slučajeva; Histologija

Report on the 20th Congress of the Serbian Association of Dermatovenereologists

The 20th Congress of the Serbian Association of Dermatovenereologists (SADV) with the international participation was held in Belgrade from the 18th to 20th of May 2017. Professor Željko Mijušković was the Congress President and Professor Lidija Kandolf Sekulović was the President of the Scientific Committee.

There were 435 participants from 20 countries at the Congress. During the three days of the Congress, 29 invited speakers from Europe, Israel and USA and 10 invited speakers from Serbia presented some of the latest developments and systematic reviews in dermato-oncology, autoimmune bullous diseases, inflammatory dermatoses and aesthetic dermatology.

On the day 1, the focus was on dermatologic oncology, a fast developing field of dermatology. The scientific programme started in the morning on the 18th of May with *Euromelanoma session* during which Matilda Bylaitė-Bučinskienė (Lithuania), Larisa Stojanović (Slovenia) and Lidija Kandolf Sekulović (Serbia) presented the achievements of Euromelanoma campaigns in their respective countries. Dušan Škiljević (Serbia) communicated on the knowledge and attitudes of adolescents concerning UV protection, Ana-Maria Forsea (Romania) presented the results from Eurodermoscopy study, and Veronique del Marmol (Belgium) concluded the session with the presentation of the future of the Euromelanoma campaign (Figure 1). *Dermoscopy session* was a gathering of the leading dermatologists in this field. Iris Zalaudek (Austria) (Figure 2), the current president of the International Society of Dermoscopy, Aimilios Lallas (Greece), the current secretary of the International Society of Dermoscopy, Harald Kittler (Austria) and Danica Tiodorović (Serbia), presented an update in dermoscopy. *Treatment of metastatic melanoma* was the last session during which the world recognized experts in the field of advanced melanoma Sanjiv Agarwala (USA),

Figure 1. Euromelanoma session participants (from left to right): Željko Mijušković, Larisa Stojanović, Ana-Maria Forsea, Lidija Kandolf Sekulović, Veronique del Marmol, Matilda Bylaitė-Bučinskienė and Dušan Škiljević

Figure 2. Prof. Iris Zalaudek delivering a lecture at the dermoscopy session

Figure 3. Fruitful discussion at the interactive case discussion session (from left to right): Janja Ocvirk, Dirk Schadendorf, Axel Hauschild and Sanjiv Agarwala

Axel Hauschild (Germany), Dirk Schadendorf (Germany) and Gal Markel (Israel), presented the newest clinical studies and results of adjuvant treatment, immunotherapy and targeted therapy of melanoma. In the second part of this session, Davorin Herceg (Croatia), Janja Ocvirk (Slovenia), Lidija Kandolf Sekulović (Serbia), Dobrica Nerić (Serbia) and Željko Mijušković (Serbia) presented interesting clinical cases of metastatic melanoma followed by a fruitful discussion held by the experts and the exchange of experience from the practice (Figure 3).

Figure 4. Inflammatory dermatoses session (from left to right): Angelo Valerio Marzano, Željko Mijušković, Larisa Prpić Massari and Ljubomir Novaković

"Inflammaton dermatoses" was the first plenary session in the second day of the Congress. Angelo Valerio Marzano (Italy) opened the session with a paper "Autoinflammatory diseases: a dermatological perspective". Larisa Prpić-Massari (Croatia), Željko Mijušković (Serbia) and Ljubomir Novaković (United Kingdom) presented their experience in biological therapy of psoriasis, personalized

Figure 5. Opening ceremony, Belgrade City Hall

treatment of psoriasis and phototherapy in psoriasis (Figure 4).

During the next plenary session "Autoimmune bullous diseases", Detlef Zillikens (Germany) and Branka Marinović (Croatia) revealed new insights into diagnosis and management of pemphigoid diseases and pemphigus. Mirjana Milinković Srećković (Serbia) reported on the incidence of autoimmune bullous diseases and Gjorgi Gocev (Macedonia) presented clinicopathological characteristics of pemphigus.

