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Case report
Prikaz slučaja
UDK 616.5-002.1-079.4
UDK 616.5-002.1-08:615.357
https://doi.org/10.2298/MPNS2210321K

PITYRIASIS LICHENOIDES ET VARIOLIFORMIS ACUTA – DILEMMAS IN DIAGNOSIS AND CHOICE OF THERAPY – A CASE REPORT

PITYRIASIS LICHENOIDES ET VARIOLIFORMIS ACUTA – DILEME U DIJAGNOZI I IZBORU TERAPIJE – PRIKAZ SLUČAJA

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Summary

Introduction. Pityriasis lichenoides et varioliformis acuta is a rare inflammatory skin disease of unknown etiology and its diagnosis is sometimes established by eliminating diseases that are considered in the differential diagnosis. Given the lack of randomized clinical trials, recommendations for therapy remain based on case reports and case series. **Case Report.** We present a 63-year-old female patient with generalized skin lesions including, papules, papulonecrotic lesions, and atrophic scars accompanied by a subjective feeling of itching that occurred 2 months before admission. The histopathological findings showed a mixed perivascular inflammatory cellular infiltrate and capillary blood vessels with thickened walls in the superficial part of the dermis as signs of vasculitis. The infiltrate was dominated by lymphocytes, neutrophils were admixed, but there were no signs of cellular atypia, which supported the clinical diagnosis of pityriasis lichenoides et varioliformis acuta. Therapy with systemic corticosteroids and doxycycline was applied, which led to the resolution of lesions. **Conclusion.** The authors would like to bring to the readers' attention a rare skin disease, pityriasis lichenoides et varioliformis acuta, point to papulonecrotic tuberculids in differential diagnosis due to similar clinical presentation, remind them of the dilemmas that may arise in case of the described lymphocytic vasculitis based on the findings of histopathological analysis, and highlight the effectiveness of doxycycline and prednisone in the therapy.

Key words: Pityriasis Lichenoides; Skin Diseases; Diagnosis, Differential; Prednisolone; Doxycycline

Sažetak

Uvod. *Pityriasis Lichenoides et Varioliformis Acuta* je retko inflamatorno oboljenje kože nerazjašnjene etiologije čija se dijagnoza ponekad postavlja eliminacinom oboljenja koja diferencijalnodijagnostički dolaze u obzir. S obzirom na nedostatak randomizovanih kliničkih studija, preporuke za terapiju ostaju bazirane na prikazima i serijama slučaja. **Prikaz slučaja.** Prikazujemo bolesnicu starosti 63 godine sa generalizovanim promenama na koži u vidu papula, papulonekrotičnih lezija i atrofičnih ožiljaka praćenih subjektivnim osećajem svraba koje su se javile dva meseca pred hospitalizaciju. Na histopatološkom nalazu su opisani perivaskularno smešten mešoviti zapaljenski infiltrat i kapilarni krvni sudovi zadebljalog zida u superficijalnom delu dermisa kao znaci vaskulitisa. U infiltratu su dominirali limfociti uz prisustvo i neutrofila ali znaci atipije ćelija nisu opisani što je ukazivalo na klinički postavljenu dijagnozu *Pityriasis Lichenoides et Varioliformis Acuta*. Primenjena je terapija sistemskim kortikosteroidima i doksiciklinom što je dovelo do rezolucije promena. **Zaključak.** Autori žele da podsete na *Pityriasis Lichenoides et Varioliformis Acuta* kao retko kožno oboljenje, diferencijalnodijagnostički navedu i papulonekrotične tuberkulide zbog slične kliničke prezentacije, podsete na dilemu koja se može javiti u slučaju opisanog limfocitnog vaskulitisa na nalazu histopatološke analize i navedu efikasnost doksiciklina i prednizona u terapiji.

