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FAMILIAL ORAL LICHEN PLANUS - A REVIEW OF THE LITERATURE AND A CASE SERIES REPORT

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Abstract

Background: Lichen planus (LP) is a complex condition with numerous and polymorphic clinical manifestations. Although oral lichen planus (OLP) usually appears as isolated cases in the population, there have been reports of this condition manifesting among members of the same family. Therefore, genetic factors represent a potential etiologic factor, as demonstrated in several studies. **Aim of the study:** To present the clinical-evolutionary characteristics and treatment response in a series of 8 different cases of OLP from 4 different families. **Results:** All patients included in the study were women, with a mean age of 44.87 years, non-smokers, and had associated general conditions such as psoriasis, autoimmune thyroiditis, or hepatitis C. The most common clinical form was the atrophic-keratotic type, involving 2-3 topographical areas, and the majority of patients reported painful symptoms. In half of the patients, we observed a good progression and significant remission. **Discussion:** A possible factor associated with the pathogenesis of OLP is genetics. Familial LP appears at younger ages and can manifest with widespread lesions. The study of familial OLP cases reveals certain clinical-evolutionary characteristics, which are sometimes atypical. **Conclusion:** Studying familial OLP cases is necessary to better understand the specific manifestation patterns and to assess treatment response. Additionally, these cases may have a higher potential for malignant transformation.

Keywords: lichen planus, familial oral lichen planus, genetic factor, case series

Introduction

Oral lichen planus (OLP) is a multifactorial dermatosis caused by an immunological mechanism, with varied clinical manifestations and a chronic, often inconsistent course. Epidemiological data show a higher prevalence in middle-aged adult women, between 50-60 years (1,2). The pathogenic mechanism is characterized by a cellular immune response involving macrophages, Langerhans cells, and activated T lymphocytes. The consequence of this complex immunological conflict is vacuolization and apoptosis of basal cells (3). Lichen planus (LP) can be localized to the skin, oral, genital, or esophageal mucosa, and sometimes even nails. In some cases, clinical lesions may exclusively affect the oral mucosa; however, multilocular involvement is not considered a criterion for disease severity or a predictor of frequent exacerbations (4-6). According to internationally accepted criteria, diagnosis is based on characteristic clinical features and histopathological findings. The etiological factors involved in triggering OLP are diverse, and in some cases, remain unidentified (7-10).

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Moreover, the pathogenic mechanism of OLP is complex, grounded in the interaction of various types of immune responses. Several exogenous or endogenous triggering factors have been described, such as dental restorative materials, systemic medication (non-steroidal anti-inflammatory drugs, antihypertensives), association with other autoimmune diseases or systemic conditions (diabetes, hypertension, hepatitis C), trauma, stress, or genetic factors (11-15).

In recent times, new research directions have emerged regarding the etiology of LP. For instance, the potential influence of oral microbiome dysbiosis on the onset and evolution of LP is being studied (16-18). On the other hand, other studies investigate the hypothesis of genetic determination in OLP, linked to genetic polymorphisms in cytokines, such as interferon-gamma (IFN-γ) or tumor necrosis factor-alpha (TNF-α) (19,20). The existence of familial OLP cases supports the genetic etiology hypothesis, although further studies are needed to confirm this theory (21-27).

Material and Methods

A retrospective review was conducted of patients with OLP monitored in the Oral Pathology Department at Carol Davila University of Medicine and Pharmacy, Bucharest, between 2006 and 2018. Eight patients from four families were identified and considered to be familial cases of LP. The diagnosis of familial OLP was established based on the simultaneous fulfillment of the following conditions: the patients were diagnosed with OLP according to the clinical and histopathological criteria approved by the World Health Organization (WHO), and the patients within a family were first- or second-degree relatives.

The clinical criteria for diagnosing OLP include symmetrical reticular keratotic lesions on the buccal mucosa. Occasionally, the clinical presentation may be polymorphic, with associated ulcerations or atrophy. The clinical diagnosis must be confirmed by histopathological examination. The histological features compatible with OLP are as follows: chronic subepithelial inflammatory infiltrate arranged in a band-like pattern, sharp epithelial-connective junction ridges, and the absence of dysplasia (28,29).

Patients who met the criteria for familial OLP were included in the study, and the following variables were analyzed: sex, age, associated general conditions, clinical characteristics of LP (type and location of lesions), associated syptomatology, and disease progression over a monitoring period of at least one year.

Results

The four families included in the study each had two affected members. The familial relationships were mother-daughter in three cases (families II, III, and IV) and sisters in one case (family I). This observation raises the hypothesis that OLP may have a genetic predisposition. All patients with familial OLP studied were women from an urban environment, aged between 22 and 69 years (mean age 44.6 years).