In the afternoon, the diagnosis and treatment of skin cancer and cutaneous lymphoma were the main topics. Michael Weichenthal (Germany), Gregor Jemec (Denmark), Aleksandar Sekulić (USA) and Caius Silviu Solovan (Romania) presented an update and emphasized the new results in diagnosis and treatment of cutaneous lymphomas, basal cell carcinoma and primary mucosal melanoma. The third and last Congress day started with the plenary session "Inflammatory dermatoses". Miloš Nikolić (Serbia) presented the update on Clinical and pathological spectrum of SCLE and SLE, Asja Prohić (Bosnia and Herzegovina) talked about Malassezia yeasts in skin diseases, Dušan Buchvald (Slovakia) reported on Allergy testing in atopic dermatitis and Đuka Ninković-Baroš (Bosnia and Herzegovina) presented a lecture on "Autoimmune chronic urticaria"

Within the aesthetic dermatology plenary session, topics like rosacea, cosmetic dermatitis, sclerotherapy for leg veins and contraindications and complications in aesthetic dermatology were presented by Snežana Minić (Serbia), Marina Jovanović (Serbia), Suzana

Први југословенски конгрес стручњака за кожне и полне болести

Вече Словенског Друштва Београд I.

Figure 6. Politika, December 18, 1927

Завршни дан конгреса југословенских стручњака за кожне болести

Унапређења у војсци

Figure 7. Politika, December 19, 1927

Figure 8. The first lifetime achievement award recipient: prof. Danilo Stevanović

Nikolovska (Macedonia) and Hana Zelenkova (Slovakia).

During the last plenary session of the Congress, Mateja Dolenc-Voljč (Slovenia) communicated on demodicosis, Milan Matić (Serbia) presented the paper on Biofilms in chronic wounds and Zoran Golušin (Serbia) presented the association of syphilis and HIV infection.

Besides plenary lectures, 18 free communications and 18 case reports were presented. Mirjana Gajić-Veljić (Serbia) received an award for the best free communication presentation and Jovan Lalošević (Serbia) received an award for the best case report presentation at the Congress.

The opening ceremony of the Congress was organized at the Belgrade City Hall on the 18th of May, with the guided tour through Serbian history represented in this recently renovated and one of the most beautiful historical buildings in Belgrade (Figure 5). At the beginning of the ceremony, the film "History of Dermatovenereology in Serbia" reminded us of the pioneers of modern dermatology in Serbia. We have celebrated the 90th anniversary of our Association: the first Congress of Yugoslav dermatologists was held in Belgrade on the 17th and 18th of December 1927 (Figure 6 and Figure 7). For this occasion and for the first time in its history, the SADV awarded a lifetime achievement award and the first winner of this award was Professor Danilo Stevanovic, internationally recognized derma-

Figure 9. SADV Honorary members with the hosts (from left to right): Dirk Schadendorf, Gal Markel, Sanjiv Agarwala, Željko Mijušković, Detlef Zillikens, Michael Weichenthal, Aleksandar Sekulić, Tatjana Radević, Ljubomir Novaković, Lidija Kandolf Sekulović and Axel Hauschild

tologist, who put the Serbian dermatology on the world map (Figure 8). Professor Danilo Stevanović was born in 1927. He graduated from the Medical School, University of Belgrade in 1953. Since then, he worked at the Institute of Dermatology and Venereology of the Clinical Centre of Serbia as a Head of the Department. From 1955 to 1957 he attended the University of Cambridge in United Kingdom, where he successfully defended the thesis entitled "Pathological Effects of Actinic Radiation on the Human Skin" and received his PhD degree in dermatovenereology. He published more than 200 articles in high-ranking international journals and described four new dermatoses.

After the welcome speech, the greeting speeches were given by the Secretary General of the European Academy of Dermatology and Venerology - Prof. Branka Marinovic (Croatia), and EADV Executive Committee member - Prof. Matilda Bylaitė-Bučinskienė (Lithuania), European coordinator of Euromelanoma skin cancer prevention campaign - Prof. Veronique del Marmol, (Belgium) and European Association of Dermato-Oncology Executive Board member Prof. Axel Hauschild. Traditionally, during the opening ceremony the new honorary members of SADV were proclaimed: Aimilios Lallas (Greece), Aleksandar Sekulić (USA), Ana-Maria Forsea (Romania), Angelo Valerio Marzano (Italy), Asja Prohić (Bosnia and Herzegovina), Detlef Zillikens (Germany), Dirk Schadendorf (Germany), Gregor Jemec (Denmark), Harald Kittler (Austria), Veronique del Marmol (Bel-

