

LICHEN PLANUS PIGMENTOSUS INVERSUS – REDAK KLINIČKI ENTITET

LICHEN PLANUS PIGMENTOSUS INVERSUS – A RARE CLINICAL ENTITY

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Sažetak

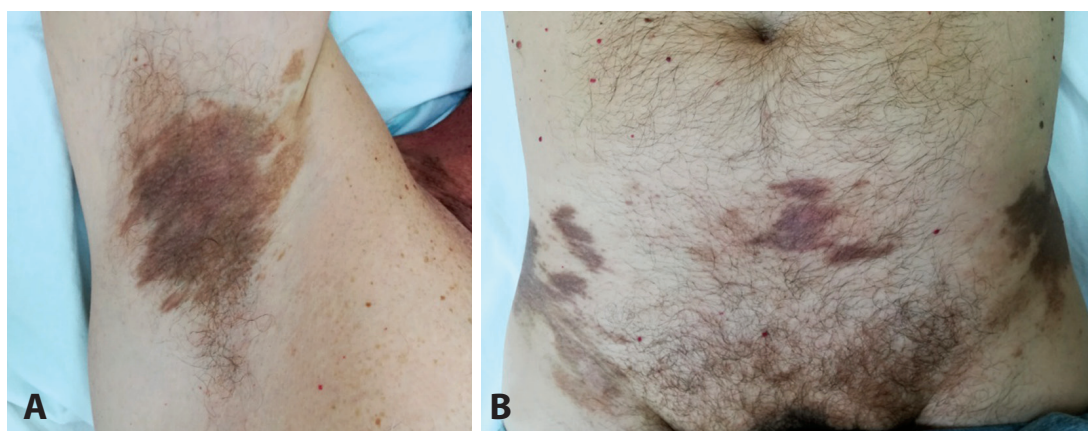
Uvod. Lichen planus pigmentosus inversus je retka forma lichen planus pigmentosus-a, koja se pretežno javlja kod osoba srednjih godina i svetle puti. Za ovu formu su uglavnom karakteristične asimptomatske hiperpigmentacije u intertriginoznim regijama. **Prikaz slučaja.** Predstavljamo pacijenta starosti 56 godina, svetle puti (Fitzpatrick fototip II) kod koga je u toku prethodna četiri meseca došlo do pojave asimptomatske, simetrične hiperpigmentacije u više kožnih pregiba. Fizikalnim pregledom, aksilarno, ingvinalno, supraklavikularno i u abdominalnim prevojima uočeno je više jasno ograničenih makula i plakova ljubičasto-smeđe boje. Histopatološki preparat pokazao je lihenoidne karakteristike sa izraženom inkontinencijom melanina u papilarnom dermu. Dijagnoza lichen planus pigmentosus inversus postavljena je na osnovu korelacije kliničkog i histopatološkog nalaza. Topikalna terapija takrolimusom dovela je do kompletne kliničke regresije. **Zaključak.** Incidencija lichen planus pigmentosus inversus je verovatno potcenjena i treba ga uzeti u obzir u diferencijalnoj dijagnozi hiperpigmentacija lokalizovanih u intertriginoznim regijama. Topikalna primena kalcineurinskih inhibitora može se smatrati dobrom terapijskom opcijom zbog minimalnih neželjenih efekata i odličnih kliničkih rezultata.

Ključne reči: lichen planus; hiperpigmentacija; poremećaji pigmentacije; diferencijalna dijagnoza; biopsija; takrolimus; topikalna primena

Abstract

Introduction. Lichen planus pigmentosus inversus is a rare variant of lichen planus pigmentosus primarily affecting light-skinned middle-aged individuals. It is characterized by asymptomatic hyperpigmented lesions in intertriginous regions. **Case report.** We report a case of 56-year-old male with Fitzpatrick skin type II, presenting with a 4-month history of asymptomatic hyperpigmentation in multiple bilateral skin folds. Physical examination revealed sharply defined purple-brown macules and plaques in the axillary, inguinal, supraclavicular regions, and abdominal skin folds. Histopathological analysis demonstrated lichenoid features with prominent melanin incontinence in the papillary dermis. The diagnosis was confirmed by correlating clinical and histopathological findings. Treatment with topical tacrolimus resulted in complete clinical regression. **Conclusion.** LPPI may be underreported and should be considered in the differential diagnosis of hyperpigmented lesions in intertriginous areas. Topical calcineurin inhibitors represent a promising therapeutic option due to their minimal side effects and favorable clinical outcomes.

