**LICHEN PLANUS: ORAL MANIFESTATIONS, DIFFERENTIAL DIAGNOSIS AND TREATMENT**

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**Sažetak**

**Uvod:** Neka od tipičnih kožnih oboljenja, kao što su Pemphigus vulgaris, Pemphigoid mucosae oris, Erythema exudativum multiforme, Sclerodremia, Dermatitis herpetiformis-Duhring i Lichen planus, lokalizuju se i u usnoj duplji.

**Cilj:** Cilj rada je da se precizira dijagnoza i terapija Lichen planusa sa manifestacijama u usnoj dupljii.

**Metode:** Analizom literature i na osnovu kliničkog iskustva lekara ispitivane su načine oralne manifestacije Lichen planusa.

**Rezultati:** Ovo oboljenje najčešće se javlja kod pacijenata srednjih godina (30 – 60 godina) i češće je kod žena nego kod muškaraca. Oralni Lichen planus retko se vidio kod dece. Bolest se javlja kod 0,5% – 2% populacije. Klinička istorija potvrđuje vezu između oralnog Lichen planusa i oralnog karcinoma, stoga ovo oboljenje treba smatrati kao prekanceroznu leziju.

**Zaključak:** Dermatoze u ustima najčešće se lokalizuju na obraznoj sluzokoži, i to u visini okluzalne linije i na sluzokoži retromolarnog predela, ali se mogu javiti i na sluzokoži jezika, poda usne duplje i usana.

**Ključne reči:** Lichen planus, oralne manifestacije, usna dupljia

**Abstract**

**Introduction:** Some of the typical skin diseases, such as Pemphigus vulgaris, Pemphigoid mucosae oris, Erythema exudativum multiforme, Sclerodremia, Dermatitis herpetiformis-Duhring and Lichen planus, can cause swelling and irritation in mucous membranes of the oral cavity.

**Aim:** The aim of the study was to precise diagnosis and treatment of oral Lichen planus manifestations.

**Methods:** Analyzing the literature data and the experience of clinicians, the most common oral lichen planus manifestations were investigated.

**Results:** This disease most commonly occurs in middle-aged patients (30-60 years) and is more common in women than in men. Oral Lichen planus is rarely seen in children. The disease presents in 0.5% to 2% of the population. Clinical history established the relation between oral Lichen planus and oral carcinoma, and therefore this disease should be considered a precancerous lesion.

**Conclusion:** Dermatoses in the mouth are localized most often in the oral mucosa, both at the height of the occlusal line and in the mucous membrane of the retromolar area, but they can also occur in the mucous membranes of the tongue, the floor of the mouth and lips.

**Key words:** Lichen planus, oral manifestations, oral cavity
Uvod

Lichen planus, pored virusnih infekcija i aftoznih lezija, zauzima treće mesto među oboljenjima na oralnoj sluzokoži. Od prvih kožnih opisa Lichen planus-a, koji je objavio Wilson 1869. godine, notirane su i sluzokožne promene od strane drugih autora1. Mogućnost da se pojave oralne lezije, bez kožnih manifestacija, prvi je opisao Audry 1894. godine2, a posebno su istaknute od strane Dubreuilh 1906. godine2, koji je ukazao na to da patohistološka slika oralnih lezija odgovara pathohistološkoj slici kožnih promena. Zatim su sledili brojni autori, koji su pored belih papula i plakovnih lezija u usnoj duplji, počeli da opisuju i brojne varijante bolesti, počevši od Poora 1905. godine3, koji je prvi opisao vezikulo-bulozne lezije, pa do opisa ulcerozne i atrofične lezije, koje su posebno obradili Lortat-Jacob i sar. 1929. godine3.

Etiologija

1. Stres – nervoza i emotivna nestabilnost veoma često su prisutne kod osoba sa ovim oboljenjem. Kliničkim pregledima utvrđeno je da se bolest javlja nedelju do dve nedelje nakon jakog emocionalnog stresa (smrt bliskog člana porodice, napetost na poslu, psihička premorenost, itd)5,6, tako da se neurogeno poreklo najviše dovodi u vezu sa ovim oboljenjem.

2. Autoimmunost – mnoge studije pokazale su da antibazalne ćelije antitela (anti-BCA), koje perzistiraju mesecima ili godinama kod pacijenata sa oralnim Lichen planus-om, mogu biti autoantitela, koja organizam stvara u borbi protiv alteriranih antibazalnih ćelija antitela7,8,9. U kožnim i oralnim promenama nađeni su depositi imuno-globulina klase IgG, IgM i komplementa C310.

3. Genetska predispozija – bolest je kosmopolitska, ali je dokazano da se češće javlja kod osoba sa HLA-A3, B5, A28, B7-B8-DRW911,12. Podaci o HLA markerima za oralni Lichen planus su u mnogome zavisi od ispitivane populacije12,13. Žene oboljene češće nego muškarci, a starosnot u kojoj se oboljenje javlja je između 30 i 60 godina14. U retkim slučajevima i deca mogu oboljeti.

