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LICHEN PLANUS: ORALNE MANIFESTACIJE, DIFERENCIJALNA DIJAGNOZA I TERAPIJA

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 duplji.

Metode: Analizom literature i na osnovu kliničkog iskustva lekara ispitivane su najčešće 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 vidi 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 ležiju.

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

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

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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 retramolar area, but they can also occur in the mucous membranes of the tongue, the floor of the mouth and lips.

Keywords: *Lichen planus*, *oral manifestations*, *oral cavity*

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Uvod

Lichen planus, pored virusnih infekcija i aftoznih lezija, zauzima treće mesto među oboljenjima na oralnoj sluzokoži. Od prvih kožnih opisa *Lichen planus*-a, koje 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 Dubreuilha 1906. godine², koji je ukazao na to da patohistološka slika oralnih lezija odgovara patohistološkoj 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

- **Stres** – nervosa 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.
- **Autoimunost** – 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 antitela^{7,8,9}. U kožnim i oralnim promenama nađeni su depoziti imuno-globulina klase IgG, IgM i komplementa C3¹⁰.
- **Genetska predispozicija** – bolest je kosmopolitska, ali je dokazano da se češće javlja kod osoba sa HLA-A₃, B₅, A₂₈, B₇-B₈-DRW₉^{11,12}. Podaci o HLA markerima za oralni *Lichen planus* u mnogome zavise od ispitivane populacije^{12,13}. Žene oboljevaju češće nego muškarci, a starosnot u kojoj se oboljenje javlja je između 30 i 60 godina¹⁴. U retkim slučajevima i deca mogu oboleti.
- **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:

- **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.
- **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 antibodies^{7,8,9}. Deposits of IgG, IgM and complement C3-class immunoglobulins were found in skin and oral changes¹⁰.
- **Genetic predisposition** - this disease is cosmopolitan, but has been shown to occur more frequently in people with HLA-A₃, B₅, A₂₈, B₇-B₈-DRW₉^{11,12}. Data on HLA markers for oral *Lichen planus* are highly dependent on the studied population^{12,13}. 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 ređi 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 lichenoidnih reakcija i inflamacije gingive^{18,19}. Ranija istraživanja ukazuju na lichenoidne reakcije koje nastaju kao produkt galvanske struje, koja se stvara između metala u ustima^{19,20}. Međutim, skorašnja istraživanja ukazuju na to da inflamacija nastaje kao rezultat interakcije ćelija 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 – najmladi 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. Bulozni 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 inflammation^{18,19}. Earlier research indicates that lichenoid reactions occur as a product of galvanic potential between metals in the mouth^{19,20}. 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 reticular, plaque-shaped, erosive and atrophic²³. 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. Bolest se javlja u vidu beličastih papula veličine čiodine glave. Uočavaju se u vidu beličastih linija ili traka. Pojedinačno, papule se mogu videti jedino lupom. Ovaj oblik često se vidi na obraznoj sluzokoži u obliku belih niti, koje su blago uzdignute iznad sluzokože. Ove linije se nazivaju i Vikamove strije²⁴. Ova forma oboljenja lokalizuje se u predelu okluzalne linije, na retromolarnom predelu, na ivicama jezika, na labijalnoj i bukalnoj površini fiksne gingive, na semimukozi usana i tvrdom nepcu²⁴. Najređe se javlja na mekom nepcu i podu 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.

Lichen planus u obliku plaka

Lichen planus u ovom obliku može se videti kao tanak sloj plaka različitih veličina, glatke i nešto svetlijе površine, u odnosu na lokalno tkivo. Najčešće lokalizacije su obraz, nepce, jezik i gingiva, a retko pod usne duplje i rumeni deo usana. Kada je reč o histološkoj slici površinskih slojeva epitela prisutne su parakeratoza i hiperkeratoza, a u subepitelnom sloju limfocitni infiltrat²⁵. Ovaj tip *Lichen planus-a* načešće se sreće kod pušača¹⁶. *Lichen planus* u plakovnoj formi često alterira u malignu formu zajedno sa erozivnim i atrofičnim oblicima²⁵.

