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REVIEW ARTICLE

Oral lichen planus – an oral potentially malignant disorder (OPMD) of the oral cavity

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ABSTRACT

Introduction. Oral lichen planus is a chronic inflammatory disease of unknown etiology, characterized by recurrent lesions, presenting as reticular lesions, sometimes accompanied by atrophic, erosive, and/or ulcerative areas. Despite being one of the most common conditions affecting the oral mucosa, oral lichen planus remains an ailment with undefined etiology and unclear pathogenesis, imprecise management, and uncertain premalignant potential.

Materials and methods. A narrative literature review study was conducted. A bibliographic search was carried out in databases such as PubMed, Hinari, SpringerLink, the National Center of Biotechnology Information, and Medline. Articles published from 1990 to 2023 were selected using various combinations of keywords: "oral lichen planus," and "epidemiology," "etiology," "pathogenesis," "symptoms," "management," "histopathology," and "malignant transformation." After processing the data from these databases, 475 full articles were found. The final bibliography comprised 50 relevant sources, considered representative of the materials published on the topic of this synthesis article.

Results. Oral lichen planus is an inflammatory condition associated with T-cell-mediated immune dysfunction. Triggers include autoimmune responses to local antigens, microorganisms, and stress. The disease results from a complex interplay of host factors, lifestyle, and environmental factors leading to T-cell-mediated immune dysregulation. Diagnosis of oral lichen planus is based on clinical features (multiple, bilateral, symmetrically distributed lesions, occurring most commonly on the buccal mucosa, dorsal tongue surface, and gingiva), histopathological findings (predominantly lymphocytic band-like infiltrate in the lamina propria, presence of apoptotic cells in the basal cell layer, absence of epithelial dysplasia), and immune-related changes (deposition of fibrinogen along the basement membrane zone, presence of granular fluorescent deposits containing IgA, IgG, and IgM in colloid bodies).

Conclusions. Oral lichen planus is a chronic inflammatory condition mediated by T-cells in response to various extrinsic antigens, modified autoantigens, or superantigens, with periods of remission and relapse and the potential for malignant transformation. The etiology and pathogenesis of this condition are complex, diagnosis relies on clinical features, histopathological findings, and immunological data, patient treatment is symptomatic, and the potential for malignant transformation varies. Nevertheless, prospective studies with large sample sizes, adequate treatment duration, and long-term follow-up are needed.

Keywords: oral lichen planus, epidemiology, etiology, pathogenesis, symptoms, histopathology, treatment, malignant transformation.

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Key messages

What is not yet known on the issue addressed in the submitted manuscript

Despite numerous studies conducted, the epidemiology, etiology, and pathogenesis of oral lichen planus (OLP) are complex and incompletely understood. The therapy administered is often unsatisfactory and is associated with a series of adverse effects. Although

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OLP is considered an oral potential malignant disorder, its potential for malignant transformation is still contradictory.

The research hypothesis

The analysis and overview of the severity of oral lichen planus lesions correlate with an increased risk of malignant transformation, suggesting it is a potential predictive marker for assessing malignant potential in affected individuals.

The novelty added by manuscript to the already published scientific literature

This article summarizes a synthesis of the most recent international publications on etiological factors and pathogenetic theories, clinical forms, diagnostic methods, therapeutic approaches, and the risk of malignant transformation of oral lichen planus.

Introduction

Oral lichen planus (OLP) is an autoimmune, chronic, inflammatory disease that affects the stratified squamous epithelium of the oral mucosa. Despite being one of the most common conditions of the oral mucosa, the etiology and pathogenesis of OLP remain uncertain. However, scientists consider OLP to be a multifactorial process involving genetic, psychological, and infectious factors, characterized by immune-mediated damage of basal epithelial cells by T lymphocytes [1-3]. The prevalence of the disease in the general population ranges from 0.1% to 4%, most commonly affecting middle-aged patients in the 30-60 age group, with women being more predisposed than men at a ratio of 1.4:1. OLP is rarely diagnosed in children and young adults [1-3]. The condition presents with white reticular lesions (often bilateral), sometimes accompanied by atrophic, erosive, and ulcerative areas, with distinct relapses and remissions. The buccal mucosa, tongue, and gingiva are the most commonly affected areas. Treatment of OLP patients is symptomatic but often yields a limited response. Although the potential for malignant transformation is uncertain, and the degree of associated risk varies, the World Health Organization (WHO) has classified OLP as a potentially malignant disorder [1, 3].