Ključne reči: Pityriasis Lichenoides; kožne bolesti; diferencijalna dijagnoza; prednizon; doksiciklin

Introduction

Pityriasis lichenoides is an uncommon inflammatory skin disease representing a spectrum of diseases that manifest in two forms: pityriasis lichenoides et varioliformis acuta (PLEVA) and pityriasis lichenoides chronica (PLC). The incidence and prevalence of PLEVA have not been precisely determined; it occurs at all ages, most often in the second and third decade of life, while it is described in children in about 20% of cases [1, 2]. The etiology of the disease is not fully elucidated and attempts are made to explain it by an inflammatory reaction triggered by infectious agents, a secondary inflammatory response to T-cell dyscrasia or hypersensitivity mediated by immune compex, while some argue that it is a T-cell lymphoproliferative disease [1, 3].

Due to the rarity of this disease and a long list of diseases included in the differential diagnosis, establishing the diagnosis is difficult and sometimes it is made by exclusion of diseases by differential diagnosis [4]. Therapy recommendations are often debated because they are based on case reports and case series,

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Abbreviations
PLEVA – pityriasis lichenoides et varioliformis acuta
PLC – pityriasis lichenoides chronica
LyP – lymphomatoid papulosis

primarily due to the self-limiting course of the disease and the consequent lack of randomized clinical trials [1]. The aim of this paper was to point to this rare entity which is often associated with dilemmas in establishing the diagnosis and choice of treatment modality.

Case Report

We hereby present a 63-year-old female patient who was hospitalized due to generalized skin lesions including papules, papulonecrotic lesions, and atrophic scars accompanied by a subjective feeling of itching. The eruptions appeared 2 months before admission, first on the skin of the front abdominal wall, followed by changes on the trunk and lower extremities, and the upper extremities and capillitium. The skin changes occurred in bursts and some resolved with atrophic and varioliform scars. The patient denied occasional medication intake and there was no apparent episode of any infection before the onset of the eruptions. She presented with arterial hypertension and diabetes, which were well controlled.

On admission, the patient was in good general condition, cardiopulmonary compensated and afebrile,

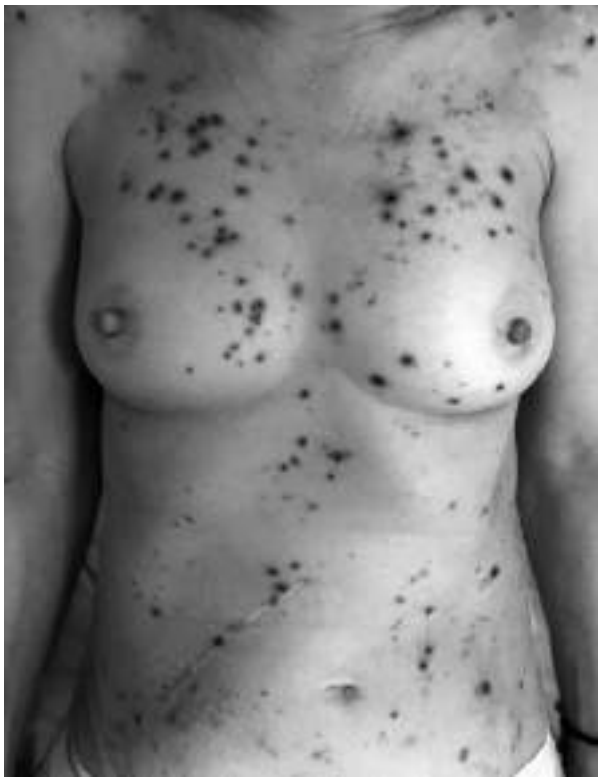

Figure 1. Polymorphic clinical presentation, anterior side of the trunk
Slika 1. *Polimorfna klinička prezentacija, prednja strana trupa*

