Oral lichen planus *

Líquen plano oral

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Abstract: Oral lichen planus (OLP) is a relatively common mucosal disease that can present isolated or associated with cutaneous lichen planus. Contrarily to its cutaneous counterpart, though, OLP tends to be chronic, relapsing, and difficult to treat. Severe morbidity is related to erosive forms, and more aggressive presentations have been described, such as the "gingivo-vulvar syndrome". This article reviews the current knowledge about the pathogenesis, clinical picture, differential and laboratorial diagnosis, prognosis, and treatment of OLP.
Keywords: Lichen planus; Lichen planus, oral; Oral medicine

Resumo: O líquen plano da mucosa oral (LPO) é afecção relativamente comum, que pode aparecer isolado ou associado ao líquen plano cutâneo, havendo, no entanto, significantes diferenças clínico-evolutivas: o LPO tende a ser crônico, recidivante e de difícil tratamento, levando a importante morbidade, principalmente em sua forma erosiva. Novas formas clínicas agressivas têm sido salientadas na literatura, como a forma gingivo-vulvar. Este artigo revisa a etiopatogenia, as formas clínicas, a diagnose diferencial e laboratorial, a prognose e o tratamento do LPO, além de mencionar, brevemente, a experiência dos autores com esta enfermidade, vivida no Ambulatório de Estomatologia da Divisão de Dermatologia do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo.
Palavras-chave: Líquen plano; Líquen plano bucal; Medicina bucal

INTRODUCTION

Lichen planus is a T-cell mediated chronic inflammatory mucocutaneous disease of unknown cause. [1] It is characterized by a papular skin eruption that occurs in most cases between 30 and 60 years of age; however, occurrence in children has been increasingly observed. [2-4] It may affect the mucous membranes, particularly the oral and genital mucosa, and very rarely, the mucosa of the anus, nose, larynx, conjunctiva and urethra. Oral mucosal lesions occur in 50 to 70% of the patients with lichen planus and may be exclusive in 20 to 30% of them. [5-7] Nonetheless, skin lesions of lichen planus were observed in 15% of the patients with diagnosis of oral lichen planus (OLP). [8] It is estimated that the prevalence of OLP varies from 0.5 to 4% of the general population, [9-13] being more common in females.[2,7,14-16] A hundred and three patients with OLP were treated at the Outpatient Clinic of Stomatology, Division of Dermatology, Clinics Hospital, University of Sao Paulo School of Medicine, between 2003 and 2010; 33 of these patients were men and 70, women (unpublished data). The objective of this study is to review the etiopathogenesis, clinical manifestations, diagnosis and treatment of OLP.

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ETIOPATHOGENESIS

Although it is believed that OLP is a T-cell mediated autoimmune disease, its cause remains unknown. [17] Current evidence suggests that the disease is related to an alteration of cell-mediated immunity, triggered by endogenous or exogenous factors, which results in an altered response to autoantigens. [18,19] Most activated T cells in the inflammatory infiltrate of OLP are CD8 +.[20,21] Activated T cells of the inflammatory infiltrate, associated with increased production of Th1 cytokines (IL-1, IL-8, IL-10, IL-12, TNF-α) increase the expression of intercellular adhesion molecules (ICAM-1) on Langerhans cells and macrophages, leading to presentation of major histocompatibility complex antigens by keratinocytes. This altered immune response results in apoptosis of keratinocytes in the basal layer and may determine disease activity.[22-27] Other mechanisms that may also be involved in the etiopathogenesis of the disease are mast cell degranulation and activation of matrix metalloproteinases.[13] Moreover, some researchers believe that the chronicity of OLP can be partly explained by a deficiency in the mechanisms of immunosuppression mediated by transforming growth factor beta; [28] however, the causes that lead to the onset of the process have not yet been fully clarified.

The relationship between OLP and hepatitis C virus is not stable, since the prevalence of this virus in patients varies based on studies, ranging from 0% to over 60%, according to the country where these studies are conducted. [1, 29-32] The rates of HCV infection in patients with LP appear to be high in Japan, Italy and Brazil [33] and low in the U.S., France, Nordic countries, UK and Germany. [31] However, results in Brazil are controversial, as a recent study shows. [34] Data by these authors show a frequent observation in our clinical practice: it is rare to diagnose HCV positivity in patients with OLP, but it is common to see OLP in individuals known to be carriers of the virus.

The difference in the prevalence of HCV infection in different geographic locations may not have been clearly explained, but it is believed to be due to differences in the socioeconomic status and to the selection bias of the subjects studied (mean age and gender) in their respective countries . [1,31,35] Given this geographical heterogeneity, the hypothesis that some genetic change may facilitate the development of OLP in a subgroup of patients with hepatitis C has been raised [31,32] A recent meta-analysis of the literature led us to conclude that " HCV infection is associated with a statistically significant risk for the development of OLP, suggesting that the presence of either HCV or certain types of lichen planus can be used as predictive markers of one another in certain geographical regions."[33] Therefore, it is suggested that research of liver abnormalities or HCV infection in patients with OLP should be conducted only in individuals with suspicious clinical and epidemiological history.