In light of the above, the purpose of this article was to provide a synthesis of the most recent data to update the understanding of the etiology, pathogenesis, epidemiology, clinical presentation, diagnosis, management, and the potential for malignant transformation of OLP.

Materials and methods

To achieve the set objective, an initial search for specialized scientific publications was conducted, and relevant articles were identified using the Google Search engine and from databases including PubMed, Hinari, SpringerLink, National Center of Biotechnology Information, and Medline. The criteria for selecting the articles included contemporary data on OLP using the following keywords: "oral lichen planus," "epidemiology," "etiology," "pathogenesis," "symptoms," "management," "histopathology," "malignant transformation," which were used in various combinations to maximize search yield.

For advanced selection of bibliographic sources, the following filters were applied: full-text articles, articles in the English language, articles published between 1990 and 2023. After a preliminary analysis of titles, original articles, editorials, narrative synthesis, systematic reviews, and meta-analyses were selected, containing relevant information and contemporary concepts regarding the etiology, pathogenesis, epidemiology, clinical presentation, diagnosis, management, and the potential for malignant transformation of OLP. Additionally, a search was conducted in the reference lists of the identified sources to highlight additional relevant publications that were not found during the initial database search.

The information from the publications included in the bibliography was collected, classified, evaluated, and synthesized, highlighting the key aspects of the contemporary understanding of OLP. To minimize the risk of systematic errors (bias) in the study, a thorough search was conducted in the databases to identify a maximum number of relevant publications for the study's purpose. Only studies meeting validity criteria were considered, and secure exclusion criteria were used to remove articles from the study. Both studies showing positive and negative results were analyzed.

When necessary, additional sources of information were consulted to clarify certain concepts. Duplicate publications, articles that did not align with the study's purpose, and those that were inaccessible for full viewing were excluded from the list of publications generated by the search engine.

Results

After processing the information identified through the Google Search engine and from the databases PubMed, Hinari, SpringerLink, National Center of Biotechnology Information, and Medline, following the search criteria, a total of 475 articles related to the topic of ozone therapy were found. After a primary analysis of the titles, 59 articles were potentially relevant for the synthesis. Upon repeated review of these sources, a final selection of 50 relevant publications was made, ultimately included in the bibliography of this work. These 50 articles were consid-

ered representative of the materials published on the subject of this synthesis article.

Publications whose content did not align with the addressed theme, even if selected by the search program, as well as articles that were not accessible for free viewing and not available through HINARI (Health Internet Work Access to Research Initiative) or in the scientific medical library of the Public Institution "Nicolae Testemițanu" State University of Medicine and Pharmacy, were subsequently excluded from the list.

Definition. Oral lichen planus (OLP) is an inflammatory condition characterized by immune-mediated T-cell dysfunction, which can manifest with varying appearances from keratotic to erythematous and ulcerative. OLP is a chronic immune-mediated disease marked by recurrent and repeated relapses and remissions, resistance to treatment, and a potential for malignancy [4-10].

The etiology of OLP is not fully elucidated and is considered multifactorial, remaining controversial. Numerous potential triggering factors are involved in the pathogenesis of OLP, including local and systemic factors related to delayed T-cell-mediated hypersensitivity [1, 4-9, 11-13].

Studies have implicated stress, anxiety, depression, genetic predisposition, pharmaceutical products, dental materials, systemic conditions, and viruses (including hepatitis type C virus - HCV and hepatitis type B virus - HBV) as causal agents, influencing the onset, development, exacerbation, or recurrence of OLP. However, the most notable risk factor is considered to be HCV infection [1, 7, 8, 11-16].