Figure 10. Congress faculty members at the welcome cocktail party (from left to right): Branka Marinović, Matilda Bylaitė-Bučinskienė, Aimilios Lallas and Danica Tiodorović

Figure 11. Congress faculty members at the City hall (from left to right): Milos Nikolic, Dusan Skiljevic, Mirjana Gajic-Veljic, Angelo Valerio Marzano, Lidija Kandolf Sekulović, Željko Mijušković

gium), Michael Weichenthal (Germany) and Mateja Dolenc Voljč (Slovenia) (Figure 9 and Figure 10). The exquisite performance of a capella Viva Vox choir given at the end of the opening ceremony made this event a memorable one. On the Presidentćs Dinner was organised for the Congress faculty at the one for the Congress Faculty at one of the popular Belgrade venues, Top of the Hub at the Usce Tower with a stunning view at Belgrade and the confluence of Danube and Sava River.

This Congress, with its rich program gave an excellent opportunity to make new and strengthen old friendships and cooperation among the dermatologists not only from Serbia, but from the region and Europe as well.

The next congress of the Serbian Association of Dermatology and Venereology will be held in 2021.

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A Report on the 26th Congress of the European Academy of Dermatology and Venereology, Geneva 2017

Geneva, a beautiful city located under the Swiss Alps at Geneva Lake, famous for being a host for many international humanitarian, political and business associations, was also the host for the 26th Congress of the European Academy of Dermatology and Venereology, held from the 13th to 17th of September, 2017.

At the same time, it was a marvelous occasion to celebrate the 30th birthday of the European Academy of Dermatology and Venereology (EADV) and there would not have been a better location for this event than Switzerland, the home of the EADV Headquarters.

The scientific programme provided a great opportunity to continue medical education and professional development through a multiplicity of finely-tuned sessions. The intensive 4-day program included 181 stimulating sessions.

The newly-structured thematic format of the sessions for different levels of knowledge - Training and Educational Forum, Review and Updates, and Expert Forum, as well as the standard Plenary Lectures, Free Communications, Clinical Cases from around Europe, Oral e-Poster presentations, Spotlights, all day Workshops, including *Aesthetic Sunday*, and Late-breaking News, met the expectations of the vast majority of the participants.

The participation of Serbian dermatovenereologists was well appreciated. The invited speakers from Serbia at the 26th EADV Congress were Prof. Miloš Nikolić and Prof. Mirjana Milinković. The oral presentations were the following:

Figure 1. Dr. Jovan Lalošević presenting a case report at the "Clinical cases from around Europe"

Prof. Miloš Nikolić was a session chair for the "Autoimmune and Autoinflammatory Diseases" and he delivered a lecture on "Clinical and Pathological Spectrum of SCLE and SLE". Prof. Nikolić was also a co-chair at the Plenary Lectures held on September 14th.

Figure 2. Prof. Miloš Nikolić, Assoc.Prof. Jelena Stojković-Filipović, Dr. Jovan Lalošević at the Exhibition hall at the Palexpo (Congress center)

Figure 3. Prof. Željko Mijušković, Prof. Lidija Kandolf-Sekulović, Prof. Ljiljana Medenica and Assoc. Prof. Dušan Škiljević at the dinner party hosted by the Congress President

Prof. Mirjana Milinković was a session chair for the: "Vasculitis, Vasculopathies and Treatment" and she delivered a lecture on "Peripheral Purpura: When is it Life-threatening?"

Assoc. Prof. Jelena Stojković-Filipović presented her scientific work "Expression of Minichromosome Maintenance Proteins in Keratinocytic Intraepidermal Neoplasia and Invasive Squamous Cell carcinoma of the Skin" at Free Communications session.

Prof. Lidija Kandolf-Sekulović delivered a lecture on "What to Know about the 8th Edition of the AJCC Staging of melanoma" at the Subspecialty Meeting Euromelanoma / EADO - European Association of Dermato Oncology.

Dr. Jovan Lalošević presented a case report "Orofacial granulomatosis in a 12-year-old girl successfully treated with intravenous pulse corticosteroid therapy and chloroquine" at the session Clinical cases from around Europe.