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 nepcu²⁶. 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 limfocitima²⁶. Bolest počinje bez simptoma, a ukoliko se i javi, smetnje su veoma blage i javljaju se u vidu zatezanja i hrapavosti sluzokože, suvoće, blagog peckanja i žarenja u ustima. Prognoza je dobra, mada retko može doći do spontanog povlačenja promena. Kod ovih varijanti, epiteljalne promene su hiperkeratotične ili obično hiperortokeratotične²⁷.

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 whitish lines or bands. Individual papules can only be seen with a magnifying glass. This type is often seen in the facial mucosa, in the form of white filaments slightly raised above the mucosa. These lines are also called Wickham's striae²⁴. They are localised in the area of the occlusal line, the retromolar area, the edges of the tongue, the labial and buccal surfaces of the fixed gingiva, to the submucosa of the lips and the hard palate²⁴. It occurs most rarely in the soft palate and the floor of the mouth. Subepithelial tissue always has a thick lymphocyte infiltration. This type of *Lichen planus* rarely goes into a malignant form. It often occurs along with other 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 infiltrate²⁵. This type of *Lichen planus* is most commonly seen in smokers¹⁶. The *Lichen planus*, in plaque form, often alters to malignant form along with erosive and atrophic forms²⁵.

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 palate²⁶. They are usually individual, but can also produce white creases. Mucosal inflammation is present. Histologically, parakeratosis and hyperkeratosis are expressed in the upper layers, while diffuse lymphocyte infiltration is present in subepithelial layer²⁶. 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 hyperkeratotic²⁷.

Nema atrofije epitelijuma, pa, prema tome, ni ulceracija. Kod nekih pacijenata lezije mogu biti konfluentne i podsećati na leukoplakiju, gde, po redu, može biti papularni, linearni ili prstenasti raspored belih područja²⁸. Pošto su generalno ove lezije asimptomatske, često se otkrivaju slučajno od strane pacijenta ili pri redovnim stomatološkim kontrolama od strane stomatologa.

Erozivno-ulcerozna forma Lichen planus-a

Ovo je veoma česta forma oboljenja. Lokalizuje se na obraznoj sluzokoži, gingivama, jeziku, nepcu i podu usne duplje. Najfređe se javlja na rumenom delu usana. Ovu formu Lichen planus-a karakteriše destrukcija oralnog epitela²⁹. Jayljaju se bule, a njihovim prskanjem nastaju erozivno-ulcerozne površine nepravilnog oblika i različite veličine. Ulcerozne površine prekrivene su žućastim fibrinoznim eksudatom i okružene su inflamiranim zonom. Erozivno-ulcerozne promene uglavnom nastaju kao posledica prskanja bula, ali postoje slučajevi kada one nastaju i bez predhodnog obrazovanja buloznih eflorescenci³⁰.

Subjektivne tegobe bolesnika su izrazite, praćene bolom koji prati ishranu, govor i konzumiranje tečnosti. Nelagodnosti i bolovi mogu biti prisutni i spontano²⁹. Mukoza je osjetljiva na mehaničke iritacije i dentalnu traumu, pre nego što se druge karakteristične lezije javi. Ove lezije imaju sjajne površine i tendenciju da se odvoje od susedne mukoze jasnom demarkacionom ivicom^{29,30}.

Histološki se vide degenerativne promene bazalnog sloja epitela sa znacima atrofije i pojmom erozija i ulceracija³¹. Oko erozivno-ulceroznih promena u epitelu izražena je čelijska infiltracija sa dominacijom neutrofilnih granulocita, dok je u subepitelu prisutna limfocitna infiltracija.

Erozivno-ulcerozna forma *Lichen planus-a* može se transformisati u maligni proces zbog moguće lichenoidne degeneracije³⁰. Postoje tri oblika erozivnog *Lichen planus-a*: bulozni, atrofični i ulcerozni oblik.

Bulozni oblik karakteriše pojava vezikula i bula ispunjenih bistrim seroznim sadržajem, sa mogućom eritrocitnom hemoragijom. Ovi oblici oboljenja nastaju nagomilavanjem tečnosti u subepitelnom vezivnom tkivu³².

Zbog tankog omotača samih vezikula, pri govoru i jelu, one pucaju i dolazi do bolnih senzacija³².

There is no epithelial atrophy and therefore no ulceration. In some patients, the lesions may be confluent and resemble leukoplakia, where there may be a papular, linear, or annular arrangement of white areas²⁸. As these lesions are generally asymptomatic, they are often detected accidentally by the patient or at regular dental checkups by the dentist.