Genetic polymorphisms of several cytokines also appear to be associated with the clinical presentation of the disease. Interferon- polymorphisms have been associated to lichen planus with exclusive oral involvement, and TNF-α polymorphisms have been associated with forms that affect the oral mucosa and skin. It is, however, hasty to say that OLP is a genetically determined disease. These findings must be confirmed by studies conducted in different geographical areas. [19]

A severe form of the disease, the so-called "vulvovaginal-gingival syndrome" of lichen planus appears to be associated with an HLA class II allele (HLA-DBQ1). [36]

Another interesting aspect to be discussed is the presence of lesions identical to those of lichen planus in graft *versus* host disease (GVHD). Clinical and histopathological findings of lichenoid oral lesions in chronic GVHD are indistinguishable from idiopathic OLP lesions. In GVHD, donor T lymphocytes attack tissue antigens of the minor histocompatibility complex of the host cell. Thus, GVHD appears as an interesting model in the study of the pathophysiology of OLP. [32]

Several authors have also shown that oral lichenoid reactions may result from contact with dental restoration materials, especially those containing amalgam, metallic mercury or ammoniated mercury. This can be shown in those cases in which the replacement of these materials leads to the improvement of OLP lesions, a fact mainly observed when there are no skin lesions and all oral lesions are in contact with the restorations. [1,32,37-40]

The importance attributed to psychological factors varies according to the authors; there is controversy over whether psychiatric disorders (anxiety, depression) are involved in the genesis of the disease or are a consequence of chronic painful lesions. In a study of 16 patients with OLP without mental complaints and without subjective need for psychiatric help, psychiatric examination showed that 5 of them had a moderate disorder and one had signs of "neurosis." Association with depression [41] is reported by some authors and refuted by others. [41,42]

CLINICAL MANIFESTATIONS

OLP may present in the following forms: reticular, atrophic, papular, erosive, bullous and erythematous. These different clinical presentations represent

variations of intensity and duration of the disease (Figures 1-6). These different forms may present simultaneously, and the predominant clinical morphology can change over time in the same patient.[43,44] OLP lesions are often bilateral and symmetrical, which differentiates them from contact lichenoid reactions of the oral mucosa. Unilateral lesions of OLP are rare and atypical. [41] The most affected sites are the buccal and gingival mucosa, back of the tongue, lip mucosa and lip vermilion. [2,4,43-45] The gingival mucosa is frequently affected, and the disease presents in the form of "chronic desquamative gingivitis." OLP lesions may appear at sites of trauma (koebnerization).

The primary lesion of OLP is a small opalescent papule, whitish and keratotic (not removable with a spatula). Lesions may be isolated or assume different patterns; for instance, arboriform, striated or annular. These features are commonly found bilaterally in the buccal mucosa. [2,6,46-50] Lesions at the back of the tongue tend to be more keratotic, isolated or plaque-like, due to the peculiar characteristics of this epithelium.[2,6,46,47] Lesions of long evolution tend to become atrophic due to epithelial tissue correction. Depapillation of the tongue caused by atrophy may result in gustatory changes, with consequent burning upon contact with certain foods.

In the erosive form, bright red well-demarcated erosions are observed, characteristically surrounded by typical papulae. When the disease progresses rapidly, bullae may be rarely observed. Pain is usually intense and can affect the patient's quality of life. [48,49]

Lesions identical to those described above may also appear in the lip vermillion and tend to diffusely affect this area; however, they almost always respect the boundary between the lip vermillion and skin of the lip, unlike some other cheilitis.

The presentation form of "desquamative gingivitis" is peculiar, and can occur isolated or associated with lesions in other areas. Painful erosions, which interfere with tooth brushing, are observed in the gingival mucosa. [45,47-49]

Residual mucosal pigmentation is common in dark-skinned individuals, often associated with the presence of active lesions (lichen planus pigmentosum).

Lesions resulting of the reaction caused by contact of the mucous membranes with dental restorations containing metal are indistinguishable from those of idiopathic lichen planus, except for the fact that they are asymmetrically distributed in the mucosa, because they are near dental restorations. [1,33,37-39] Of the 103 patients, 4 presented these characteristics (unpublished data).