Figure 2. Skin eruption consisting of livid erythematous papules, some of which are covered with necrotic eschar or central sanguinolent crusts, posterior side of the trunk
Slika 2. *Kožne promene u vidu lividno eritematoznih papula, od kojih su neke prekrivene nekrotičnom esharom ili centralnom sangvinolentnom krustom, zadnja strana trupa*

without adenopathy or other clinical signs on physical examination. Numerous erythematous livid papules with a diameter of several millimetres to 1 cm were present on the trunk and lower extremities, some of which were covered with necrotic eschar or with central sanguinolent crusts **(Figures 1 and 2)**. Individual changes of similar characteristics were present on the skin of the upper extremities and capillitium, while the skin of the face, palms and soles as well as visible mucous membranes were spared. Individual atrophic and varioliform scars up to 1 cm in diameter were registered on the skin of the pretibial area of lower legs, on both sides **(Figure 3)**.

Laboratory tests, including a full blood cell count with differential, markers of inflammation, liver and kidney function tests, urine, serum protein electrophoresis, immunoglobulins G, M and A, C3 and C4 complement components, antinuclear antibodies to primate liver and Hep-2 cells, beta-2 microglobulin, Treponema pallidum serology (venereal disease research laboratory, Treponema pallidum hemagglutination) as well as the QuantiFERON-TB Gold test, were within reference values or negative. X-ray of the lungs and heart as well as ultrasonography of the upper abdomen showed no pathological changes.

The histopathological findings showed a diffusely hyperkeratotic epidermis with flattened rete ridges and focal necrosis of the papillary dermis. The

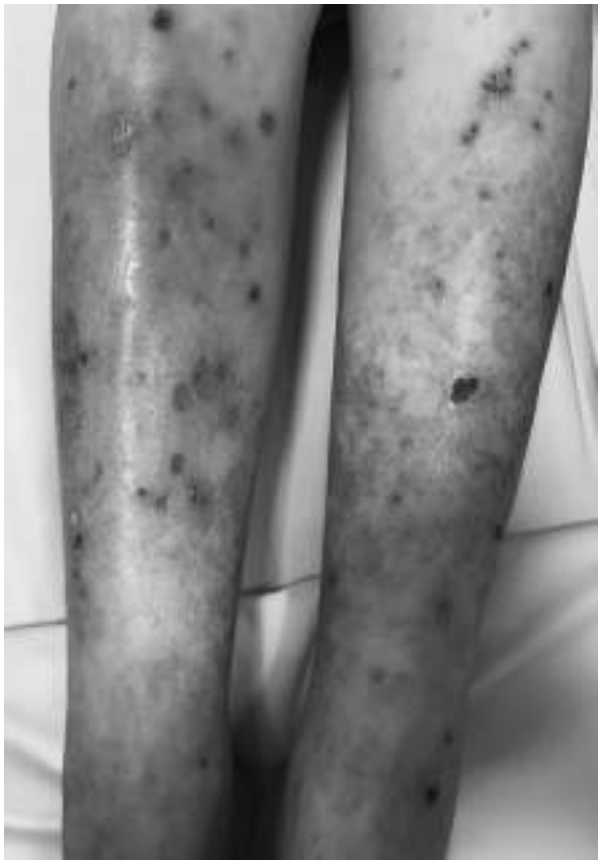

Figure 3. Atrophic and varioliform scars, postinflammatory hyperpigmented macules and ulceronecrotic lesions, pretibial area of lower legs
Slika 3. *Atrofični i varioliformni ožiljci, postinflamatorne hiperpigmentovane makule i ulceronekrotične lezije, pretibijalna regija potkolenica*

epidermis showed ulcerations and crusts on the surface. In addition, both moderately dense mixed perivascular inflammatory cellular infiltrate and capillary blood vessels with thickened walls were described in the superficial part of the dermis as signs of vasculitis. The infiltrate was dominated by lymphocytes, neutrophils were admixed, but there were no signs of cellular atypia, which indicated the clinical diagnosis of PLEVA **(Figure 4)**.