Key words: Lichen Planus; Hyperpigmentation; Pigmentation Disorders; Diagnosis, Differential; Biopsy; Tacrolimus; Administration, Topical



Slike 1a i 1b. Hiperpigmentovane makule i plakovi u desnoj aksili (a), ingvinalnoj i abdominalnoj regiji (b)

Figures 1a and 1b. Hyperpigmented macules and plaques in the right axillary (a), inguinal and abdominal region (b)

Uvod

Lichen planus pigmentosus inversus (LPPI) je retka forma lichen planus pigmentosus-a (LPP), koja se pretežno javlja kod osoba srednjih godina i svetle puti, ali je takođe opisana i kod osoba drugih starosnih grupa [1]. Ovaj klinički entitet prvi su opisali Pok (Pock) i sar. 2001. godine [3]. Etiologija i patogenеза LPPI i dalje nisu do kraja rasvetljene. Klinički se karakteriše pojavom asimptomatskih ili blago pruriginoznih, svetlo do tamnobraon, lividnih, sivkastih ili tamnocrvenih makula i plakova u intertriginoznim i fleksornim regijama kože [1, 2, 4]. Kako često može da liči na druga kožna oboljenja, kao što su kontaktni dermatitis sa postinflamatornim hiperpigmentacijama, eritrazma, acanthosis nigricans, erythema fixum, erythema dyschromicum perstans (EDP) i još neke kliničke imitatore, biopsija kožne lezije je neophodna za definitivnu dijagnozu [1, 2, 8]. Lečenje LPPI je neretko veoma zahtevno, s obzirom na to da je ova dermatоза često rezistentna na lečenje lokalnim kortikosteroidima [4, 6] i takrolimusom [6], kao i opštom kortikosteroidnom terapijom [5, 9].

Cilj našeg rada je da informiše kliničare o postojanju ovog retkog kliničkog entiteta, koji je često neopravdano zanemaren i neprepoznat.

Prikaz slučaja

Muškarac starosti 56 godina, svetle puti (Fitzpatrick fototip II), javio se na našu Kliniku