4. Pušenje – Gorsky i sar.15 razmatrali su mogućnost korelacije između različitih kliničkih manifestacija lihena i pušenja, gde je

Introduction

Lichen planus, in addition to viral infections and aphthous ulcers, ranks third place among oral mucosal diseases. The first skin descriptions of Lichen planus were published by Wilson in 1869, but mucous changes were also noted by other authors1. The possibility of the appearance of oral lesions without skin manifestations was first described by Audry in 1894, and especially highlighted by Dubreuilh in 19062, who indicated that the pathohistological changes of oral lesions corresponds to the pathohistological changes of skin changes. This was followed by a number of authors who, in addition to white papules and plaque lesions in the oral cavity, began to describe numerous variants of the disease, starting with Poor in 19053, who first described vesicular-bullous lesions, then ulcerative and atrophic ones, which were specifically described by Lortat-Jacob et al. in 19293.

Etiology

The exact etiology is unknown, but several predisposing factors can be the cause of oral Lichen planus (OLP)4. The most important factors in the onset of this disease are:

1. Stress - nervousness and emotional instability are very common in people with this disease. Clinical examinations indicate that the disease occurs one to two weeks after severe emotional distress (death of a close family member, tension at work, mental fatigue, etc.)5,6, so that the neurogenic origin is most associated with this disease.

2. Autoimmunity - Many studies have shown that anti-basal antibodies (anti-BCA), which persist for months or years in patients with oral Lichen planus, may be autoantibodies that occur against altered anti-basal antibodies7,8,9. Deposits of IgG, IgM and complement C3-class immunoglobulins were found in skin and oral changes10.

3. Genetic predisposition - this disease is cosmopolitan, but has been shown to occur more frequently in people with HLA-A3, B5, A28, B7-B8-DRW911,12. Data on HLA markers for oral Lichen planus are highly dependent on the studied population12,13. Women are affected more often than men, with an onset time between ages 30 and 6014. In rare cases, children may be affected.
primećeno da je osetljivost sluzokože povezana sa pušenjem. Neumann-Jensen i sar.16 naveli su da je OLP bio redi kod pušača nego kod nepušača17, tako da se pušenje ne može zasigurno obeležiti kao jedan od faktora koji su izazivači OLP.

• Stomatološki materijali – amalgam, zlato, kompozitni ispuni, kao i metali (kobalt, nikl, paladijum), koji se otpuštaju iz određenih dentalnih ispuna, tj. iz slojeva samih materijala ispuna, dovode do lihenoidnih reakcija i inflamacije gingive18,19. Ranija istraživanja ukazuju na lihenoidne reakcije koje nastaju kao produkt galvanske struje, koja stvara između metala u ustima19,20. Međutim, skorašnja istraživanja ukazuju na to da inflamacija nastaje kao rezultat interakcije čelija medijatora i samih materijala kod pacijenta koji su duže vreme bili izloženi ovoj reakciji.

Klinička slika

Oralni Lichen planus pojavljuje se kod 0,1% – 4% osoba, u zavisnosti od pregledane populacije. Generalno je oboljenje koje se vezuje za ljude srednje i starije životne dobi, od koga češće oboljevaju žene nego muškarci, u odnosu 2:1. Mada postoji određeni procenat pacijenata sa oralnim promenama koji su stariji od 60 godina, rang godina je sličan godinama pacijenata koji imaju samo kožne promene. Postoji i mali broj pacijenata kojima su potvrđene oralne promene u ranom životnom dobu – najmlađi je imao 7 godina2. Ovo predstavlja retkost u slučajevima kožnih promena. Oralne lezije obično su bilateralne i zahvataju bukalnu mukozu (nivo okluzalne linije i retromolarni predeo) u oko 90% svih slučajeva21. Mesta najfrekventnijih pojavljivanja oboljenja su jezik (njegove ivice i dorzalna površina), semimukoza usana, pod usne duplje, gingiva, alveolarni greben i najređe nepce22. Lichen planus se u ustima može pojaviti u šest različitih oblika. Najčešće forme su retikularna, u obliku plaka, erozivna forma i atrofični tip23. Bullozni i papilarni tipovi obično se nalaze u kombinaciji sa drugim oblicima. Pacijenti sa oralnim Lichen planus-om mogu imati periode remisije i egzacerbacije.

Smoking habits - Gorsky et al.15 considered the possibility of a correlation between different clinical manifestations of lichen and smoking, where it was observed that mucosal sensitivity was associated with smoking. Neumann-Jensen et al.16 stated that OLP was less frequent in smokers than in non-smokers17 so that smoking could not be linked as one of the contributing factors to OLP with certainty.

Dental materials - amalgam, gold, composite fillings, as well as metals (cobalt, nickel, palladium) released from certain dental fillings, i.e., from the layers of the filling materials themselves lead to lichenoid reactions and gingival inflammation18,19. Earlier research indicates that lichenoid reactions occur as a product of galvanic potential between metals in the mouth19,20. However, recent research indicates that inflammation occurs as a result of mediator cells and the materials themselves in patients who have been exposed to this reaction for a long time.