Systemic corticosteroid (oral prednisone at a dose of 0.5 mg/kg), antihistamine and antibiotic therapy (cephalexin) was prescribed based on the antibiogram, considering that Staphylococcus aureus was isolated from the swab of the skin lesions. Upon completion of antibiotic therapy with cephalexin in the duration of 10 days, doxycycline was prescribed at a daily dose of 100 mg for 2 weeks, with further gradual reduction of the dose of corticosteroids for a month until withdrawal, which resulted in regression of skin lesions within 3 months, with post-inflammatory hyperpigmented macules and individual varioliform scars. In addition, the total duration of the disease was 7 months without recurrence in the follow-up period of one year.

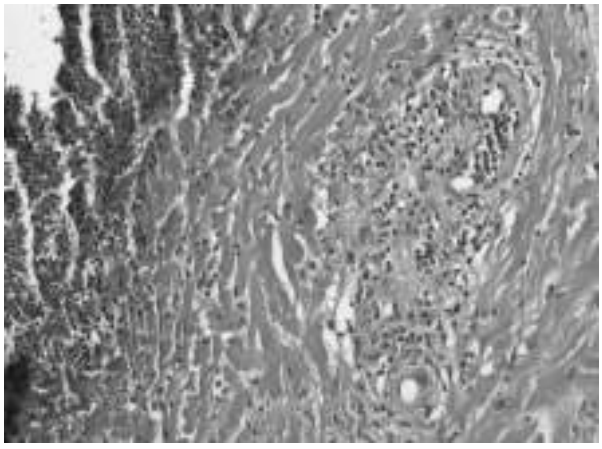

Figure 4. Histopathological finding of the lesion showing necrosis of the epidermis and papillary dermis with ulceration and crust on the surface and mixed perivascular inflammatory cellular infiltrate with signs of vasculitis; The infiltrating cells show no signs of atypia; HE x 200
Slika 4. *Histopatološki nalaz lezije pokazuje nekrozu epidermisa i papilarnog dermisa sa ulceracijom i krustom na površini kao i mešoviti perivaskularno smešten inflamatorni infiltrat sa znacima vaskulitisa. U infiltratu nema znakova atipije ćelija. HE, x 200*

Discussion

Clinical manifestations of PLEVA include eruptions of erythematous macules with rapid progression into inflammatory papules with pityriaziform desquamation. In further progression, the scale thickens and remains present centrally while separating on the periphery of papules that may undergo necrosis with the consequent appearance of centrally located ulcerations or evolve into PLC lesions. It is characterized by recurrent crops of skin lesions and the consequent polymorphic clinical picture, as well as sequelae in the form of post-inflammatory hypo- or hyperpigmented macules and varioliform scars, which was also the case in our patient [5]. The distribution of lesions is most often central in the area of the trunk and flexor surfaces of the proximal extremities, but other types of distribution, such as peripheral or diffuse, may be seen as in our patient, which prompted us to consider other differential diagnoses [1].

The list of diseases included in the differential diagnosis described in the literature is extensive and includes: lymphomatoid papulosis, cutaneous vasculitis, arthropod bite reactions, disseminated herpes simplex virus infection or varicella zoster virus infection, Gianotti-Crosti syndrome, erythema multiforme, pityriasis rosea, psoriasis guttata, secondary syphilis, pityriasis lichenoides-like mycosis fungoides, polymorphic light reaction, lichen planus, exanthematic eruptions to drugs, etc. [4, 6–8]. We included lymphomatoid papulosis (LyP) and cutaneous vasculitis into differential diagnosis, which is in compliance with literature data, but also tuberculosis papulonecrotica cutis, i.e. papulonecrotic tuberculides, which the authors did not notice in the differential diagnosis when reviewing the avail-

able literature on PLEVA. However, a review article from 2022 included PLEVA in the differential diagnosis for papulonecrotic tuberculides, due to a similar clinical presentation [9]. During the diagnostic processing of our patient, a heart and lung X-ray, QuantiFERON-TB Gold test and skin biopsy were performed in order to rule out the granulomatous nature of the disease.