There were 1 e-Poster from Serbia, presented by Dušan Škiljević and Jelena Perić.

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FORTHCOMING EVENTS

Dermatology and Venereology Events 2017/2018

DATE	MEETINGS, CONGRESSES, SYMPOSIA	ABSTRACT SUBMISSION DEADLINE	MORE INFORMATION AT
21-23 January, 2018	Updates in Wound Technology Paris, France	18 September, 2017	www.cicatrisations2018.org
7-9 February, 2018	7th Conference of the European Hidradenitis Suppurativa Foundation Roterdam, The Netherlands	16 March, 2017	www.ehsf2018.com
	Meeting of the Serbian Medical Society's Section of Dermatology and Venereology, Clinical Center of Vojvodina	No abstract submission	www.sld.org.rs
16-20 February, 2018	AAD Annual Meeting, San Diego, California, United States	1 September, 2017	www.aad.org
14-17 March, 2018	3rd International Dermatology and Cosmetology Congress (INDERCOS 2018) Istanbul, Turkey	4 February, 2018	www.indercos.org
15-17 March, 2018	1st World Congress of Trichoscopy Warsaw, Poland	30 January, 2018	www.hairnails2018.com
13-14 April, 2018	Specialist Course, Cryosurgery, Barcelona Spain	15 January, 2018	www.eadv.org
13 April, 2018	Meeting of the Serbian Medical Society's Section of Dermatology and Venereology, Military Medical Academy, Belgrade, Serbia	No abstract submission	www.sld.org.rs
26-29 April, 2018	7th Congress of FUE Europe- European Organization of Hair Restoration Professionals, Malaga, Spain		www.fue-europe.org
3-6 May, 2018	15th EADV Spring Symposium, Budva Montenegro	23 November, 2017	www.eadvbudva2018.org
19-22 May, 2018	Australasian College of Dermatology, 51st Annual Scientific Meeting, Gold Coast, Queensland, Australia	3 November, 2017	www.acdasm.com
7-9 June, 2018	18th ESPD Anuual Meeting, London, United Kingdom	15 January, 2018	www.espd2018.com
7-8 June, 2018	2nd International Keloid Symposium, Rome, Italy	30 April, 2018	www.keloidsymposium.com
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	8 March, 2018	www.ifpaworldconference.com
27-30 June, 2018	2018 IUSTI World& European Congress, Dublin, Ireland	15 March, 2018	www.iustidublin2018.com

28 June-1 July, 2018	13th World Congress of the International Academy of Cosmetic Dermatology (IACD), Dubrovnik, Croatia	10 March, 2018	www.wcocddu-brovnik2018.org
5-6 September, 2018	Bradykinin Symposium 2018, Berlin, Germany	30 June, 2018	www.bradykinin-symposi-um.de
7 September, 2018	Angioedema school, Berlin, Germany	30 June, 2018	www.bradykinin-symposi-um.de
12-16 September, 2018	27th EADV Congress, Paris France	13 March, 2018	www.eadvparis2018.org
4-6 October, 2018	ESTRO School, Multidisciplinary management of non-melanoma skin cancer, Brussels, Belgium		www.estro.org
11-13 October, 2018	22nd BDD, Belgrade, Serbia	1 June, 2018	www.udvs. org
29-30 October, 2018	6th International Conference on HIV/AIDS, STDs and STIs, San Francisci, USA		www.hiv-aids-std.confer-enceseries.com
6-9 November 2018	14th Congress of the EADO, Barcelona, Spain	10 September, 2018	www.congresseado-melanomacenters2018.com
9-11 November, 2018	EADV Course- Skin Cancer, Trieste, Italy		www.eadv.org
14-17 November 2018	CILAD 2018, Sao Paulo, Brasil	10 September, 2018	www.cilad2018.com
5-6 December, 2018	GA2LEN Global Urticaria Forum (GUF 2018), Berlin, Germany	10 September, 2018	www.globalurticariaforum.org

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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 sho uld 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/.

1.4. Cover Letter

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.

2. Tables and illustrations

Tables should capture information concisely

and precisely. Including data in tables, rather than in the text, reduces the length of the article itself.