Clinical feature

Oral Lichen planus occurs in 0.1-4% of individuals depending on the population examined and is generally a disease of middle and older-aged people, more frequently in women than in men with a ratio of 2:1. Although there is a certain percentage of patients with oral changes that are older than 60 years, the range of the years is similar to the age of patients who have only skin changes. There is also a small number of patients with oral changes that occur at an early age-the youngest patient was 7 years old2. This is a rare case. Oral lesions are usually bilateral and involve the buccal mucosa (occlusal line level and retromolar area) in about 90% of all cases21. The most frequently it appears on the tongue (its edges and dorsal surface), the submucosa of the lips, the floor of the mouth, the gingiva, the alveolar ridge and the most rarely in the palate22. Lichen planus can occur in the mouth in six different forms. The most common forms are reticulate, plaque-shaped, erosive and atrophic21. Bullous and papillary types are usually found in combination with other forms. Patients with oral Lichen planus may have periods of remission and exacerbation.
Retikularna forma Lichen planus-a

Ovo je najčešća forma Lichen planus-a u ustima. Bolešć se javlja u vidu beličastih papula veličine čodione glave. Uočavaju se u vidu beličastih linija ili traka. Poredi uložno, papule se mogu videti jedino lupom. Ovaj oblik često se vidi na obraznoj sluzokozi, ali i na dorzalnoj strani jezika i tvrdom javljaju simetrično, na obraznoj sluzokoži, istim oblicima

Lichen planus u obliku plaka

Lichen planus u ovom obliku može se videti kao tanak sloj plaka različitih veličina, glatke i nesvjetlje površine, u odnosu na lokalno tkivo. Najčešće lokalizacije su obraz, nepcu, jezik i gingiva, a retko pod usne duplje. U subepitelnom tkivu uvek se vidi gusta infiltracija limfocitima. Ovaj oblik Lichen planus-a retko prelazi u maligni oblik. Često se javlja zajedno sa drugim oblicima.

Papilarna forma Lichen planus-a

Papilarna forma Lichen planus-a klinički se vidi kao mala bela papula veličine 0.5 mm, a može se pojavljivati zajedno sa ostalim oblicima Lichen planus-a. Papule se javljaju simetrično, na obraznoj sluzokoži, ali i na dorzalnoj strani jezika i tvrdom nepcu. Obično su pojedinačne, ali mogu i da konfluiraju stvarajući bele tvorevine. Prisutna je inflamacija sluzokože. Histološki, izražena je parakeratoza i hiperkeratoza u gornjim slojevima, dok je subepitelno prisutna difuzna infiltracija limfocitima. Bolest počinje bez simptoma, a ukoliko se i jave, sjenično su veoma blago i javljaju se u vidu zatezanja i hrapavosti sluzokože, suvoše, blagog pečkanja i žarenja u ustima. Prognoza je dobra, mada retko može doći do spontanog povlačenja promena. Kod ovih varijanti, epitelijalne promene su hiperkeratočične ili obično hiperortokeratočične.

Reticular form of Lichen planus

This is the most common type of Lichen planus in the mouth. The disease occurs in the form of whitish papules the size of a chiodine head. They are seen as smooth and slightly more tangle surface than the surrounding tissue. The most common localizations are the cheek, palate, tongue, and gingiva, and rarely in the floor of the mouth. In the histological feature of the superficial layers of the epithelium, parakeratosis and hyperkeratosis are present, and in the subepithelial layer a lymphocytic infiltrate. This type of Lichen planus is most commonly seen in smokers. The Lichen planus, in plaque form, often alters to malignant form along with erosive and atrophic forms.

Plaque form of Lichen planus

It is seen as a thin layer of plaque of various sizes, a smooth and slightly more tangled surface than the surrounding tissue. The most common localizations are the cheek, palate, tongue, and gingiva, and rarely in the floor of the mouth. In the histological feature of the superficial layers of the epithelium, parakeratosis and hyperkeratosis are present, and in the subepithelial layer a lymphocytic infiltrate. This type of Lichen planus is most commonly seen in smokers. The Lichen planus, in plaque form, often alters to malignant form along with erosive and atrophic forms.

Papillary form of Lichen planus

This form is characterized by small white pinpoint papules size of 0.5 mm that are asymptomatic. It can occur along with other forms of Lichen planus. Papules occur symmetrically on the facial mucosa, but also on the dorsal side of the tongue and the hard palate. They are usually individual, but can also produce white creations. Mucoosal inflammation is present. Histologically, parakeratosis and hyperkeratosis are expressed in the upper layers, while diffuse lymphocytic infiltration is present in subepithelial layer. The disease starts without symptoms, and if they do occur, the disturbances are very mild in the form of tightness and roughness of the mucous membranes, dryness, gentle burning and burning in the mouth. The prognosis is good, although there may rarely be a spontaneous withdrawal of changes. In these variants, the epithelial changes are hyperkeratotic.
Erozivno-ulcerozna forma Lichen planus-a

This is a very common form of the disease. It localizes to the buccal mucosa, gingiva, tongue, palate and floor of the oral cavity. Most rarely, it occurs on the lips vermilion. This form of Lichen is characterized by the destruction of the oral epithelium. When bullae occur, their bursting results in irregularly shaped erosive-ulcercative surfaces of varying sizes. The ulcerative surfaces are covered with a yellowish fibrinous exudate and are surrounded by an inflamed zone. Erosive-ulcerative changes mainly occur as a consequence of bullae bursting, but there are cases when they occur without prior formation of bullous efflorescence.