Erosive-ulcerative form of Lichen planus

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 vermillion. This form of Lichen is characterized by the destruction of the oral epithelium²⁹. When bullae occur, their bursting results in irregularly shaped erosive-ulcerative 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 efflorescence³⁰.

Patients' subjective ailments are pronounced, with the pain accompanying diet, speech and fluid consumption. Discomfort and pain can also be present spontaneously²⁹. 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^{29,30}.

Histologically, degenerative changes of the basal layer of the epithelium with signs of atrophy and the appearance of erosions and ulceration are seen³¹. 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 degeneration³⁰. 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 tissue³². Due to the thin coating of the vesicles, they burst when speaking and eating and lead to painful sensations³².

Ovaj oblik najčešće se vidi na bukalnoj sluzokoži. U bazalnom sloju epitelia izražena je hidropsna degeneracija. Dominantna je infiltracija limfocitima, koja se povećava posle prskanja bula^{32,33}. Subjektivne smetnje su jako izražene i postoje bolovi prilikom užimanja hrane, a prisutni su i spontani bolovi. Ove dve forme moraju se redovno kontrolisati zbog mogućnosti maligne alteracije.

- Atrofični oblik (eritematozni oblik) predstavlja redi 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*)¹⁰. Ova atrofična forma može se javiti i kao rezultat zarastanja erozivno-ulceroznih oblika i manifestovati se epitelnom atrofijom. Promene na gingivi najčešće su izražene u gornjoj vilici u predelu fiksne gingive u obliku ograničenih atrofičnih pora. Gingivalni epitel postaje tanak i suv, pa je sklon povredama, dok u bazalnom sloju postoji hidropsna degeneracija, a u subepitelnom sloju uočava se gusta infiltracija limfocitima^{10,19}.

- Ulcerozni oblik – ovu formu *Lichen planus-a* karakteriše destrukcija oralnog epitelia. Ulcerozne površine su pokrivene beličasto-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 bukalnoj sluzokoži³⁴.

- 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 konvertirni enzimski ((ACE)) inhibitori), antimalariske, fenilamino-pirimidinske derivata (Imatinib) i injekcije zlata (Tabela 1)^{35,36}. Lokalizovane lichenoidne reakcije mogu biti udružene sa hipertenzivnim reakcijama na merkurijalne soli oslobođene iz amalgamskih nadogradnjai²⁰. Ovako nastale lichenoidne reakcije mogu se svrstati u IV tip reakcija hipersenzitivnosti³⁷.

Kod lichenoidne reakcije, erupcije imaju tendenciju ka unilateralnoj pojavi.

This form is most commonly seen on buccal mucosa. Hydropic degeneration is expressed in the basal layer of the epithelium. Lymphocyte infiltration is dominant, which increases after bursting of bullae^{32,33}. Subjective ailments are very pronounced, pain is aggravated by eating, and also a spontaneous pain is present. These two forms must be regularly monitored for the possibility of malignant alteration.

- **The atrophic form** (erythematous form) is a less common form of *Lichen planus*. It most commonly occurs on the dorsal side of the tongue and gingiva. The epithelium of the tongue is atrophic, becoming thin with pronouncedly redness and inflammation. Filiform and fungiform papillae disappear and the tongue is smooth and polished (*Lingua glabra*)¹⁰. This atrophic form can also occur as a result of the healing of erosive-ulcerative forms and manifest itself with epithelial atrophy. Gingival changes are most commonly expressed in the upper jaw in the fixed gingival area, in the form of limited atrophic pores. The gingival epithelium becomes thin and dry so it is prone to injuries, while in the basal layer there is a hydropic degeneration, and dense lymphocyte infiltration is observed in the subepithelial layer^{10,19}.

- **The ulcerative form** is characterized by destruction of the oral epithelium. The ulcerative surfaces are covered with whitish-yellowish fibrinous exudates and are surrounded by an inflammation zone on the part of the mucosa corresponding to the zone of inflammation. Ulcerative lesions are the result of damaged bullae, but they can also occur without the formation of bullous efflorescences.

The two particular forms that occur in this disease are Grinspan syndrome and lichenoid reactions.