– Submit tables in separate files, not included in the manuscript. Tables are to be double spaced and numbered sequentially, with Arabic numbers (Table 1, Table 2, etc.), in order of text citation. Each column, including the first, must have a heading. Provide a brief title for each table. Put all explanatory matter in footnotes, including any nonstandard abbreviations used in the table.

– Figures should be submitted in a separate file, not included in the manuscript document. Cite figures consecutively, as they appear in the text, with Arabic numbers (Fig. 1, Fig. 2, Fig. 3, etc.). Each figure must be assigned a title, as well as a legend. Legends should appear on a separate page, not with each figure. The Legend Page is to be numbered in sequence after the last page of the references list. Figures should be professionally drawn, as sharp black-and-white or color photographs. If photographs of persons are used, either the subjects must not be identifiable, or their pictures must be accompanied by written permission to use them.

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.

4. Author's Statements

– Conflict of Interest

To ensure fair and objective decision-making, authors must declare any associations that pose a conflict of interest (financial, personal or professional) in connection with evaluated manuscripts. If there are no conflicts of interest, the following statement should be included *before the References* (or at the end of the *Acknowledgments sectio*n):

Conflict of interest: Authors state no conflict of interest.

– Informed Consent

The protection of privacy is a legal right that must not be breached without individual informed consent. In cases where the identification of personal information is necessary for scientific reasons, authors should obtain full documentation of informed consent, including written permission from the patient prior to inclusion in the study.

The following (or similar) statement should be included *in the Methods section*:

Informed consent: Informed consent has been obtained from all individuals included in this study.

– Authorization for the use of human subjects

Manuscripts containing information related to human use should clearly state that the research has complied with all relevant national regulations and institutional policies and has been approved by the authors' institutional review board or equivalent committee. Copies of the guidelines and policy statements must be available for review by the Managing Editor if necessary. The editors reserve the right to seek additional information or guidance from reviewers on any cases in which concerns arise. All investigation with human subjects must have been conducted by following the tenets of the Helsinki Declaration, what is more authors must identify the committee or review board approving the experiments, and provide a statement indicating approval of the research. The following (or similar) statement should be included *in the Methods section*:

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

– Authorization for the Use of Experimental Animals

Manuscripts containing information related to animals use should clearly state that the research has complied with all relevant national regulations and institutional policies and has been approved by the authors' institutional review board or equivalent committee. Copies of the guidelines and policy statements must be available for review by the Managing Editor if necessary. The editors reserve the right to seek additional information or guidance from reviewers on any cases in which concerns arise. The research using animal subjects should be conducted according to the Principles of Laboratory Animal Care and similar documents. For manuscripts reporting experiments on live vertebrates or higher invertebrates, authors must identify the committee approving the experiments, and must confirm that all experiments were performed in accordance with relevant regulations. The following (or similar) statement should be included *in the Methods section*:

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If the manuscript does not contain any study that requires human or animal ethical approval, the following statement should be included in the *Methods section*:

Ethical approval: The conducted research is not related to either human or animals use.

5. Additional Information

Accepted manuscripts are edited and returned to the corresponding author for proof. Then a final version of the manuscript will be requested in a defined period of time. Authors will be notified of acceptance or rejection by email, within approximately 4 weeks after submission.

– Open access: Every article published in the Serbian Journal of Dermatology and Venereology will immediately be accessible on www.udvs.org to everyone at no charge.

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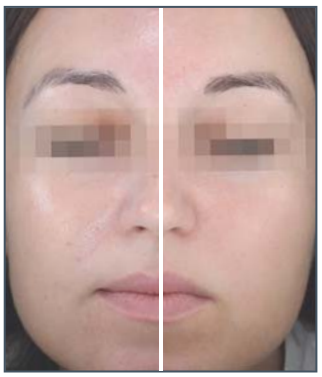

TRENUTNI MATIRAJUĆI EFEKAT[1]

(1) Split-face application of product (right-hand side) and a control sunscreen SPF50+ (left-hand side), clinical photography after 5 min. Example shown, individual results may vary. (2) Product application (n = 1059 patients with acne-prone skin, 50% received acne medication) twice daily for four weeks. Patient and dermatologist assessment. (3) After a two-week treatment period with daily product application, physician's evaluation in patients with acne-prone skin (n = 35).

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