Patients' subjective ailments are pronounced, with the pain accompanying diet, speech and fluid consumption. Discomfort and pain can also be present spontaneously. The mucosa is sensitive to mechanical irritation and dental trauma before other characteristic lesions appear. These lesions have glossy surfaces and tend to separate from the adjacent mucosa with a clear demarcation border.

Histologically, degenerative changes of the basal layer of the epithelium with signs of atrophy and the appearance of erosions and ulceration are seen. Around the erosive-ulcerative changes in the epithelium, cellular infiltration with the dominance of neutrophilic granulocytes is pronounced, while lymphocytic infiltration is present in the subepithelium. The erosive-ulcerative form of Lichen planus could be transformed into a malignant one due to the possible lichenoid degeneration. There are three forms of erosive lichen planus: the bullous, atrophic, and ulcerative form.

The bullous form is characterized by the appearance of vesicles and bullae filled with clear serous content with possible erythrocyte hemorrhage. They are formed by the accumulation of fluid in the subepithelial connective tissue. Due to the thin coating of the vesicles, they burst when speaking and eating and lead to painful sensations.
Ovaj oblik najčešće se vidi na bukaloj sluzokoži. U bazalnom sloju epitela izražena je hidropsna degeneracija. Dominantna je infiltracija limfocitima, koja se povećava posle prskanja bula. Subjektivne smetnje su jako izražene i postoje bolovi prilikom uzimanja hrane, a prisutni su i spontani bolovi. Ove dve forme moraju se redovno kontrolisati zbog mogućnosti maligne alteracije.

- **Atrofični oblik** (eritematozni oblik) predstavlja red oblik Lichen planus-a. Najčešće se javlja na dorzalnoj strani jezika i gingivi. Epitel jezika je atrofičan, istanjuje se uz izrazito crvenilo i inflamaciju. Filiformne i fungiformne papile nestaju, a jezik je gladak i kao poliran (Lingua glabra). Ova atrofična forma može se javiti i kao rezultat zarastanja erozivno-ulceroznih oblika i manifestovati se epitelnom atrofijom. Promene na gingivi najčešće se izražene u gornjoj vilici i u predelu fiksne gingive u obliku ograničenih atrofičnih pora. Gingivalni epitel postaje tanak i suv, pa se sklone povredama, dok u bazalnom sloju postoji hidropsna degeneracija, a u subepitelnom sloju uočava se gusta infiltracija limfocitima.

- **Ulcerozni oblik** – ovu formu Lichen planus-a karakteriše destrukcija oralnog epitela. Ulcerozne površine su pokrivene beličastim žućkastim fibrinoznim eksudatom, a okružene su zonom inflamacije na delu sluzokože koji odgovara zoni inflamacije. Ulcerozne lezije posledica su oštećenih bula, ali one mogu nastati i bez stvaranja buloznih eflorescencija.

Kao posebna dva oblika, koja se javljaju u okviru ovog oboljenja, postoje i Grinspanov sindrom i lichenoidne reakcije.

- **Grinspanov sindrom** predstavlja oblik oralnog Lichen planus-a koji se javlja zajedno sa Diabetes mellitus-om i hipertenzijom. Često su izražene i kožne promene, a u ustima su promene najčešće na bukaloj sluzokoži.

- **Lichenoidne reakcije** mogu biti izazvane lekovima ili nekim drugim supstancama. Brojni lekovi mogu da učestvuju u lichenoidnim erupcijama (LDEs) uključujući i nesteroidne antiinflamatorne lekove (NSAIDs), antihipertenzivne lekove (naročito angiotenzinski konvertni enzimi ((ACE) inhibitori), antimalarike, fenilamino-pirimidinske derivate (Imatinib) i injekcije zlata (Tabela 1). Lokalizovane lichenoidne reakcije mogu biti udružene sa hipertenzivnim reakcijama na merkurijalne soli oslobodene iz amalgamskih nadograđnja. Ovakvo nastale lichenoidne reakcije mogu se svrstati u IV tip reakcija hipersenzitivnosti.

Kod lichenoidne reakcije, erupcije imaju tendenciju ka unilateralanj pojav.
Dijagnoza se postavlja na osnovu biopsije i hematološki indirektnih imunofluorescencije, gde se vidi niz od perli, kao potvrda lichenoidne erupcije. U nalazu se vidi obilje difuznog lichenoidnog infiltrata sa dubokim perivaskularnim limfocitnim infiltratom.