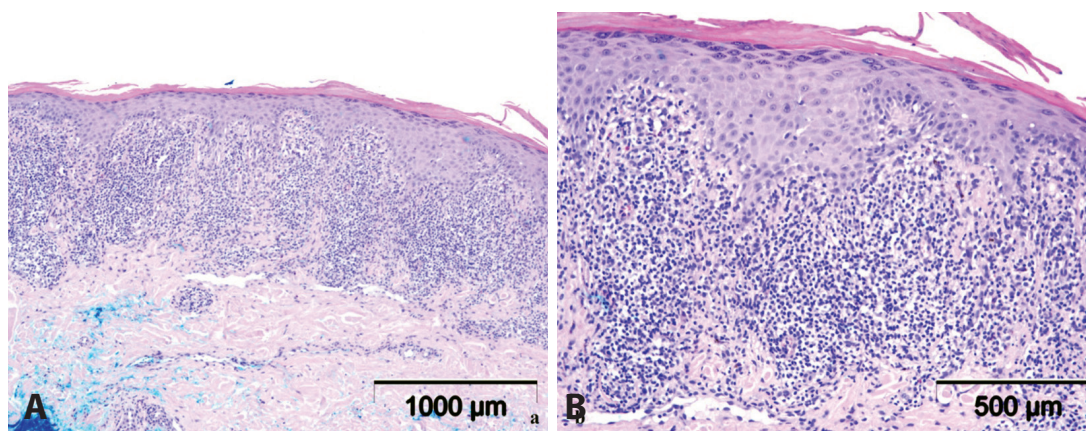
Introduction

Lichen planus pigmentosus inversus (LPPI) is a rare variant of lichen planus pigmentosus (LPP), predominantly affecting light-skinned middle-aged individuals, although cases have been reported across different age groups [1]. This clinical condition was initially described in 2001 by Pock et al. [3]. The exact cause and development of LPPI remains unclear. Clinically, LPPI manifests as asymptomatic to mildly pruritic light to dark brown, violaceous, grey, or dark red macules and plaques in intertriginous and flexural body regions [1, 2, 4]. Due to its resemblance to other skin disorders such as contact dermatitis with postinflammatory hyperpigmentation, erythrasma, acanthosis nigricans, fixed drug eruption, and erythema dyschromicum perstans (EDP), a skin biopsy is essential for a definitive diagnosis [1, 2, 8]. Treatment of LPPI is often challenging as it typically does not respond to local therapies like topical corticosteroids [4, 6], topical tacrolimus [6], or oral corticosteroids [5, 9].

The purpose of this report is to raise awareness among clinicians about this uncommon clinical entity, which is frequently overlooked and misdiagnosed.

Case report

A 56-year-old healthy Caucasian male with Fitzpatrick skin type II presented with a 4-month history of asymptomatic, enlarging



Slike 2a i 2b. Histopatološki nalaz (hematoksilin-eozin bojenje; originalno uveličanje (a) x 100, (b) x 200)

Figures 2a and 2b. Histopathological finding (hematoxylin-eosin stain; original magnification (a) x 100, (b) x 200)

zbog pojave asimptomatskih hiperpigmentacija u više kožnih pregiba obostrano, u toku prethodna četiri meseca. Nije bilo povezanosti pojave lezija sa upotrebom lekova, traumom, korišćenjem novih ulja, parfema niti antiperspiranata. Takođe, pacijent je negirao izlaganje suncu pre pojave lezija. Porodična anamneza je bila negativna za postojanje poremećaja pigmentacije.

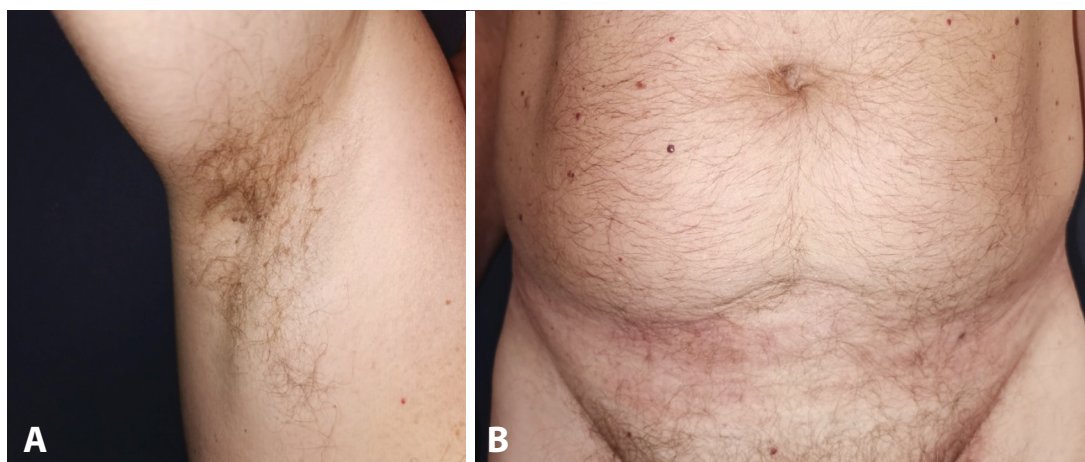
Dermatološkim pregledom utvrđeno je postojanje multiplih jasno ograničenih lividno-mrkih makula i plakova, koji su zahvatali aksilarne, ingvinalne, poplitealne i supraklavikularne kožne prevoje i abdominalne kožne nabore, obostrano (**Slike 1a i 1b**). Kapilicijum, nokti i vidljive sluznice bili su bez promena, a takođe nije bilo znakova periferne limfadenopatije. Klasične lezije lichen planus nisu nađene na predilekcionim mestima. Biopsija kože pokazala je postojanje hipergranuloze, zupčaste akantoze, bazalnu vakuolnu degeneraciju, rasute apoptotične keratinocite i trakasti dermalni limfocitni infiltrat, kao i izraženu inkontinenciju pigmenata i brojne melanofage u površnom dermisu (**Slike 2a i 2b**). Rutinske laboratorijske analize bile su u granicama referentnih vrednosti, dok su virusološki testovi na virus humane imunodeficijencije, virus hepatitisa B i hepatitisa C bili negativni. Dijagnoza je postavljena na osnovu korelacije kliničkog i histopatološkog nalaza.