There appears to be no correlation between the extent and severity of oral and skin lesions of lichen planus. [8] Concomitant extraoral involvement such as scalp, nails, conjunctiva, esophagus, larynx, urethra, vagina, vulva and perianal region can result in severe morbidity. The association between severe forms of oral and vulvar lichen planus has been recently highlighted ("vulvovaginal-gingival syndrome"). [36,50,51]

Several publications, especially articles in dental journals, address a supposedly "premalignant" potential of OLP lesions. Indeed, several studies have been conducted on the subject, with essentially inconclusive results with regard to possible "risks of malignancy" [1,52-55]. In our opinion, the development of squamous-cell carcinoma in lesions of lichen planus

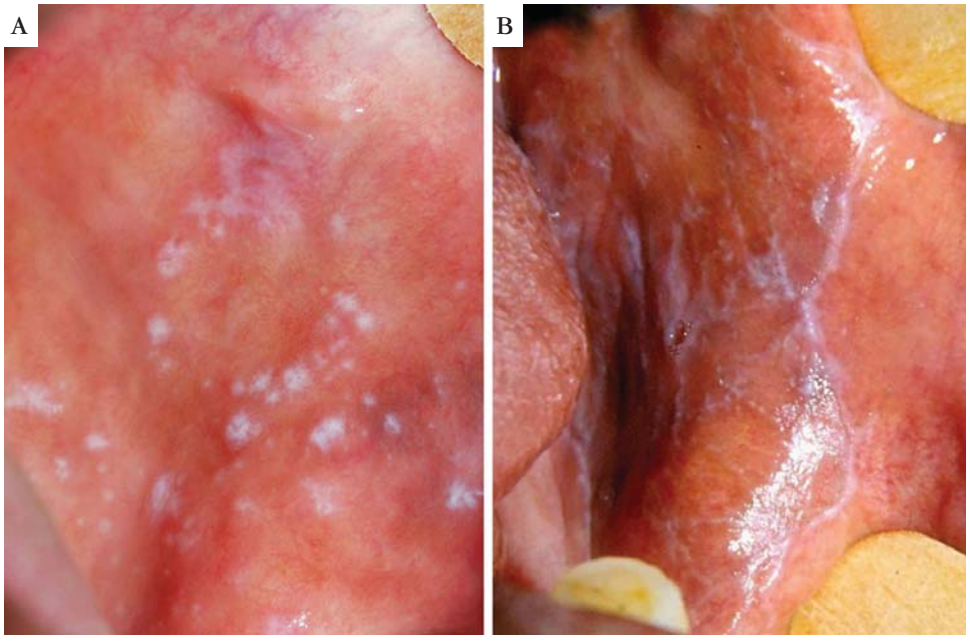

Figure 1: A. To the left: typical keratotic papules; B. To the right: confluence of reticular lesions

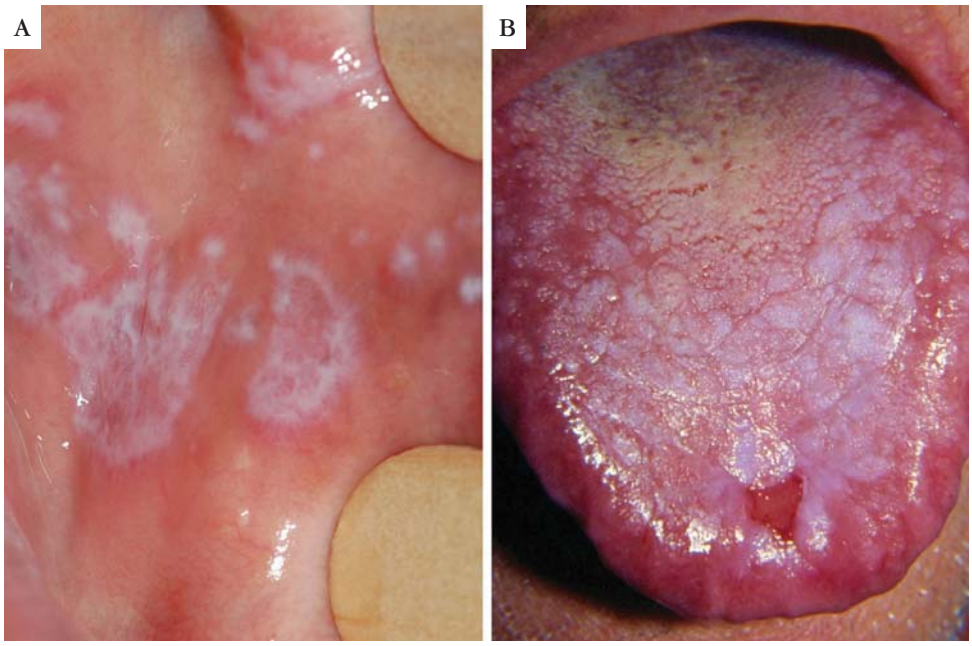

Figure 2: A. To the left: confluence of annular lesions; B. To the right: symmetrical papules forming a keratotic plaque, atrophy and erosion symmetrically distributed

only occurs in very old atrophic-cicatricial lesions, but this is rare. Dermatologists are very familiar with thi situation when it affects the skin, but this phenomenon may involve the mucous membranes (Marjolin's ulcer). Other conditions that may present atrophic-cicatricial lesions in the oral mucosa may also be rarely associated with carcinomas, such as lupus erythematosus and syphilitic glossitis. [56] Among our 103 patients, three presented with lesions of squamous-cell carcinoma associated with OLP, all of whom with highly cicatricial disease of long evolution (unpublished data).

Unlike cutaneous lichen planus, which in most cases progresses by short-term outbreaks that almost always respond well to treatment or even regress after a few months, OLP is characterized by its chronicity, persistence and resistance to therapy.