Pathogenesis. Previous studies have found that OLP is an autoimmune, localized disease induced by the dysfunction of T cells with an unknown internal or external predisposing factor. Activated cytotoxic T lymphocytes accumulate in the superficial *lamina propria*, as a band-like infiltrate and release a large quantity of inflammatory mediators, initiating the apoptosis of basal keratinocytes and their vacuolar degeneration. Over time, this leads to basal membrane disturbances and chronicization of the disease. Likely, OLP is a cell-mediated immune cytotoxic reaction to a variety of extrinsic antigens, modified autoantigens, or superantigens [1, 5, 8-10, 12, 17-20].

The pathogenesis of OLP may involve both antigen-specific and non-specific mechanisms. Antigen-specific mechanisms in OLP include antigen presentation by basal keratinocytes and the destruction of antigen-specific keratinocytes by cytotoxic T cells. Superantigens are considered antigens that mediate excessive, non-specific activation of T cells [9].

Accumulated data support the vital role of immunological mechanisms in the pathogenesis of OLP, particularly in the massive production of various cells and inflammatory mediators. It is conceived that the disease results from the complex interaction of host factors, lifestyle, and environmental factors, leading to T cell-mediated immune dysregulation [9, 19, 20].

Epidemiology. OLP most commonly develops in middle-aged and elderly adults of both sexes, with a predominance in women (1.4:1-2.0:1) [1, 4, 5, 14, 16-18, 21]. The exact prevalence and incidence of OLP are not well known and vary significantly. Due to the lack of clear diagnostic criteria, the use of a common methodology in epidemiological studies, and a consensus on the true prevalence of OLP, it remains challenging to determine accurate figures. According to epidemiological studies, the average global prevalence ranges from 1.01% to 1.27%, with variations based on the studied geographical area, ranging from 0.35% to 2.6% [1, 4, 5, 15, 17, 22]. The prevalence also varies from 0.1% to 5.0% in the general population and differs between genders – 0.96% among men and 1.57% among women [4, 11, 17, 23].

In two recent systematic reviews and meta-analyses published in 2020 and 2021, OLP had a global prevalence of 0.89-1.01% among the general population and 0.98% among patients. However, this indicator exhibited significant geographical differences ($p<0.001$). A higher prevalence of OLP was observed in non-Asian countries, among women, and among individuals aged 40 and older [6, 24, 25].

Clinical Presentation. The symptoms of OLP vary depending on the clinical type and the severity of the lesions. Approximately 82% of OLP patients are either asymptomatic or report nonspecific symptoms in the oral cavity, such as roughness, burning or pain, discomfort, irritation, xerostomia, bleeding, and dysgeusia. Symptoms are particularly pronounced when consuming hot or spicy foods, leading to difficulties in chewing, swallowing, and speaking. Over time, red or white patches appear on the oral mucosa, which gradually progress to erosions and ulcers, intensifying the symptoms and causing higher levels of anxiety, depression, and a reduced quality of life [1, 3, 14, 16, 26].

The clinical manifestations of OLP are diverse and polymorphic and can appear in various clinical forms, often associated with each other. This complexity can pose a diagnostic and therapeutic challenge due to its refractory and recurrent nature [4, 8, 16]. The characteristic clinical features of OLP present as white papules that enlarge and coalesce to form a reticular, annular, or plaque-like pattern with or without atrophy or erosion [1, 6, 8, 14, 16, 17, 22, 27].

From a clinical perspective, six distinct types of OLP are emphasized:

• Reticular or typical keratotic form (30% of cases): This is the most common form, characterized by numerous keratotic lines or slightly raised grayish-white streaks that intersect (the so-called Wickham striae), creating a lace-like or reticular pattern. These striae are usually located bilaterally and symmetrically on the buccal mucosa, but they can also be observed on the tongue, less frequently on the gums and lips. This form typically does not cause clinical symptoms and is often detected during routine examinations.