The diagnosis of PLEVA is made based on medical history, physical examination and skin biopsy for histopathological analysis, which is of great use when differentiating it from other skin diseases with similar clinical presentation [10]. The histopathological findings in LyP include a wedge-shaped or perivascular dermal infiltrate of pleomorphic lymphoid cells that resemble Reed Sternberg cells, as well as epidermal necrosis with the presence of ulceration, thus ruling out this disease in our patient. Differentiating PLEVA from LyP is of key importance considering the different prognosis of the disease and the significant risk of malignant transformation of LyP into cutaneous lymphoma. In case of a diagnostic dilemma, immunohistochemical staining is important, which was not necessary in our case. In PLEVA, CD8+ T-cells are dominant, which speaks in favour of the diagnosis, while the presence of atypical CD30+ cells excludes it and indicates LyP [4, 11, 12]. In PLEVA, perivascular and diffuse infiltrates of lymphocytes and histiocytes are described, i.e. superficial perivascular interface dermatitis, which at first resembles lymphocytic vasculitis and may lead to a diagnostic dilemma, also present in our case. However, unlike cutaneous vasculitis, true fibrinoid necrosis of blood vessels is absent in PLEVA [2, 4]. It is important to emphasize the importance of feedback and communication with pathologists in order to establish adequate diagnosis of the disease.

Bearing in mind the unclear etiology of the disease, PLEVA therapy is still a subject of discussion. Given the tendency of the disease towards spontaneous resolution, the evaluation of therapeutic modalities is limited due to the lack of adequate control groups and the impossibility of conducting randomized prospective studies [6]. Recommendations remain based on retrospective studies as well as case reports and case series that generally recommend antibiotics and/or phototherapy as effective therapeutic modalities, with corticosteroids as adjunctive therapy in severe cases of PLEVA [7]. Antibiotics with anti-inflammatory properties, such as tetracycline in adults and erythromycin in children, are most often prescribed until the skin lesions are in complete remission, usually up to 3 months [13, 14]. A review article from 2019 on PLEVA in adults by Bellinato et al., suggested the use of methotrexate or erythromycin with or without topical corticosteroids as the first therapeutic option, but in our case, therapy with doxycycline and systemic corticosteroids resulted in a positive therapeutic response without the need for the use of methotrexate [13]. In refractory cases, in addition to methotrexate, successful therapy with acitretin, dapsone and cyclosporine is described in the literature [15, 16].

Gelmetti et al. assumed that the distribution of lesions is of importance in predicting the course of the disease, and that patients with a diffuse distribution of lesions had the shortest average course of the disease (11.4 months), while those with a peripheral distribution, the longest (31.3 months). In case of patients with the central distribution, it was associated with an intermediate duration of the disease (17.3 months) [17]. These data are not in accordance with some recent publications such as the research conducted by Ersoy-Evans et al. in which the median duration for the diffuse form of the disease was 22 months and 12 months for the central and peripheral forms [18]. In our case of diffuse distribution, complete resolution occurred within 7 months.

Conclusion

In conclusion, we would like to bring to the readers' attention a rare skin disease, pityriasis lichenoides et varioliformis acuta, which is often associated with dilemmas in establishing the diagnosis and deciding on the choice of therapy. The differential diagnosis includes papulonecrotic tuberculides, due to similar clinical manifestations with the diffuse form of pityriasis lichenoides et varioliformis acuta. Also, we wish to point out the dilemma that can occur in the case of described lymphocytic vasculitis when interpreting the findings of histopathological analysis. Unlike in cutaneous vasculitis, there is no true damage to blood vessels with fibrinoid necrosis in pityriasis lichenoides et varioliformis acuta. The use of doxycycline and prednisone was effective in our patient, but spontaneous resolution of the lesions cannot be ruled out either.

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Rad je primljen 8. III 2023.
Recenziran 19. III 2023.
Prihvaćen za štampu 21. III 2023.
BIBLID.0025-8105:(2022):LXXV:9-10:321-325.