Za razliku od pravog Lichen planus-a, lekom izazvane lichenoidne erupcije nestaju nakon ukidanja leka. Lichenoidne erupcije izazvane lekovima izuzetno retko napadaju bukalnu sluzokožu, kada se javlja bela trakasta šara. Mišljenje je da lekovi samo prikrivaju latentno oboljenje Lichen planus ili širenje predhodnog poremećaja, pre nego što indukuju novo oboljenje.

The resulting lichenoid reactions can be classified as type IV hypersensitivity reactions. In lichenoid reactions, eruptions tend to be unilateral.

The diagnosis is made based on biopsy and hematologically indirect immunofluorescence, where a series of beads is seen as confirmation of a lichenoid eruption. A diffuse lichenoid infiltrate with deep perivascular lymphocytic infiltrate is also noticed.

Unlike the real Lichen planus, the medication-induced lichenoid eruptions disappear after the discontinuation of the medications. Medication-induced lichenoid eruptions extremely rarely attack buccal mucosa when a white stripe pattern occurs. It is thought that medications only mask the latent disease of Lichen planus or the spread of a previous disorder, before inducing a new disease.

### Table 1. Medications that can trigger a lichenoid reaction

| Lekovi koji mogu izazvati lichenoidnu reakciju | Medications which trigger a lichenoid drug eruption |
|---------------------------------------------|---------------------------------------------------|
| Allopurinol                                  | Furosemide                                        |
| Angiotensin                                  | Zlatne smeše                                      |
| Arsenične smeše                              | Polycarbonate                                     |
| Amalgam                                     | Mepacrine                                         |
| β-blokatori                                  | Nickel                                             |
| Bizmut                                      | NSAIDs                                             |
| Chloroquine                                  | Nylon                                             |
| Quinidine                                    | Streptomycin                                      |
| Tolbutamide                                  | Tetracycline                                      |

### Dijagnoza oralnog Lichen planus-a

Dijagnostika OLP-a sastoji se od kliničkog pregleda, uzimanja uzoraka za patohistološku dijagnozu i histohemijske ili imunohistohemijske analize tkiva.

**Patohistološka ispitivanja** – na histološkom preparatu biopsiranog uzorka vide se tri glavne karakteristike:
- hiperkeratoza i parakeratoza gornjih slojeva;
- hidropsna degeneracija bazalnog sloja epitelia;
- gusta infiltracija limfocita u gornjem korijumu ispod epitelja;
- kod kožnih lezija moguća je pojava i tzv. "shaped teeth" may occur with skin lesions.

### Diagnosis of oral Lichen planus

The diagnosis of OLP consists of clinical examination, sampling for pathohistological diagnosis, histochemical or immunohistochemical analysis of the tissue. **Pathohistological examination** - the histological preparation of a biopsied specimen shows three main characteristics:
- hiperkeratoza and parakeratoza of the upper layers,
- hydrophic degeneration of the basal layer of the epithelium,
- dense infiltration of lymphocytes in the upper corium beneath the epithelium,
- "shaped teeth" may occur with skin lesions.
Immunofluorescent examination is performed with lichen papules where the aggregates of IgG, IgM, and the C3 complement component are observed. The cellular infiltrate in lamina propria consists of T-lymphocytes, with a higher percentage of T4 lymphocytes compared to the T8. An evident predominance of T4 lymphocytes with compared to T8 lymphocytes in lamina propria in Lichen planus relative to their ratio in normal mucosa (e.g. Leucoplakia) should be examined because this may be an important differential diagnostic information. Activated T-lymphocytes secrete interferon, which in turn induces HLA-DR synthesis by keratocytes. Interleukin production by T4 lymphocytes activates T8 lymphocytes, which direct their cytotoxicity to keratocytes. Cytotoxicity can be increased by the presence of HLA-DR class II antigens on the keratinocyte membrane. When it comes to Lichen planus, a numerous keratocytes positive for HLA class II antigens were present at the basement membrane level. A considerable amount of Langerhans cells can also be found in the epithelium. This increase of Langerhans cells and basal keratocytes, positive for HLA class II antigens, may have diagnostic significance when comparing lichen planus lesions with other oral lesions.

Differential diagnosis of Lichen planus

Differential diagnosis includes all white lesions that have an oral manifestation:
- **Leukoplakia** - in leukoplakia, the changes are asymmetrical and represent a united white surface, while the surrounding mucosa is not inflamed. In Lichen planus, the changes are symmetrical, reticulate, with inflamed surrounding mucosa. In ambiguous cases, the diagnosis is established by the biopsy.
- **Sundanerasti nevus obrazu** - appears on the mucous membranes of the cheeks immediately after birth. The mucous membrane is whitish, with spongy like tissue and high density. It is sometimes possible to remove the whitish plaque mechanically, so that parts of normal mucosa can also be seen, which is impossible to do in Lichen planus. Diagnosis is done through histological examination - finding of hyperplasia is characteristic, and lamina propria is normal with a slight infiltration of inflammatory cells in the subepithelium.
**Erythematodes** – oboljenje koje se prvo isključuje zbog prisustva karakterističnih promena na licu. Kod *Erythematodes*-a lezije su na sluzokoži u obliku lako uzdignutih belih površina, okruženih karakterističnim radijalnim teleangiectatičnim proširenjima krvnih sudova, koji grade karakteristični haloo43. U histološkoj slici *Erythematodes*-a postoje hiperkeratoza, hidropsna degeneracija baznog sloja epitelja, degeneracija kolagenih vlakana u vezivnom tkivu sa perivaskularnom infiltracijom limfocita 45. Histološka slika *Lichen planus*-a bitno se razlikuje.