- **Grinspan syndrome** is a form of oral *Lichen planus* that occurs with Diabetes mellitus and hypertension. Often, skin changes are also pronounced, and changes in the mouth are most common in the buccal mucosa³⁴.

- **Lichenoid reactions** can be induced by drugs or other substances. Numerous drugs can participate in lichenoid eruptions (LDEs) including non-steroidal anti-inflammatory drugs (NSAIDs), antihypertensive drugs (especially angiotensin converting enzyme (ACE) inhibitors), antimarialials, phenylaminopyrimidine derivatives (Imatinib) and gold injections (Table 1)^{35,36}. Localized lichenoid reactions may be associated with hypertensive reactions to mercury salts released from amalgam superstructures²⁰.

Dijagnoza se postavlja na osnovu biopsije i hematološki indirektne imuno-fluorescencije, gde se vidi niz od perli, kao potvrda lichenoidne erupcije³⁷. 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 šara³⁸. Mišljenje je da lekovi samo prikrivaju latentno oboljenje *Lichen planus* ili širenje predhodnog poremećaja, pre nego što indukuju novo oboljenje³⁸.

The resulting lichenoid reactions can be classified as type IV hypersensitivity reactions³⁷. 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 eruption³⁷. 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 occurs³⁸. It is thought that medications only mask the latent disease of *Lichen planus* or the spread of a previous disorder, before inducing a new disease³⁸.

Tabela 1. Lekovi koji mogu izazvati lichenoidnu reakciju
Table 1. Medications that can trigger a lichenoid reaction

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

Dijagnoza oralnog *Lichen planus*-a

Dijagnostika OLP-a sastoji se od kliničkog pregleda, uzimanja uzoraka za patohistološku dijagnozu i histohemiske ili imunohistohemiske 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 epitelia;
 -kod kožnih lezija moguća je pojava i tzv. "testerastih zuba"²⁴.

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:
 -hyperkeratosis and parakeratosis of the upper layers,
 -hydropic 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 lesions²⁴.

Imunofluorescentna ispitivanja rade se iz lihenskih papula gde se uočavaju agregati IgG-a, IgM-a i komponente komplementa C₃. Čelijski infiltrat u *lamini proprii* sastoji se od T-limfocita, i to većeg procenta T₄ limfocita u odnosu na T₈ limfocite³⁸. Čistu predominaciju T₄ limfocita u odnosu na T₈ limfocite u *lamini proprii* kod *Lichen planus*-a, u odnosu na njihov odnos u normalnoj mukozi (npr. kod Leucoplakie), treba podvući, zato što ovo može biti važan diferencijalno-dijagnostički podatak. Aktivirani T-limfociti sekretuju interferon, koji zauzvrat indukuje sintezu HLA-DR od strane keratocita⁴⁰. Producija interleukina od strane T₄ limfocita aktiviraju T₈ limfocite, koji svoju citotoksičnost usmeravaju na keratocite. Citotoksičnost može biti povećana prisustvom HLA-DR klase II antiga na membrani keratocita⁴⁰. Kod *Lichen planus*-a, brojni keratociti, pozitivni za HLA klasu II antiga, bili su prisutni u nivou bazalne membrane⁴¹. Takođe se u epitelu može naći znatna količina Langerhansovih ćelija⁴¹. Ovo povećanje Langerhansovih ćelija i bazalnih keratocita, pozitivnih za HLA klasu II antiga, može imati dijagnostičku značajnost kada se upoređuju lezije *Lichen planus*-a sa drugim oralnim lezijama^{40,41}.

Diferencijalna dijagnoza *Lichen planus*-a

Diferencijalno-dijagnostički, u obzir dolaze sve bele lezije koje imaju oralnu manifestaciju:

- **Leucoplakia** – promene kod leukoplakije su asimetrične i predstavljaju objedinjenu površinu bele boje, dok okolna sluzokoža nije inflamirana²⁸. Kod *Lichen planus*-a promene su simetrične, mrežastog izgleda, sa inflamiranom okolnom sluzokožom. U nejasnim slučajevima dijagnoza se utvrđuje biopsijom.
- **Sunderasti nevus obraz** – javlja se na sluzokoži obraza odmah nakon rođenja. Sluzokoža je beličasta, sunđerasta i zgusnuta⁴². Nekada je moguće beličaste naslage mehanički ukloniti, pa se vide i delovi normalne sluzokože⁴², što je kod *Lichen planus*-a nemoguće odraditi. U postavljanju dijagnoze pomažu i histološka ispitivanja – karakterističan je nalaz hiperplazije, a *lamina propria* je normalna, sa blagom infiltracijom ćelija inflamacije u subepitelu.