Nakon potvrde dijagnoze, pacijentu je propisana 0,05% klobetasol propionat mast, dva puta dnevno tokom dve nedelje. Kako nije primećeno poboljšanje, terapija je promenjena

hiperpigmentacijama utičući na više kožnih pregiba obostrano. Nije bilo povezanosti pojave lezija sa upotrebom lekova, traumom, korišćenjem novih ulja, parfema niti antiperspiranata. Takođe, pacijent je negirao izlaganje suncu pre pojave lezija. Porodična anamneza je bila negativna za postojanje poremećaja pigmentacije.

Physical examination revealed multiple sharply defined purple-brown macules and plaques involving axillary, inguinal, popliteal, supraclavicular regions, and abdominal skin folds (**Figures 1a and 1b**). The scalp, nails, and visible mucous membranes were unaffected, and there were no signs of lymphadenopathy. Classical lesions of lichen planus were not found on the predilection sites. Skin biopsy revealed hypergranulosis, irregular acanthosis, basal cell vacuolization, scattered apoptotic keratinocytes, and band-like dermal lymphocytic infiltration, accompanied by prominent pigment incontinence and numerous melanophages in the superficial dermis (**Figures 2a and 2b**). Routine laboratory analyses were within normal ranges, while virological tests for human immunodeficiency virus (HIV), hepatitis B, and hepatitis C virus were negative. The diagnosis was established based on the correlation of clinical and histopathological findings.

Upon confirmation of the diagnosis, our patient was prescribed topical clobetasol propionate 0.05% ointment twice daily for 2 weeks. However, due to lack of improvement, the treatment was switched to topical tac-



Prilozi 3a i 3b. Kompletna klinička regresija kožnih lezija

Figures 3a and 3b. Complete clinical regression of skin lesions

na primenom topikalnog preparata 0,1% takrolimus, što je dovelo do potpune kliničke regresije kožnih lezija u toku narednih šest meseci (**Slike 3a i 3b**). Tokom perioda praćenja od 18 meseci nije zabeležen relaps kožnih promena.

rolimus 0.1% twice daily, which resulted in complete clinical regression of skin lesions within 6 months (**Figures 3a and 3b**). During the follow-up period of 18 months, no relapses were noted.

Diskusija

Kao što sam naziv sugerise, lichen planus pigmentosus inversus (LPPI) predominantno zahvata intertriginozne zone, najčešće aksile. Drugi prevoji – cervikalni, ingvinalni i poplitealni, takođe mogu biti zahvaćeni, ali i neke neočekivane zone, kao što su postaurikularni sulkusi, abdomen i struk [4, 10]. Prvih sedam slučajeva LPPI prijavili su Češkoj Pok i saradnici 2001. godine [3] kod pacijenata svetle puti, sa promenama lokalizovanim u aksilama i preponama. Iako se ovaj klinički entitet najčešće manifestuje bilateralnom pojavom hiperpigmentovanih mrkih ili sivkastih ovalnih makula, papula i plakova, lokalizovanih na intertriginoznim, fleksornim zonama i kožnim prevojima, unilateralna prezentacija je takođe prijavljena [11]. U najvećem broju slučajeva lezije zahvataju više regija istovremeno, međutim, opisane su i lezije ograničene na jednu zonu kože [12]. Do sada nisu prijavljene prateće promene na noktima, kosi i mukozama.