**Mechanička oštećenja oralnog epitelja** nastaju kod neurotičkih osoba zbog grijanja obrazne sluzokože. Klinički i po lokalizaciji liče na *Lichen planus*. Dijagnoza se postavlja na osnovu anamneze i kliničkih razlika. Polje koje je mehanički oštećeno u obliku nepravilnih beličastih zgrušavanja sa diskretnim erozijama 43. Lokalizacija je uvek u predelu okluzalne linije. Ova mehanička oštećenja ne pokazuju polimorfnost u obliku belih mrežastih formacija, linija ili plaka, kao što je slučaj kod *Lichen planus*-a 45.

**Kandidičija** – hronične forme, lokalizovane na sluzokoži obrazra, mogu da se javi u obliku belih linija. Moguća je izražena suvoća i gubitak fleksibilnosti epitela, pa obliku belih linija. Moguća je izražena na sluzokoži obraza, mogu da se javje u formi nepravilnih beličastih zgrušavanja sa diskretnim erozijama 43. Lokalizacija je uvek u predelu okluzalne linije. Ova mehanička oštećenja ne pokazuju polimorfnost u obliku belih mrežastih formacija, linija ili plaka, kao što je slučaj kod *Lichen planus*-a 45.

**Pemphigus vulgaris** – diferencijalno-dijagnostički u obzir dolaze samo erozivno-ulcerozne i vezivno-bulozne forme *Lichen planus*-a 30. Dijagnostička razlika uočava se na osnovu anamneze i kliničkih razlika. Polje koje je mehanički oštećeno u obliku nepravilnih beličastih zgrušavanja sa diskretnim erozijama 43. Lokalizacija je uvek u predelu okluzalne linije. Ova mehanička oštećenja ne pokazuju polimorfnost u obliku belih mrežastih formacija, linija ili plaka, kao što je slučaj kod *Lichen planus*-a 45.

**Pemphigoid mucosae oris** – ova dermatoza koristi se u diferencijalnoj dijagnozi buloznih formi *Lichen planus*-a, jer je karakteriše prisustvo keratotikih belih lezija, kao i činjenica da je prisutnija kod starijih osoba ženskog pola 46.

**Lingua geographica** – diferencijalno-dijagnostički, ova pojava je akutnog, benignog toka, a promene se spontano javljaju i gube. Nisu fiksne karaktere, već migriraju na druga područja jezika 47, za razliku od *Lichen planus*-a, koji je hronično i na terapiju rezistentno oboljenje, dok su promene koje se javljaju na jeziku fiksno karaktere 47.

**Erythematodes** – A disease that is first excluded by the presence of characteristic changes on the face. In *Erythematodes*, lesions on the mucous membranes are in the form of slightly raised white surfaces, surrounded by characteristic radial telangiectatic extensions of blood vessels, which build characteristic halo 43. In the histological picture of *Erythematodes* there is hyperkeratosis, hydropic degeneration of the basal layer of the epithelium, degeneration of collagen fibers in connective tissue with perivascular infiltration of lymphocytes 43. The histological picture of *Lichen planus* differs significantly.

**Mechanical damage to the oral epithelium** - occurs in neurotic persons due to the chewing of the facial mucosa. Clinically and locally, it resembles *Lichen planus*. The diagnosis is made on the basis of history and clinical differences. The field that is mechanically damaged is in the form of irregular white mottled coagulation with discrete erosion 43. Localization is always in the area of the occlusal line. These mechanical defects do not show polymorphism in the form of white mesh formations, lined or plaque as is the case with *Lichen planus* 47.

**Candidiasis** - Chronic forms, localized to the buccal mucous membranes, can occur in the form of white lines. Extreme dryness and loss of flexibility of the epithelium are possible, so the resulting changes show a similarity to *Lichen planus* 47. Spongiosis and infiltration of the epithelium by neutrophilic granulocytes are seen in the pathohistological findings in candidiasis, as well as epithelial hyperplasia 44.

**Pemphigus vulgaris** – Differential-diagnostich, only the erosive-ulcerative and connective-bullous forms of *Lichen planus* are considered 40. Diagnostic difference is observed by microscopic findings of segregated Tzanck cells, which are absent in *Lichen planus*, as well as by finding of acantholytic cells in intraepithelial bullae 45.

**Pemphgoid mucosae oris** – This dermatosis is used in the differential diagnosis of bullous forms of *Lichen planus* as it is characterized by the presence of keratotic white lesions, as well as by the fact that it is more present in older women 46.