Immunofluorescence 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 T₈³⁸. 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 keratocytes⁴⁰. 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 membrane⁴¹. When it comes to *Lichen planus*, a numerous keratocytes positive for HLA class II antigens were present at the basement membrane level⁴¹. A considerable amount of Langerhans cells can also be found in the epithelium⁴¹. 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^{40,41}.

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 inflamed²⁸. In *Lichen planus*, the changes are symmetrical, reticulate, with inflamed surrounding mucosa²⁸. In ambiguous cases, the diagnosis is established by the biopsy.
- **Sponge cheek nevus** - appears on the mucous membranes of the cheeks immediately after birth. The mucous membrane is whitish, with spongy like tissue and high density⁴². It is sometimes possible to remove the whitish plaque mechanically, so that parts of normal mucosa can also be seen⁴², 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 teleangiektatičnim proširenjima krvnih sudova, koji grade karakteristični haloo⁴³. U histološkoj slici *Erythematodes*-a postoje hiperkeratoza, hidropsna degeneracija bazalnog sloja epitela, degeneracija kolagenih vlakana u vezivnom tkivu sa perivaskularnom infiltracijom limfocita⁴³. Histološka slika *Lichen planus*-a bitno se razlikuje.

Mehanička oštećenja oralnog epitela nastaju kod neurotičnih osoba zbog grickanja 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 je nepravilnih beličastih zgrušavanja sa diskretnim erozijama⁴³. 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*-a²⁵.

Kandidoza – hronične forme, lokalizovane na sluzokoži obraza, mogu da se javе u obliku belih linija. Moguća je izražena suvoća i gubitak fleksibilnosti epitela, pa nastale promene pokazuju sličnost sa *Lichen planus*-om⁴⁴. Patohistološkim nalazom, kod kandidoze vide se spongioza i infiltracija epitela neutrofilnim granulocitima, kao i hiperplazija epitela⁴⁴.

Pemphigus vulgaris – diferencijalno-dijagnostički u obzir dolaze samo erozivno-ulcerozne i vezivno-bulozne forme *Lichen planus*-a³⁰. Dijagnostička razlika uočava se mikroskopskim nalazom segregovanih Cankovih ćelija, kojih nema kod *Lichen planus*-a, kao i nalazom akantolitičnih ćelija u intraepitelijalnim bulama⁴⁵.

Pemphigoid mucosae oris – ova dermatоза koristi se u diferencijalnoj dijagnozi buloznih formi *Lichen planus*-a, jer je karakteriše prisustvo keratotičnih belih lezija, kao i činjenica da je prisutnija kod starijih osoba ženskog pola⁴⁶.

Lingua geographica – diferencijalno-dijagnostički, ova pojava je akutnog, benignog toka, a promene se spontano javljaju i gube. Nisu fiksног karaktera, već migriraju na druga područja jezika⁴⁷, za razliku od *Lichen planus*-a, koji je hronično i na terapiju rezistentno oboljenje, dok su promene koje se javljaju na jeziku fiksног karaktera⁴⁷.

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 halo⁴³. 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 lymphocytes⁴³. 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 whitish coagulation with discrete erosion⁴³. Localization is always in the area of the occlusal line. These mechanical defects do not show polymorphism in the form of white mesh formations, lines or plaque as is the case with *Lichen planus*²⁵.

Candidosisa - 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*⁴⁴. Spongiosis and infiltration of the epithelium by neutrophilic granulocytes are seen in the pathohistological findings in candidosis, as well as epithelial hyperplasia⁴⁴.

Pemphigus vulgaris – Differential-diagnostic, only the erosive-ulcerative and connective-bullous forms of *Lichen planus* are considered³⁰. 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 bullae⁴⁵.

Pemphigoid 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 women⁴⁶.

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 tongue⁴⁷, unlike *Lichen planus*, which is a chronic and therapy-resistant disease, while changes occurring in a tongue are of a fixed character⁴⁷.