Autori sugerisu da spoljni okidači, kao što su trenje i Kebnerov fenomen usled mehaničke iritacije uskom odećom, mogu da imaju uzročnu ulogu u nastanku lezija [4, 5]. Na osnovu pregledane literature može se smatrati da je imunopatogeneza LPPI slična patogenezi LPP,

Discussion

As implied by its name, lichen planus pigmentosus inversus (LPPI) primarily manifests on intertriginous areas, notably in the axillae. Other affected skin folds include cervical, inguinal, and popliteal regions, with some uncommon localizations such as post-auricular sulci, abdomen, and waist also reported [4, 10]. The initial seven cases of LPPI were documented in 2001 by Pock et al. in Caucasian individuals in the Czech Republic, predominantly affecting the axillae and groins [3]. Although typically characterized by bilateral hyperpigmented dark-brown or grey ovoid macules, papules, and plaques on intertriginous and flexural areas, unilateral presentations have also been observed [11]. Furthermore, while most cases involve multiple affected regions concurrently, isolated lesions limited to a single site have been documented as well [12]. No abnormalities of the nails, hair, or mucous membranes have been noted in LPPI cases.

Authors have suggested potential triggering factors such as friction and the Koebner phenomenon resulting from external mechanical stress, such as tightly fitting clothing, which may contribute causatively to LPPI development [4,5]. According to reviewed litera-

koju odlikuje citotoksični efekat CD8⁺ T-limfocita na bazalne keratinocite, što vodi inicijalnoj brzom infiltraciji limfocita i lihenoidnim histopatološkim odlikama sa značajnom inkontinencijom pigmenta u površnom dermisu [1, 2], što je viđeno i u našem slučaju. LPPI je povezivan sa virusnom infekcijom hepatitisa C, nekim endokrinopatijama i autoimunskim bolestima [1, 6]. Koegzistencija sa lezijama klasičnog lichen planus takođe je opisana [7]. Većina pacijenata ipak ima spontanu pojavu kožnih promena [2, 9, 13], kao što je bio slučaj i sa našim pacijentom.

Postavljanje dijagnoze LPPI može da bude izazovno, s obzirom na to da brojne druge dermatoze klinički mogu da liče na ovu dermatozu. U dostupnoj literaturi najčešće pominjane diferencijalne dijagnoze bile su lichen planus pigmentosus (LPP), acanthosis nigricans, erythema fixum, erythema dyschromicum perstans (EDP), postinflamatorne hiperpigmentacije, eritrazma i druge [11, 13]. Biopsija i kliničko-patološka korelacija su neophodne za razlikovanje LPPI od većine pomenutih entiteta, imajući u vidu da promene na koži često nisu dovoljno specifične. Inverzna lokalizacija lezija je odlučujuća za postavljanje dijagnoze LPPI umesto klasičnog LPP. Lezije EDP takođe mogu da se lokalizuju u intertriginoznim regijama, a histopatološki često nalazimo bazalnu vakuolnu degeneraciju sa inkontinencijom pigmenta [14]. Međutim, odsustvo lihenoidnog dermalnog infiltrata, kao i pojava promena kod osoba sa tamnijim fototipovima, karakteristike su koje mogu da razlikuju ovu dermatozu od LPPI. Dakle, intertriginозна lokalizacija hiperpigmentovanih lezija kod svetloputih pacijenata, zajedno sa trakastim lihenoidnim histopatološkim obrascem, glavni su faktori koji pomažu u razlikovanju LPPI od njegovih kliničkih imitatora [9, 13, 15].

Iako LPPI ima blag klinički tok, ishodi mogu da variraju od spontane regresije, do višegodišnjeg perzistiranja promena [5, 11]. Iz tog razloga, lečenje ove dermatoze predstavlja izazov kako za lekara, tako i za pacijenta [16]. Još uvek ne postoje opšte terapijske preporuke za lečenje LPPI. Potentni topikalni kortikosteroidni preparati, topikalni inhibitori kalcineurina, kao što je takrolimus, kao i sistemski kortikosteroidi, mogu biti efikasni modaliteti lečenja. Međutim, rezultati lečenja su nekonzistentni, s obzirom na značajnu rezistenciju kožnih promena [4–6, 9]. Lokalna primena takrolimusa

ture, the immunopathogenesis of LPPI mirrors that of LPP, characterized by the cytotoxic effect of CD8⁺ T-lymphocytes on basal keratinocytes, leading to an initial rapid inflammatory infiltrate and lichenoid histopathological features with notable melanin incontinence in the upper dermis [1,2], as observed in our patient's case. LPPI has been associated with hepatitis C virus infection, certain endocrinopathies, and autoimmune diseases [1, 6]. Coexistence with classic lichen planus has also been documented [7]. However, most patients typically report a history of spontaneous onset of skin lesions [2,9,13], consistent with our patient's presentation.