DIAGNOSIS

The diagnosis is achieved through clinical and histopathological examination. Histopathological manifestations include acanthotic (keratotic lesions), atrophic (old lesions), prominent or absent (erosive lesions) epithelium. There is liquefaction of the basal layer associated with superficial lymphocytic inflammatory infiltrate at the junction of the epithelium with

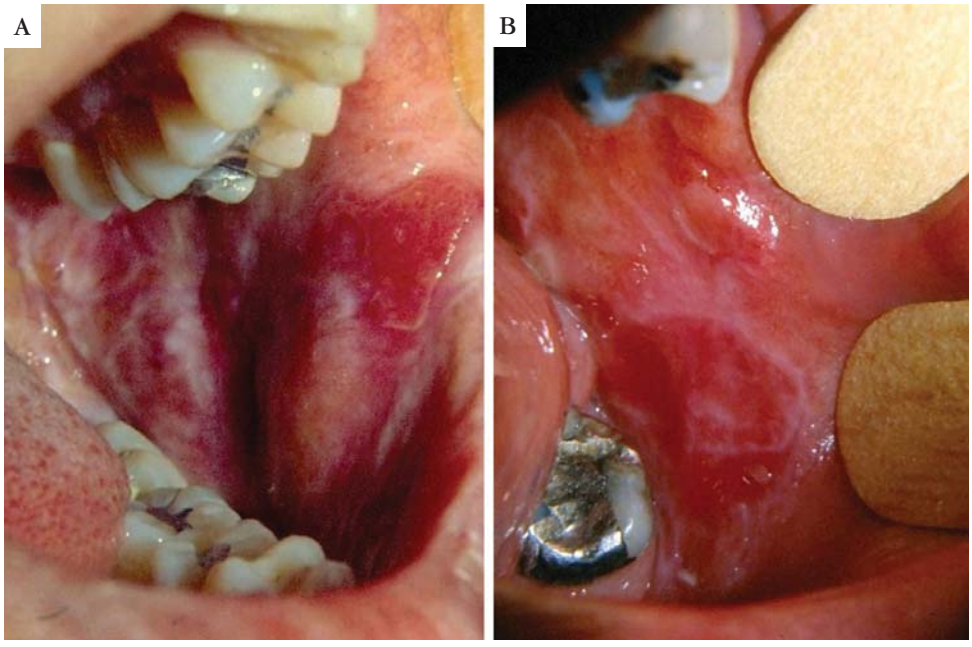

Figure 3: A. To the left: erosions surrounded by whitish lesions; **B.** To the right: lesion in the vicinity of a dental restoration

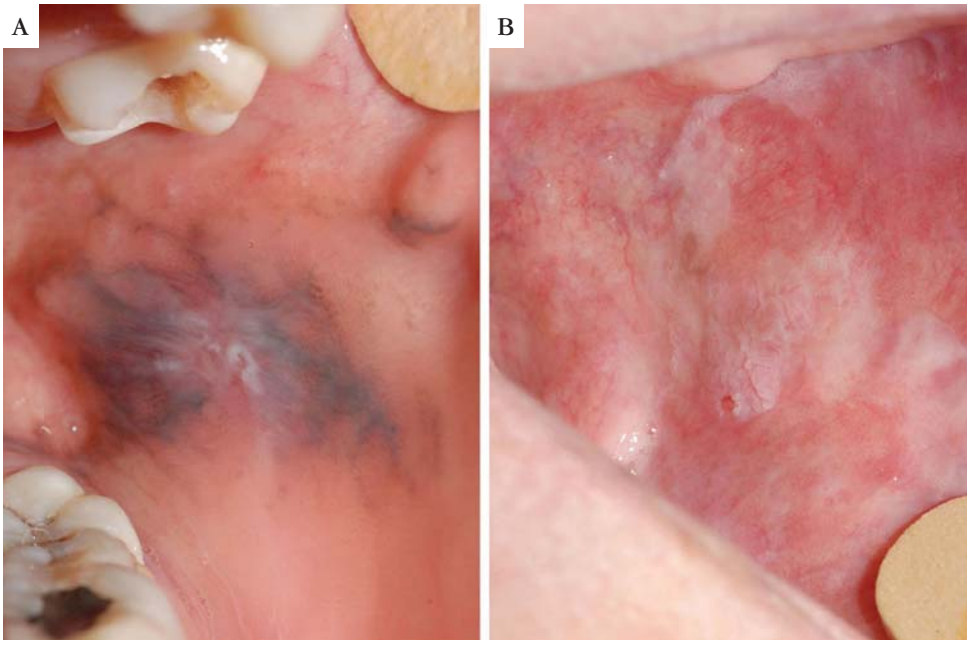

Figure 4: A. To the left: pigmentation and whitish lesions; **B.** To the right: atrophic-cicatricial aspect in a case of long evolution

lamina propria. Numerous eosinophilic spheric bodies are seen in the conjunctival epithelium, known as cytoid bodies, apoptotic bodies or Civatte bodies, in adittion to varying degrees of pigment leakage (Figure 7). [1,2,50] Interface inflammation reaching excretory portions of minor salivary glands has been recently characterized by our group ("salivary lichen planus", an analogy with lichen planopilaris). [57]