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-Küstnerov test)⁴⁹ i *in vitro* (precipitinske reakcije, dvostruka difuzija u gelu, imunoelektroforeza, test degranulacije bazofila, Sholliev 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 primenjuje i lokalna administracija antisептика⁵⁰⁻⁵². Kortikosteroidi za oralnu aplikaciju koriste se u tečnom stanju⁵⁰. Oralnim putem, kortikosetroidi aplikuju se u obliku tečnosti⁵⁰. Veoma efikasno se primjenjuje i penicilin u visokim dozama. Ova terapija se zasniva na delovanju penicilina na samu adherenciju streptokoka na oralne epitelne ćelije, koje se smatraju mogućim pokretačima antigene aktivnosti keratinocita⁵².

Hiruška ekskizija, 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 alteracija, 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, dosta uticaja na osnovnu terapiju ovog oboljenja⁵⁵.

Erythema exudativum multiforme – differential diagnosis is mainly a clinical one. If necessary, it is virological (exclusion of primary HSV infection). A biopsy is not indicated. Immunohistochemical studies may indicate the presence of immune responses in the basement membrane area (fibrinogen, IgM, C₃)⁴⁸.

Stomatitis allergica – may be different from the erosive-ulcerative form of *Lichen planus* on the basis of anamnesis, clinical picture and in vivo tests (exposure test, epicutaneous Patch testing, puncture test - Prick test, multiple stab test, intradermal tests, the Prausnitz-Küstner test)⁴⁹ and in vitro (precipitin reactions, double diffusion in gel, immunoelectrophoresis, basophil degranulation test, Shelly's test, lymphocyte transformation test).

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.

Lečenje retikularnih i papuloznih formi oralnog Lichen planus-a

Terapija ovakvih oralnih manifestacija simptomatskog je karaktera. Koriste se sedativi, antimalarici, ignipunkcija, vitamini sa lokalnom obradom usne duplje i posebnim higijensko-dijjetetskim režimom⁵⁶.

Sedativi su indikovani kod neurotičnih bolesnika⁵⁷. Daje se heksahidroadifen-hlorid (benifen) 2 do 3 puta dnevno, po jedna dražeja posle jela⁵⁷. Indikovan je i diazepam (apaurin) u dozi od 3 dražeje od 2 mg do 5 mg dnevno⁵⁷. Antimalarici (resorchin i dr.) uz neslanu dijetu u izveznim slučajevima daju dobre rezultate. Primenjuju se u tebletama od 25 mg 3 puta dnevno po jedna tableta. Lečenje traje sedam dana⁵⁶. Ukoliko nema gastrointestinalnih smetnji, lečenje resorchinom nastavlja se na sledeći način: bolesnici sledećih 7 dana piju 2 puta dnevno po jednu tabletu. U poslednjoj turi od 7 dana bolesnici ordiniraju po jednu tabletu dnevno. U sledećih mesec dana bolesnici primaju samo doze za održavanje od ½ tablete dnevno⁵⁰.

Ignipunkcija se izvodi pod lokalnom anestezijom i može dati dobre rezultate⁵⁰.

Vitamini A, B i D lokalno se koriste za premazivanje obolelih mesta ili parenteralno²².

Lokalno, stomatolog odstranjuje zubne naslage – dentalni plak, zubni kamenac i izvršava korekciju neprikladnih radova (loše plombe i protetski radovi). Higijensko-dijjetetski režim obuhvata zabranu upotrebe žestokih pića, ljute i jako začinjene hrane, kao i pušenja.

Lečenje bulozno-vezikuloznih i erozivno-ulceroznih formi oralnog Lichen planus-a

Terapija za ove oblike oralnog *Lichen planus*-a ciljana je i ima u vidu oslobođanje od nelagodnosti, zarašćivanje erozivnih lezija i povećanje epitelijalne istanjenosti na područjima atrofije. Kod ovih formi oralnog *Lichen planus*-a primenjuju se kortikosteroidi, tuberkulostatici, vrši se hirurški zahvat, a ređe se koristi i ultravioletno zračenje^{50,53,54}.

Kortikosteroidi aplikuju se u vidu spreja, parenteralno i intralezijski.