• Plaque form: This form is characterized by homogeneous white patches and may clinically resemble leukoplakia but has a multifocal distribution. The plaques typically have a slightly elevated or smooth, flat surface and are most commonly found on the dorsal surface of the tongue and the buccal mucosa.

• Atrophic (erythematous) or exudative-hyperemic form: This type features the appearance of red patches with very fine white streaks. It can be associated with the erosive or reticular form. The proportion of atrophic and keratinized areas typically varies throughout the affected area. The attached gingiva is most commonly affected with an irregular distribution in quadrants. Clinical symptoms include a burning sensation in the oral cavity, sensitivity, and discomfort.

• Erosive (ulcerative) form: This form may present ulcers at the center of the lesion. The ulcer is typically covered with a white, fibrinous membrane and is surrounded by erythematous mucosa. The disease's progression is dynamic, involving new areas from week to week. White streaks are observed around the ulcer on clinical examination.

• Papular form: This is a rare form that contains small, white, raised, pinpoint-sized papules and may generate fine lace-like patterns.

• Bullous form: This is a rare form; it involves blisters that can range from a few millimeters to several centimeters in diameter. They are present for a short duration, after which they rupture, leaving painful ulcers. These lesions are more commonly found in the area of the third molars. They can also occur, though less frequently, on the tongue, gums, and lip mucosa. The bullous form is typically associated with the reticular form [3, 6, 8, 10, 13, 16, 20, 26-28].

The reticular, papular, and plaque forms of OLP, known as "non-erosive lesions" or "predominantly white forms," are often asymptomatic and are frequently detected incidentally by a dentist [1, 3, 5, 13, 16]. On the other hand, the atrophic/erosive, ulcerative, and bullous lesions, referred to as "erosive lesions" or "predominantly red forms," cause severe symptoms, primarily pain and a burning sensation, limiting food intake and oral hygiene. These symptoms significantly affect oral health-related quality of life, with a substantial impact on overall health, regardless of age and gender. The erosive form is the most severe and recurrent clinical variant, and erosive and bullous forms can transform into ulcerative forms [1, 5, 13, 16, 21, 29].

OLP lesions are typically multiple, bilateral (less commonly unilateral), more or less symmetrical, and can appear solitarily or simultaneously in various combinations, involving the oral mucosa (60-70% of cases), the dorsal surface of the tongue, gums, lower lip mucosa, and palate. According to the results of several studies, the first three locations, which are prone to trauma, are the most common (80-90% of cases), while the floor of the mouth, hard palate, and lip mucosa are rarely affected [2, 3, 8, 10, 20, 26, 28, 30].

OLP is often accompanied by skin lesions or involves other squamous mucous membranes. Approximately 15-20% of OLP patients develop skin lesions, and around 20% have concurrent genital lesions. Among patients with cutaneous lichen planus, OLP lesions occur in up to 60-70% of cases [9, 11, 15-17, 20, 27, 31].

Diagnostics. Because OLP is a condition with malignant potential, early and accurate diagnosis is crucial, allowing for timely and appropriate management and improving the patient's quality of life [1, 16, 29, 32]. However, the diverse clinical presentation and the asymptomatic nature of the most common subtype of OLP make the disease an underdiagnosed health problem [1, 16, 29, 32].

Currently, there are no widely accepted diagnostic criteria for OLP. Diagnosis is based on clinical and histological criteria and includes: (1) detailed medical history and a comprehensive mucocutaneous clinical examination; (2) cytological examination; (3) hematological examination; and (4) biopsy with histopathological and immunofluorescence examination [1, 4, 10, 11, 16, 20, 27, 33]. However, classic OLP lesions (bilateral, reticular, with Wickham striae) can be diagnosed based on clinical appearance alone. The clinical presentation of rarer forms can be significantly different from classic OLP and, therefore, may be challenging to diagnose based solely on clinical examination [1, 16, 20, 27, 33].