Biopsies should be preferably done in keratotic areas to avoid erosions, because they are devoid of epithelium, making microscopic examination difficult. [58,59]

Histopathological analysis of specimens of OLP was not always uniform in the analyzed studies. Van der Meij and Van der Waal found that in 42% of cases, in which there was full agreement on the clinical diagnosis of the disease, there was no consensus on histopathological diagnosis [60]. On the other hand, in 50% of the cases in which there was a consensus, there was no clinical agreement. In our opinion, diagnosis is safe if proper clinical and pathological criteria are followed, dismissing the possibility of other diseases such as traumatic keratosis, lupus erythematosus, erythema polymorphe and incipient tumors. [59,50]

Direct immunofluorescence from perilesional

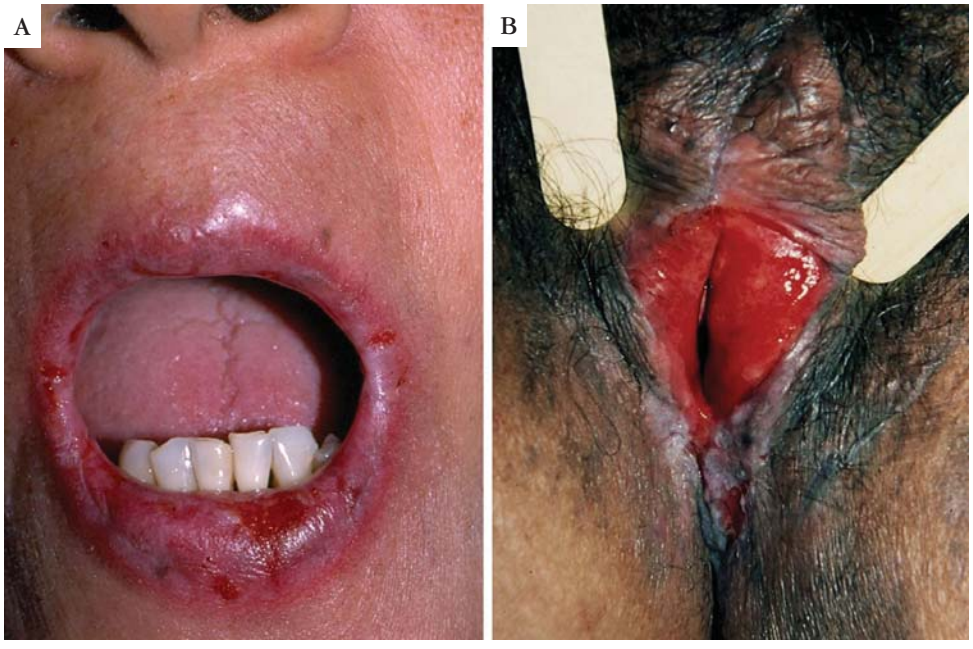

Figure 5: A. Vulvovaginal-gingival syndrome:" erosions, synechiae and reduction of the oral and vulvar orifices in one patient