Kada govorimo o upotrebi u obliku spreja, koristi se polusintetski kortikosteroid triamcinolom sa halkinolom – poznat kao Kenalog S. Aplikuje se nekoliko puta dnevno.

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 (Resorchin 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 Resorchin 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 used^{50,53,54}.

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.

U obliku spreja može se dati i retinoidna kiselina (0,9%) sa ciljem da redukuje keratinizaciju⁵⁸. Neki pacijenti reaguju i na terapiju grizeofulvinom⁵⁹. Za uporne lezije preporučuju se i betametazon (0,1%) i fluocinonid (0,01%), za lokalnu upotrebu⁵⁹. Može se savetovati i briancinolon acetonid (0,1%), za ispiranje pre uzimanja sistemskog prednisona od 40 mg⁶⁰.

Parentralno, daju se prednison, dexamethason i drugi polusintetski kortikosteroidi⁵³. Parentralna terapijska doza prepisuje se na sledeći način: prve dve nedelje terapije, radi smanjenja akutnih simptoma, ordiniraju se visoke doze kortiko preparata (1 mg/kg), a zatim se doza postepeno smanjuje (po 10 mg) na svaka tri dana, sve do odgovarajuće doze održavanja pomoću koje će promene stagnirati ili potpuno nestati⁶¹.

Intralezijsko davanje kortikosteroida primenjuje se da bi se izbegla ili ublažila njihova sporedna dejstva, pa se Kenalog 40 ili Kenalog 10 aplikuju u same erozivno-ulcerozne površine. Inicira se najviše do 3 mg, a ukupna doza ne sme biti veća od 80 mg⁶¹.

Hirurško lečenje je indukovano ako histopatološki nalaz pokazuje značajan stepen displazije, a sastoji se u odstranjivanju obolelih mesta, uz česte recidive⁵³.

U okviru terapije uključuju se i antiseptične vodice za ispiranje usta (sa dodatkom za kontrolu plaka i redukciju sekundarne infekcije)⁶² i analgetične vodice (za redukciju nelagodnosti)⁶².

Upotreba raznih topikalnih preparata – solubilne betametazonske tablete (koriste se rastvorene u vodi i služe za ispiranje usta), sprejevi (beklometason), jake steroidne pomade (npr. fluocinonid) pomešane sa nekom adhezivnom bazom – mogu dovesti do pojave oralne kandidoze i zakomplikovati tretman bolesti⁶³. Topikalna antifungicidna terapija često je indikovana kod bolesnika sa simptomatskim oralnim *Lichen planus*-om⁶⁴. Superinfekcija oralnom kandidom može egzacerbirati oralne simptome *Lichen planus*-a, pa zbog toga treba na vreme početi sa lečenjem oralne kandidoze. Nystatin ili amphotericin odgovarajući su medikamenti, ali mogu biti neprihvatljivi kod pacijenata sa soričnom atrofičnom mukozom⁶⁵. Zbog toga su miconasol gel i sistemski fluconasol više indikovani⁶⁶.

Some patients also respond to Griseofulvin therapy⁵⁹. 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 mg⁶⁰.

Prednisone, Dexamethason, and other semi-synthetic corticosteroids are administered parenterally⁵³. 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 completely⁶¹.

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 mg⁶¹.

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 common⁵³.

A therapy also includes antiseptic mouthwash (with plaque control and secondary infection reduction supplement)⁶² and analgesic mouthwash (for discomfort reduction)⁶².

The use of various topical preparations - betamethasone soluble tablets (used dissolved in water for mouthwashing), sprays (beclomethasone), strong steroid pomades (e.g. fluocinonide) mixed with an adhesive base - can lead to the oral candidiasis and complicate the treatment of the disease⁶³. Topical antifungal therapy is often indicated in patients with symptomatic oral *Lichen planus*⁶⁴. 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 mucosa⁶⁴. Therefore, miconazole gel and systemic fluconasol are more indicated⁶⁶.

Zaključak

Većina manifestnih oblika u usnoj duplji ovog oboljenja ima kompletну 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 sumnjičiva promena, kao što su nodularne, verukozne, mrljaste ili "somotno-crvene" pojave na mukozi. Pacijenta treba savetovati da prijavi bilo koje specifične promene na lezijama ili simptome. Idealno je napraviti i fotografiski 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 slučajevе 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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