Significant changes have been made over the years regarding the diagnosis of OLP. In 1978, the World Health Organization (WHO) developed a set of clinical and histopathological criteria for the diagnosis of this condition. These criteria were typical but nonspecific, and they were not able to distinguish between OLP and oral lichenoid lesions (OLL). In 2003, van der Meij and van der Waal made modifications to these criteria, confirming the absence of epithelial dysplasia in the diagnosis of OLP. The most recent diagnostic approach for OLP was published in 2016 [11]. The authors compared the criteria established by the WHO with those modified by van der Meij and van der Waal. They reported mild to moderate clinicopathological correlation in the definitive diagnosis of OLP and recommended associating clinical and histopathological features for a definitive diagnosis. The latest modified classification is that of the American Academy of Oral and Maxillofacial Pathology (2016), which includes clinical and histopathological characteristics capable of correctly distinguishing OLP from OLL:

• Clinical Criteria: (a) symmetrical multifocal distribution; (b) white and red lesions presenting one or more of the following forms: reticular/papular, atrophic (erythematous), erosive (ulcerative), plaque-like, vesicular; (c) lesions are not exclusively located in places where smokeless tobacco products are placed; adjacent and in contact with dental restorations; (d) the onset of lesions does not correlate with the initiation of treatment with a medication or the use of products containing cinnamon.

• Histopathological Criteria: (a) predominantly lymphocytic infiltrate in a band-like or irregular pattern in the *lamina propria* limited to the epithelium - *lamina propria* interface; (b) hydropic degeneration of basal cells; (c) lymphocytic exocytosis; (d) absence of epithelial dysplasia; (e) absence of architectural changes in the verrucous epithelium [10-12, 16, 22].

Therefore, marginal tissue biopsy, including both lesions and areas with a normal appearance, is considered the "gold standard" for diagnosing OLP. The histopathological features of OLP are characteristic and consist of epithelial

hyperkeratosis, hydropic or vacuolar degeneration of basal epithelial cells, atrophy, or "sawtooth" acanthosis of spinous epithelial cells, a homogenous eosinophilic deposit at the junction between connective tissue and epithelium, band-like lymphocytic infiltrate in the superficial *lamina propria*, apoptotic keratinocytes in the lower epithelial layer with the formation of colloid or civatte bodies [1, 8, 9, 11, 12, 17, 20, 27, 34-36].

Direct immunofluorescence examination of tissue in cases of OLP demonstrates the deposition of fibrinogen along the basal membrane zone (at the mucosa-submucosa interface) in 90-100% of cases. At the level of civatte bodies, the method highlights the presence of granular fluorescent deposits containing IgA, IgG, and IgM. Indirect immunofluorescence examination detects anti-basal cell antibodies [1, 11, 12, 20, 24, 35, 36].

So, the diagnosis of OLP is based on clinical characteristics, histopathological findings, and immunological data [8, 33, 37]. The most widely accepted histopathological features of OLP are three, which should be present concurrently:

• Chronic cellular inflammatory subepithelial infiltration, limited to the surface of the connective tissue, in a dense and well-defined "band-like" pattern, predominantly composed of lymphocytes.

• Hydropic degeneration of the basal layer of keratinocytes (basal epithelium), forming colloid bodies (Civatte).

• Absence of dysplasia in the epithelial layer [1, 5, 8, 9, 20, 26, 27, 30, 37].

The differential diagnosis of reticular OLP includes leukoplakia, oral lichenoid lesions (OLL), and discoid lupus. The differential diagnosis of erosive OLP includes the following conditions in the oral cavity: cheek chewing or biting (*morsicatio buccarum*), hypersensitivity mucositis, OLL, chronic oral candidiasis, oral squamous cell carcinoma (OSCC), benign pemphigus, pemphigus vulgaris, and systemic diseases (discoid lupus erythematosus, erythema multiforme). Differential diagnosis of OLP from other diseases is particularly challenging in non-reticular forms, which often require biopsy with histopathological examination and immunofluorescence testing. [1, 8, 33, 34, 38, 39].