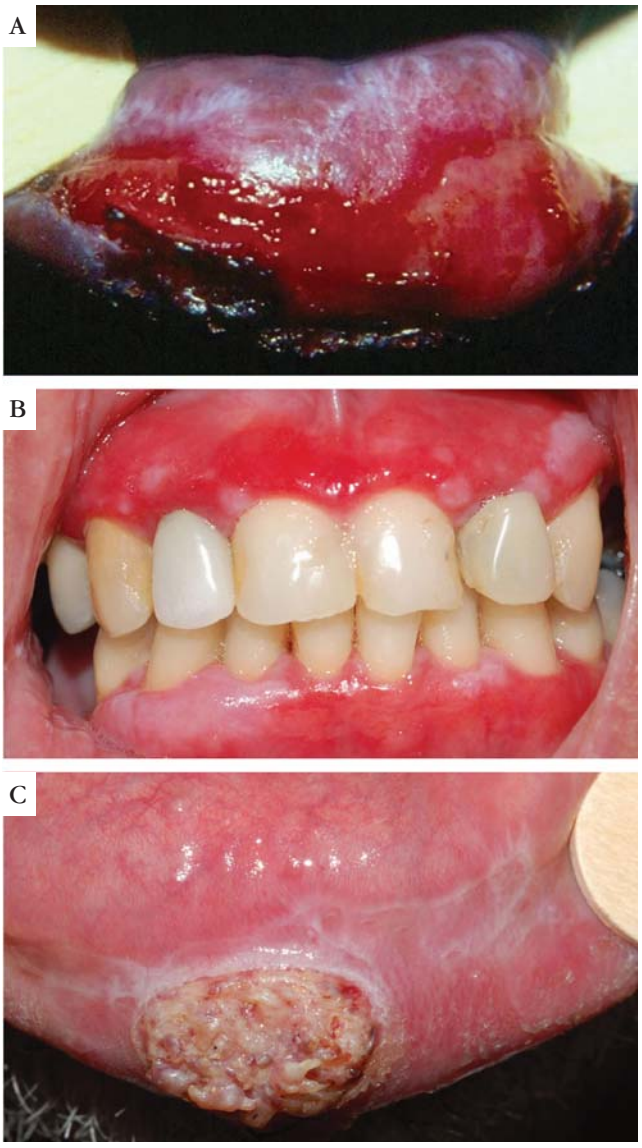

Figure 6: A. Striated lesions and erosions restricted to the lip vermillion; **B.** desquamative gingivitis-erosive aspect with keratotic areas, **C.** Squamous-cell carcinoma over atrophic-cicatricial area

biopsy may be useful to differentiate OLP from other mucosal diseases with an inflammatory component of the interface, especially lupus erythematosus, erythema polymorphe and drug eruptions. The most common finding in OLP is the presence of IgM deposits and, less frequently, of IgA and C3 in subepithelial cytoid bodies. [5]

DIFFERENTIAL DIAGNOSIS

It depends on the morphology of the lesions. Reticular papular lesions should be differentiated from discoid lupus erythematosus, candidiasis, morsicatio buccarum (mucosal exfoliation due to the habit of nibbling) and other traumatic injuries, mucous patches of secondary syphilis, pilous leukoplakia and

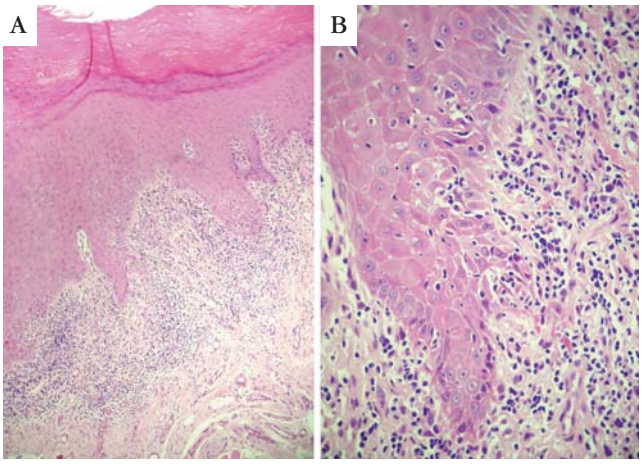

Figure 7: A. To the left: Histopathological aspect of papular lesion in the mucosa - hyperkeratosis, irregular acanthosis, hydropic degeneration of basal layer and inflammatory infiltrate forming a band in the superficial portions of lamina propria. (Hematoxylin-eosin); **B.** To the right: detail showing epithelial ridge with degeneration of the basal layer and many dyskeratotic keratinocytes ("Civatte bodies"). The inflammatory infiltrate is predominantly lymphocytic. (Hematoxylin-eosin)

incipient squamous-cell carcinoma. Erosive lichen planus should be adequately differentiated from aphthae, mucous membrane pemphigoid, pemphigus vulgaris, drug reactions, erythema polymorphe and acute lesions of lupus erythematosus. The differential diagnosis of the pigmented form is done with multiple causes of mucosal pigmentation.

It is sometimes difficult to clinically diagnose "desquamative gingivitis" when lesions in other sites are absent. Mucous membrane pemphigoid, pemphigus vulgaris and OLP may present as desquamative gingivitis of very similar clinical aspect; therefore, it is essential to conduct histopathological examination and direct immunofluorescence for proper diagnosis.

TREATMENT

The treatment of OLP aims to relieve the symptoms and minimize the functional impact of the disease. No treatment is effective for all cases of OLP because its cause is unknown. [5] Professional experience is, therefore, important. One should take into account the extent of lesions and severity of symptoms. Hence, treatment is individualized for each patient. Exclusive reticular papular lesions are asymptomatic and do not require treatment. Sequelae are observed in exclusively atrophic lesions and these lesions do not respond to any treatment. Erosive lesions are those that require drug therapy because of severe pain.

Oral hygiene practices are important, especially periodontal care given by a professional dentist, when gingival lesions are present, since tartar and dental

plaques can stimulate local inflammation and exacerbate disease activity. [1,61-63] Replacement of metal restorations is indicated when reactions to these substances are suspected. Improvement occurs more commonly in those cases in which all the lesions are located in areas close to the restorations. [37-39]

The drugs most often prescribed are potent topical corticosteroids - mouthwash, ointment or orabase paste, used two to three times a day. It is important to note that creams are never recommended for use in the oral mucosa, and orabase paste is only used for intraoral lesions (wet); lesions located in the lip vermillion should be treated with ointments. Oral and intralesional corticosteroids are almost never used by us in cases of exclusive intraoral manifestation, as the therapeutic target (inflammatory infiltrate) is easily topically treated, if we consider that only bare lesions (erosive) will be treated.