**Lingua geographica** – differential-diagnostic, this phenomenon is acute, benign, and the changes occur and disappear spontaneously. They are not of a fixed character, but migrate to the other areas of the tongue 47, unlike *Lichen planus*, which is a chronic and therapy-resistant disease, while changes occurring in a tongue are of a fixed character 47.
Erythema exudativum multiforme – diferencijalna dijagnoza je uglavnom klinička. Po potrebi je virusološka (isključivanje primarne infekcije HSV). Biopsija nije indikovana. Imunohistohemijska ispitivanja mogu ukazati na prisustvo imunoloških reakcija u zoni bazalne membrane (fibrinogen, IgM, C3)⁴⁸.

Stomatitis allergica – diferencijalno-dijagnostički, može se razlikovati od erozivno-ulcerozne forme Lichen planus-a na osnovu anamneze, kliničke slike i izvođenjem testova in vivo (test ekspozicije, epikutani – Patch test, proba ubodom – Prick test, test multipnih uboda, intradermalni testovi, Prausnitz-Kustnerov test)⁴⁹ i in vitro (precipitinske reakcije, dvostruka difuzija u gelu, imunoelektroforeza, test degranulacije bazofil, Shellijev test, test limfocitne transformacije).

**Terapija oralnog Lichen planus-a**

Lečenje se sastoji u interdisciplinarnom postupku uklanjanja predisponirajućih faktora za OLP. U terapiji oralnog lichen planus-a ordiniraju se kortikosteroidi topikalno i sistemski, uz koje se primjenjuje i lokalna administracija antiseptika⁵⁰-⁵². Kortikosteroidi za oralnu aplikaciju koriste se u tečnom stanju⁵⁰. Oralnim putem, kortikosteroidi se aplikiraju u obliku tečnosti⁵⁰. Veoma efikasno se primjenjuje i penicilin u visokim dozama. Ova terapija se zasniva na delovanju penicilina na samu adherenciju streptocoka na oralne epitelne ćelije, koje se smatraju mogućim pokretačima antigenične aktivnosti keratinocita⁵².

Hiruška ekscizija, krioterapija, CO₂ laser i ND:YAG laser koriste se u terapiji OLP-a⁵³. U principu, hirurgija se ostavlja za visoko rizične slučajeve, kada je u pitanju maligna alternacija, tj. za uklanjanje visko rizičnog displastičnog područja⁵³. Fotohemoterapija je nova metoda uklanjanja rizičnih područja lihena u okviru koga se koriste ultraljubičasti A (UVA) talasi, dužine od 320 nm do 400 nm⁵⁴. Od novijih metoda, danas se sve više uvodi i relaksacija, meditacija i hipnoza, koje takođe imaju, pokazalo se, došta uticaja na osnovnu terapiju ovog oboljenja⁵⁵.

**Oral Lichen planus therapy**

The treatment consists of an interdisciplinary procedure for eliminating predisposing factors for OLP. In oral lichen planus therapy, corticosteroids are administered topically and systemically, with the use of topical administration of antiseptics⁵⁰-⁵². Oral administration of corticosteroids is conducted in the form of a liquid⁵⁰. Penicillin is administered very effectively in high doses⁶. This therapy is based on the effect of penicillin on the adherence of streptococci to the oral epithelial cells, which are considered to be possible drivers of antigenic activity of keratinocytes⁵².

Surgical excision, cryotherapy, CO₂ laser, and ND: YAG laser is used in OLP therapy⁵³. In general, surgery is performed only for high-risk cases of malignant alteration, i.e., to remove the high-risk dysplastic area.⁵³ Photochemotherapy is a new method of removing lichen risk areas using ultraviolet A (UVA) waves, 320 to 400 nm in length⁵⁴. Relaxation, meditation, and hypnosis are increasingly being used as the new methods today, which also appear to have a significant impact on the underlying therapy of the disease⁵⁵.
Treatment of reticular and papular forms of oral Lichen planus

Therapy of such oral manifestations is symptomatic. Sedatives, antimalarials, ignipuncture, vitamins with local treatment of the oral cavity and a special hygienic-diet regime are used56.

Sedatives are indicated in neurotic patients57. Hexahydrodiphene chloride (Benifen) is given 2-3 times a day after each meal57. Diazepam (Apaurin) from 2-5 mg 3 times a day is also indicated57. Antimalarials (Resorcin et al.) with unsalted diets in certain cases produce good results. It is administered 3 times a day (25 mg tablets). The treatment lasts for seven days56. If there are no gastrointestinal disorders, treatment with Resorcin is continued as follows: patients take 2 times a day one tablet for the next 7 days. In the last round of 7 days, patients take 1 tablet per day. For the next month, patients only receive maintenance doses of ½ tablet per day50.

Ignipuncture is performed under local anesthesia and can produce good results50.

Vitamins A, B, and D are used topically to coat affected areas or parenterally22.