Management. In patients with non-erosive lesions (reticular, papular, or plaque-like) with typical clinical manifestations (bilateral and symmetrical lesions), a biopsy to confirm the clinical diagnosis is not obligatory. In the case of erosive lesions (atrophy/erosion, ulcerative, or bullous), a biopsy is necessary, especially for lesions with suspected dysplastic changes or malignant transformation.

The management of OLP includes: (1) Establishing the diagnosis based on medical history, clinical examination, and comprehensive tests – histopathological examination, direct and indirect immunofluorescence tests; (2) Informing the patient about the condition – a chronic, recurrent disease with periods of exacerbation and remission; (3) Treatment; (4) Long-term periodic monitoring to detect early dysplastic and malignant transformation changes.

Currently, a wide range of therapeutic options is available for the management of OLP, but none of them are curative [1, 6, 10, 19, 20, 33, 40-42]. Due to the unknown etiology, the therapeutic approach to OLP is symptomatic, depending on the type of lesion, associated symptoms, clinical presentation, the extent of the disease, and potential side effects of medications. The primary goals of OLP treatment are to alleviate discomfort and stress through patient education and oral hygiene measures, eliminate local irritating or aggravating factors in the oral cavity, alleviate distressing symptoms, reduce inflammation, expedite and extend periods of remission, and decrease the risk of malignant transformation [1, 2, 10-12, 17, 20, 27, 33, 35, 41-43].

Patients with asymptomatic non-erosive lesions do not require immediate treatment unless they become inflamed, ulcerated, or painful, but regular monitoring is necessary. Patients with symptomatic erosive forms require immediate and effective drug treatment to alleviate the clinical picture and improve the quality of life of the patients. According to the data in the literature, up to 20% of OLP lesions can spontaneously regress without treatment [1, 2, 10-12, 17, 20, 27, 35, 41-44]. Since OLP is an immunologically mediated condition, the drugs of choice for treatment are corticosteroids, administered topically, intralesionally, or systemically, followed by topical calcineurin inhibitors, and, if necessary or prophylactically, antifungal agents. Resistant lesions require systemic therapy with corticosteroids or immunosuppressants [1, 4-6, 8, 10, 11, 17, 19, 20, 23, 27, 30, 35, 36, 41, 45].

The management of OLP includes: (1) Pharmacological treatment: inflammatory/symptomatic therapy with topical, intralesional, or systemic corticosteroids; topical calcineurin inhibitors (immunosuppressants); topical or systemic retinoids (immunomodulators); immunosuppressants like azathioprine and methotrexate, and lycopene (an antioxidant); (2) non-pharmacological treatment: this may involve phototherapy with ultraviolet rays, photodynamic therapy, and laser therapy; (3) surgical excision: this is recommended for patients with isolated, persistent, or treatment-resistant erosions. However, it's important to note that therapeutic outcomes are often disappointing [1, 2, 6, 10, 12, 19, 20, 27, 30, 33, 35, 41, 43, 45].

Eliminating predisposing factors and maintaining meticulous oral hygiene are necessary to prevent recurrences. Additionally, continuous clinical monitoring of patients with OLP is required to assess therapeutic responses and any changes in the appearance of lesions [11, 12, 30].

Prognosis. One of the most significant concerns regarding OLP is its increased potential for malignant transformation into OSCC [22, 32]. Previous studies have found that if there is a risk, it is very difficult to quantify it, possibly so low that it's challenging to determine if OLP is genuinely associated with a significant risk of malignant transformation [22, 32]. Regardless of the incidence of malignant transformation, in 1978, the WHO defined OLP as a "potentially malignant disorder," representing a generalized condition with a significantly increased risk of OSCC [22, 28, 32].

The hypothesis for the relationship between OLP and OSCC is chronic inflammation, which over time contributes

to the formation of critical DNA lesions leading to the development of OSCC [46].