The potency of topical corticosteroids and their frequency of use should be reduced as clinical manifestations and symptoms improve. The intraoral use of topical steroids is safe and well tolerated. The most common adverse effect is oral candidiasis, which can be prevented with the prophylactic use of topical nystatin and by advising the patient not to sleep with dental prostheses.

Erosive gingival lesions are particularly resistant. As previously mentioned, in addition to drug treatment, there should be specialized periodontal monitoring, which has been shown to be very useful. The use of molded dentures to improve contact of the drug with the mucosa is sometimes prescribed. We have not found any need for their use; in addition, exaggerated contact of a potent corticosteroid with the gingival mucosa can lead to retraction. [63]

The topical calcineurin inhibitors - tacrolimus and pimecrolimus - were introduced in the treatment of OLP at the beginning of the last decade. They are topical immunosuppressive drugs that have been used as steroid sparers in OLP and have shown interesting therapeutic results.[64-69] Tacrolimus ointment is used at a concentration of 0.1% and pimecrolimus ointment is used at a concentration of 1%. The ointment must be applied twice daily, but use may be increased to four times daily until remission or symptomatic relief. [1,32] Adverse reactions include burning and stinging at the application site. Systemic levels of pimecrolimus and tacrolimus were detected after application to the oral mucosa. [68,69] In theory, it is suggested that these drugs may increase the frequency of carcinomas in OLP, because in addition to acting on the immune system, they would also act directly on cells. For instance, according to Becker et al,[54,70] tacrolimus appears to interfere with a few important intracellular signaling pathways, especially those related to p53 protein, whose mutation is present in several types of cancers. Therefore, the potential systemic absorption and malignancy of such agents reinforce the need for further long-term evaluation of these drugs.

Some authors have reported efficacy of topical retinoids in the treatment of OLP, especially when used in combination with topical corticosteroids for reticular or hyperkeratotic lesions. [71-73]. Imiquimod has been recently used in a small series of cases.[74] We have not used these drugs.

Several anti-inflammatory drugs commonly used in dermatology, such as levamisole, sulfone, griseofulvin and chloroquine were used by several authors, with anecdotal results and without scientific basis. [3,75-78]

Immunosuppressive therapies such as PUVA, methotrexate, azathioprine and mycophenolate mofetil can be attempted in very severe and resistant cases. [79-82]

CO_2 laser treatment has been attempted by some health professionals, but in our opinion, the method lacks scientific basis for this indication (laser is not used in the treatment of cutaneous lichen planus).[83,84]

Patients should be periodically followed-up due to the need to gradually reduce the medication and, especially, monitor atrophic-cicatricial lesions.

Individuals with concomitant psychopathology, especially those with symptoms of depression or anxiety, may deserve specialized care. [1,85] ❑

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QUESTIONS

1. It is correct to state the following about oral lichen planus:

a- It is more common in women
b- It is more typical in adolescence
c- It is accompanied by skin lesions in 5 to 15% of cases
d- It is believed that approximately 10% of the population will present with at least one manifestation in their lifetime

2 - It is correct to state the following about oral lichen planus:

a- Cells in the inflammatory infiltrate are predominantly lymphocytes b
b- Idiopathic oral lichen planus-specific antigen has been recently individualized
c- Apoptosis of keratinocytes in the basal layer is an important occurrence in the disease
d- Unlike the skin, the infiltrate is predominantly constituded by T lymphocytes

3 - It is correct to state the following about the relationship of oral lichen planus with hepatitis C virus:

a- It varies according to the region of study.
b- The rates are high in patients in Germany, United Kingdom and the United States
c- The medical literature indicates whether to investigate the presence of hepatitis C virus in all patients with OLP
d- Studies uniformly show that the ratio is high in Brazil

4 - It is incorrect to state the following about oral lichen planus:

a- the "vulvovaginal-gingival syndrome" appears to be associated with an HLA class II allele (HLA-DBQ1)
b- Clinical and histopathological findings of lichenoid oral lesions in chronic graft versus host disease are indistinguishable from findings of idiopathic OLP lesions
c- Genetic polymorphisms of several cytokines also appear to be associated with the clinical presentation of the disease
d- In GVHD, donor T lymphocytes attack tissue antigens of the minor histocompatibility complex of the host cell.