Diagnosing LPPI can be challenging due to the potential for clinical resemblance to several other dermatoses. The primary differential diagnoses, as documented in the literature, include lichen planus pigmentosus (LPP), acanthosis nigricans, fixed drug eruption, erythema dyschromicum perstans (EDP), postinflammatory hyperpigmentation, or erythrasma [11, 13]. Biopsy and clinicopathologic correlation are essential to differentiate LPPI from these entities, as clinical findings alone are often insufficient. The inverse distribution of lesions is critical for distinguishing LPPI from classic LPP. While EDP lesions can also occur in intertriginous regions and show basal vacuolar degeneration with pigment incontinence on histopathology [14], the absence of a lichenoid dermal infiltrate and the occurrence in individuals with darker phototypes can differentiate EDP from LPPI. Therefore, key clues to differentiate LPPI from mimickers include its occurrence in fair-skinned individuals, localizes in intertriginous regions, and characteristic band-like lichenoid histopathological patterns [9, 13, 14].

Although LPPI generally follows a benign clinical course, outcomes can range from spontaneous regression to persistent lesions lasting for years [5, 11]. Consequently, therapeutic management is often challenging for both patients and physicians [15]. There are no standardized treatment guidelines for LPPI. Treatment options such as medium to high-potency topical corticosteroids, topical calcineurin inhibitor tacrolimus, and systemic corticosteroids appear promising but yield inconsistent results since skin lesions often exhibit resistance to these therapies [4-6, 9]. Topical tacrolimus may be considered a fa-

imponuje kao najbolja terapijska opcija zbog minimalno izraženih neželjenih efekata i zadovoljavajućeg kliničkog odgovora [8, 17].

Dostupni podaci iz literature ukazuju na to da je LPPI uglavnom monofazna bolest, te da se recidivi ne očekuju nakon odgovarajućeg lečenja. U tom smislu, redovne dermatološke kontrole nisu neophodne nakon povlačenja lezija.

Zaključak

Incidencija LPPI je verovatno potcenjena, što vodi čestom neprepoznavanju ovog kliničkog entiteta. Intertriginozna lokalizacija lezija kod svetloputih pacijenata, trakasti lichenoidni patohistološki obrazac, kao i blag klinički tok govore u prilog ovoj dijagnozi. LPPI treba razmotriti u diferencijalnoj dijagnozi drugih hiperpigmentacija lokalizovanih u fleksornim regijama. S obzirom na nedovoljna znanja o etiologiji i imunopatogenezi ovog stanja, trenutno nema opštih preporuka za lečenje. Izbegavanje faktora rizika i lokalna primena takrolimusa mogu se smatrati dobrim inicijalnim terapijskim pristupom.

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avorable therapeutic choice due to minimal side effects and satisfactory clinical outcomes [8, 16].

Available data suggest that LPPI is typically a monophasic disease, with relapses not anticipated following adequate treatment. Consequently, dermatologist follow-ups are unnecessary once lesions have resolved.

Conclusion

LPPI is likely underdiagnosed and frequently misdiagnosed due to its relatively low incidence. The characteristic intertriginous distribution in light-skinned individuals, along with a band-like lichenoid histopathological pattern and the benign clinical course, support the diagnosis. LPPI should be considered in the differential diagnosis of hyperpigmented lesions located in flexural areas. Currently, due to limited understanding of its etiology and immunopathogenesis, there are no standardized treatment recommendations for LPPI. However, initial therapeutic approaches may include avoiding triggering factors and considering topical tacrolimus.

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