Previous prospective and retrospective studies have found a potential for malignant transformation of OLP ranging from 0.07% to 6.5% over observation periods ranging from 0.5 to 22 years [3, 5, 22, 28]. According to WHO data, this figure varies from 0.4% to 12.5%, with an average rate of 1.09% [11, 15, 16, 23, 27, 30, 34, 47].

According to the results of a systematic literature review published in 2016, which evaluated data from 38 studies between 1995 and 2014 with a total of 16,032 cases of OLP, the rate of malignant transformation of the condition varied from 0% to 5.8% [48]. According to the results of six recent systematic reviews and meta-analyses and a study published in 2023, which evaluated data from eight systematic reviews published between 2014 and 2023, the rate of malignant transformation of OLP ranged from 0.44% to 1.4% [22, 49, 50]. A meta-analysis based on 10 high-quality studies highlighted a higher proportion of malignant transformation (2.28%) [49]. The highest prevalence of malignant transformation was reported in the erosive, atrophic, and ulcerative subtypes of OLP, which involve the hard palate, tongue, labial mucosa, and gingiva [1, 5, 6, 16, 22, 46]. Given the consistent evidence of the risk of oral malignancy, patients with OLP should be carefully monitored for the early development of OSCC [32, 49].

Therefore, OLP is a potentially malignant condition with a rate of malignant transformation ranging from 0% to 12.5% depending on the follow-up period. Studies have listed the following risk factors for the malignant transformation of OLP: lesion localization on the tongue, the red type (atrophic or erosive form), tobacco and alcohol consumption, and HCV [22, 46, 47]. The wide range of OLP malignant transformation rates obtained in these analyses can be attributed to differences in the diagnostic criteria used, the average follow-up periods, and the number of cases evaluated [48].

Conclusions

1. OLP is a chronic inflammatory condition with periods of remission and relapse, harboring a malignant potential, and most likely being a result of a cell-mediated reaction to a variety of extrinsic antigens, modified autoantigens, or superantigens. Both the etiology and pathogenesis of this disease are complex and incompletely understood, necessitating further research, especially due to the risk of malignant transformation.

2. The diagnosis of OLP is based on clinical characteristics, histopathological results, and immunological data:

- Clinical criteria: (a) multifocal symmetric distribution; (b) white and red lesions that exhibit one or more of the following forms: reticular/papular, atrophic (erythematous), erosive (ulcerative), plaque-like, bullous; (c) lesions are not exclusively localized in the sites of smokeless tobacco placement; adjacent to and in contact with dental restorations; (d) the onset of lesions does not correlate with the initiation of treatment with a drug or the use of products containing cinnamon.
- Histopathological criteria: (a) predominantly band-like or irregular lymphocytic infiltrate in the *lamina propria* limited to the epithelium - *lamina propria* interface; (b) hydropic degeneration of basal cells; (c) lymphocytic exocytosis; (d) absence of epithelial dysplasia; (e) absence of architectural changes in verrucous epithelium.

3. The management of OLP includes: (1) pharmacological treatment: anti-inflammatory/symptomatic therapy (topical, intralesional, or systemic corticosteroids), topical calcineurin inhibitors (immunosuppressants), topical or systemic retinoids (immunomodulators), immunosuppressants (azathioprine, methotrexate), lycopene (antioxidant); (2) non-pharmacological treatment: ultraviolet phototherapy, photodynamic therapy, and laser therapy; (3) surgical excision, recommended for patients with isolated and persistent OLP erosions resistant to conservative treatment.

4. The elimination of predisposing factors and maintaining meticulous oral hygiene are necessary for preventing relapses, and continuous clinical monitoring of patients with OLP is required to monitor therapeutic responses and any changes in lesion appearance.

Competing interests

None declared.

Ethical statement

No approval was required for this study.

Authors' contribution

The authors contributed equally to the research of the scientific literature, the selection of the bibliography, the reading, and analysis of biographical references, the writing of the manuscript and its peer review. All authors have read and approved the final version of the article.

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