Locally, the dentist removes dental plaque, calculus and corrects inappropriate fillings and prosthetic work. The hygiene and diet regimen includes a ban on the use of booze, hot and spicy foods, as well as smoking.

Treatment of vesicular-bullous and erosive-ulcerative forms of oral Lichen planus

Therapy for these forms of oral Lichen planus is targeted and involves relief from discomfort, healing of erosive lesions and increasing the thinness of the epithelial barrier in areas of atrophy. Corticosteroids and tuberculostatics are administered and surgical procedure is performed with these forms of oral Lichen planus, and ultraviolet radiation is rarely used50,53,54.

Corticosteroid sprays are administered parenterally and intralesionally. Semi-synthetic corticosteroid triamcinolone spray - known as Kenalog Spray is administered several times a day. Retinoic acid (0.9%) may also be administered in the form of a spray in order to reduce keratinization58.
Some patients also respond to Griseofulvin therapy. Betamethasone topical 0.1% and Fluocinonide topical 0.01% are recommended for the treatment of persistent lesions. Triamcinolone acetonide (0.1%) in a form of a rinse may be advised before taking systemic Prednisone of 40 mg.

Prednisone, Dexamethasone, and other semi-synthetic corticosteroids are administered parenterally. The parenteral dosage is as follows: for the first two weeks of therapy in order to reduce acute symptoms, high doses of cortico-preparations (1mg/kg) are administered, and then the dose is gradually reduced (by 10 mg) every three days until the appropriate maintenance dose is achieved within which changes will stagnate or disappear completely.

Intralesional administration of corticosteroids is used to avoid or alleviate their side effects, so Kenalog-40 or Kenalog-10 is applied to the erosive-ulcerative surfaces. The maximum injection is up to 3 mg and the total dose should not exceed 80 mg.

Surgical treatment is induced if the histopathological findings indicate a significant degree of dysplasia and consist of the removal of affected areas, but relapses are common.

A therapy also includes antiseptic mouthwash (with plaque control and secondary infection reduction supplement) and analgesic mouthwash (for discomfort reduction).

The use of various topical preparations - betamethasone soluble tablets (used dissolved in water for mouthwashing), sprays (beclometasone), strong steroid pomades (e.g., fluocinonide) mixed with an adhesive base - can lead to the oral candidiasis and complicate the treatment of the disease. Topical antifungal therapy is often indicated in patients with symptomatic oral Lichen planus. Oral candida superinfection may exacerbate the oral symptoms of Lichen planus, so oral candidiasis should be treated promptly. Nystatin or Amphotericin are appropriate medicines but may be inadequate in patients with soric atrophic mucosa. Therefore, miconazole gel and systemic fluconasol are more indicated.
**Zaključak**

Većina manifestnih oblika u usnoj duplji ovog oboljenja ima kompletnu benignu prirodu, tako da mogu ući u remisiju i nakon nekoliko godina. Međutim, kod malog procenta slučajeva (0,4% do 3,3%) oralne lezije prelaze u maligne promene. Iz ovog razloga, dugotrajne tokove ovog oboljenja treba pratiti i treba raditi rebiopsije, ako postoji bilo koja sumnjiva promena, kao što su nodularne, verukoze, mrljaste ili "somotno-crvene" pojave na mukozi. Pacijenta treba savetovati da prijavi bilo koje specifične promene na lezijama ili simptome. Idealno je napraviti i fotografski zapis pacijentovih promena prilikom svakog narednog kontrolnog pregleda. Postoje sugestije, da ako ima erozivnih i atrofičnih formi oralnog Lichen planus-a, postoji veća šansa za malignom transformacijom i da te slučajevre treba nadzirati kontinuirano u narednom periodu. Oralni Lichen planus je često oralno oboljenje sa kojim se susreću stomatolozi prilikom pregleda pacijenta. Neophodno je da se prisutne lezije precizno identifikuju i primeni adekvatna terapija. Pravilno uzimanje anamneze, razumevanje patogeneze i kliničke slike veoma je važno za sprovođenje adekvatnog lečenja svih oralnih manifestacija ovog, danas, veoma čestog kožnog oboljenja.

**Conclusion**

Most of the manifestations in the oral cavity of this disease have a complete benign nature, so they can go into remission after several years. However, in a small percentage of cases (0.4-3.3%), oral lesions undergo malignant changes. For this reason, the long-term course of this disease should be monitored and a rebiopsy should be performed if there is any suspicious change, such as nodular, verrucous, or “velvet-red” in the mucosa. The patient should be advised to report any specific lesion changes or symptoms. It is also ideal to make a photographic record of the patient's changes at each subsequent checkup.

There is also suggestion that if there are erosive and atrophic forms of oral Lichen planus, there is a greater chance of malignant transformation and that these cases should be monitored continuously over the coming period. Oral Lichen planus is a common oral disease encountered by dentists when examining a patient. It is imperative that the present lesions are accurately identified and an appropriate therapy should be administered. Proper anamnesis, understanding of pathogenesis and clinical presentation is very important for the adequate treatment of all oral manifestations of this, nowadays, very common skin disease.
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