5 - It is correct to state the following about oral lichen planus:

a- The replacement of dental materials produces a 50% improvement of OLP lesions
b- Oral lichenoid reactions may result from contact with dental restoration materials, especially those containing gold
c- Restorations containing amalgam, metallic or ammoniated mercury are not suspected of causing lichenoid reactions
d- Lesions that improve with the replacement of restorations are only those that are in contact with them

6 - It is correct to state the following about oral lichen planus:

a- The different clinical forms (reticular, atrophic, papular, erosive, etc.) mainly reflect differences in genetic susceptibility
b- Bilateral and symmetrical lesions are usually caused by drugs
c- The predominant clinical morphology can change over time in the same patient
d- Keratotic lesions tend to be intensely symptomatic

7 - It is correct to state the following about oral lichen planus:

a- Whitish papules are easily removed with a spatula
b- Atrophy of the mucosa of the tongue develops quickly
c- Typical papulae are almost never observed in erosive forms of the disease
d- Atrophy of the mucosa of the tongue may lead to gustatory changes

8 - It is incorrect to state the following about oral lichen planus:

a- Lesions in the lip vermillion tend not to advance to the skin of the lip
b- Due to the characteristics of the epithelium, lesions in the lip vermillion do not become erosive
c- Lichen planus pigmentosus is associated with whitish lesions
d- Bullous lesions are rare

9 - It is incorrect to state the following about oral lichen planus:

a- There appears to be no correlation between the extent and severity of oral and skin lesions of lichen planus.
b- The "vulvovaginal-gingival syndrome" results in severe morbidity
c- Concomitant extraoral involvement such as scalp, nails, conjunctiva, esophagus, larynx, urethra, vagina, vulva and perianal area may rarely occur
d- Erosive lesions rarely affect the gingiva

10 - It is incorrect to state the following about oral lichen planus:

a- Study results are essentially inconclusive as to the potential "risk of malignancy" of the lesions
b- Squamous cell carcinoma only develops in old lesions
c- Other atrophic and cicatricial conditions of the mucosa may predispose to tumors
d- Sarcomas may rarely occur in erosive lesions of long evolution

11 - It is correct to state the following about oral lichen planus:

a- Its psychogenic cause is well documented
b- Psychiatric disorders are always present regardless of the clinical form of the disease.
c- There is controversy over whether psychiatric disorders are involved in the genesis of the disease or are the consequence of chronic painful lesions.
d- Cases in individuals with mucocutaneous forms of the disease have a lower correlation with psychiatric disorders than those with only mucosal lesions.

12 - It is correct to state the following about oral lichen planus:

a- It is characterized by chronicity, persistence and resistance to therapy.
b- Skin lesions take longer to disappear
c- It often disappears without treatment
d- If there are concomitant skin lesions, they tend to be more severe

13 - It is correct to state the following about the histopathology of oral lichen planus:

a- The epithelium is acanthotic and parakeratotic
b- Degenerate basal layer dismisses the diagnosis
c- The infiltrate never reaches the salivary gland duct
d- "Civatte bodies" are eosinophilic

14 - It is correct to state the following about desquamative gingivitis:

a- Immunofluorescence is not useful in the differential diagnosis
b- Its features allow for easy clinical diagnosis of its causes
c- Cases of lichen planus must be distinguished from those of lupus erythematosus
d- Cases of oral lichen planus only occur in the gingiva

15 - It is correct to state the following about the treatment of oral lichen planus:

a- Corticosteroids are the only effective medication
b- Lesions in the lip vermillion are treated with creams
c- Orabase paste is inappropriate for use in the lip vermillion
d- Atrophic lesions improve with oral treatment

16 - It is correct to state the following about the treatment of oral lichen planus:

a- Periodontal treatment should only be prescribed after complete healing of the lesions
b- Erosive lesions improve with treatment with steroid ointments
c- Corticosteroid injections are used to treat reticular or papular forms of the disease
d- Orabase paste should not be used to treat erosive lesions

17 - It is correct to state the following about the treatment of oral lichen planus:

a- The use of molded dentures is safe because it does not lead to retraction
b- Oral corticosteroid is the treatment of choice
c- Creams will chemically bind to saliva facilitating adherence to the mucosa
d- Prophylaxis of oral candidiasis should be done if topical corticosteroids are used

18 - It is incorrect to state the following about the treatment of oral lichen planus:

a- Although there is no study to confirm this, retinoids are excellent to treat erosive lesions
b- Calcineurin inhibitors have been increasingly used
c- Drugs such as levamisole, sulfone, griseofulvin and chlororquine need to be further studied
d- There is no scientific basis for the use of lasers

19 - It is correct to state the following about the prognosis of oral lichen planus:

a- It is a high-risk disease, with considerable risk of malignancy
b- Atrophy of the papillae of the tongue, although clinically visible, does not affect the patient
c- After the disease is controlled, it is better to abruptly suspend treatment to avoid the side effects of medication
d- Idiopathic cases are more difficult to control than those associated with dental restorations

20 - It is correct to state the following about biopsies in oral lichen planus:

a- They must always be performed in areas of erosion
b- They should be avoided in gingival lesions
c- They must be sent for direct immunofluorescence in all cases
d- They are diagnostic in most cases

Answers

Immunopathology of allergic contact dermatitis. An Bras Dermatol. 2011;86(3):419-33.

1d	7c	13b	19d
2c	8b	14b	20d
3a	9b	15a	
4c	10d	16a	
5a	11b	17a	
6c	12c	18d	

Papers

Information for all members: The EMC-D questionnaire is now available at the home-page of the Brazilian Annals of Dermatology: www.anaisdedermatologia.org.br. The deadline for completing the questionnaire is 60 days from the date of online publication.