The general characteristics of the studied patients are presented in Table I.

Table I. General characteristics of patients with familial OLP in the study cohort.

Patients	Family	Age at diagnosis	Gender	Area	Employment
1	I	22	Female	Urban	Employed
2	I	32	Female	Urban	Employed

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3	II	57	Female	Urban	Employed
4	II	35	Female	Urban	Employed
5	III	69	Female	Urban	Retired
6	III	50	Female	Urban	Employed
7	IV	60	Female	Urban	Retired
8	IV	34	Female	Urban	Employed

Analyzing the clinical form at the time of diagnosis in the familial LP cases included in this study, we observed primarily the atrophic-hyperkeratotic form in families II, III, and one patient from family IV, while the second member of family IV had an acute, predominantly ulcerative clinical form. Both members of family I initially presented with the keratotic form. Regarding lesion location and the number of affected topographical areas, most patients had lesions in more than three areas of the oral cavity. In all cases, the buccal mucosa displayed symmetric, bilateral reticular keratotic lesions. Additionally, most patients reported painful symptoms, such as burning sensations exacerbated by the consumption of acidic or spicy foods and beverages. The clinical characteristics of patients with familial OLP are presented in Table II.

Table II. Clinical characteristics of patients with familial OLP in the study cohort

Patients	**Family**	**Lesion type***	**Lesion distribution****	**Symptoms*****
1	I	K	B	+
2	I	K	B, T (dorsal)	-
3	II	A-K	B, T (dorsal and ventral)	+
4	II	A-K	B, G	+
5	III	A-K	B, G, T (ventral)	-
6	III	A-K	B, G	-
7	IV	A-K	B	+
8	IV	E-K	B, G	+

*K-Keratotic, A- Atrophic, E-Erosive; **B- Buccal mucosa, T-Tongue, G- Gingiva; *** + symptomatic, - asymptomatic

None of the patients in the study cohort presented with extraoral manifestations of LP; the lesions were localized exclusively to the oral mucosa. Regarding associated general pathology, we noted the presence of conditions that occur more frequently in patients with OLP. An exception was family I, where neither of the two members had associated systemic diseases. Autoimmune chronic thyroiditis was the most frequently associated condition in the studied cases. All these aspects are presented in Table III.

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Table III. Associated general conditions in the studied cases

Patients	Family	Associated conditions
1	I	No
2	I	No
3	II	Diabetes
4	II	Autoimmune thyroiditis
5	III	Autoimmune thyroiditis
6	III	Autoimmune thyroiditis
7	IV	HCV infection
8	IV	Psoriasis

Regarding the recommended treatment, 5 patients received topical applications of Clobetasol 0.05%, and 2 patients also received topical Tretinoin 0.05%. One patient received topical treatment with only a vitamin A derivative. The therapeutic regimens were adjusted based on the progression of lesions and individual response to treatment.

The 8 patients included in the study were monitored for at least 1 year. At the last follow-up, four of them showed favorable progression and 90% remission of the initial lesions. Three patients had only a 30% improvement in clinical appearance and symptomatology, while one case experienced a significant exacerbation.

Discussion

Familial OLP is rarer compared to non-familial LP, and the study of reported cases reveals several characteristics such as an earlier average age of onset, occasional significant exacerbation periods throughout the disease course, and atypical clinical forms with multiple localizations. In this study, it is observed that the age at which LP was diagnosed (44.87 years) is lower compared to non-familial cases reported, and all patients are female. This observation is consistent with other similar studies that reported an early onset for familial OLP cases. For instance, a study conducted in Spain at the University of Murcia, which included 13 patients with a familial history of OLP, mostly women (11), had an average age of 42 years (26).

Another study conducted in China at Qingdao Municipal Hospital, which included 18 patients with familial OLP from 8 different families, also found a predominance of females (n=13), with the most represented age range being between 40 and 49 years (21).

Familial lichen planus is described in the literature as having an early onset and polymorphic clinical forms, with a tendency for frequent exacerbations. This study aligns with this observation. The patients included in the study exhibited extensive clinical forms affecting 3 or more different localizations. All patients presented with bilateral reticular keratotic lesions on the buccal mucosa, which is also an important criterion for the clinical diagnosis of OLP. A similar study also found a higher frequency of keratotic or atrophic-hyperkeratotic forms accompanied by reduced symptomatology (26). In a retrospective study conducted in China, the reticular keratotic form was reported as predominant, followed by erosive and atrophic forms, with the most frequent localization being the buccal mucosa, followed by the tongue and gingiva (21).

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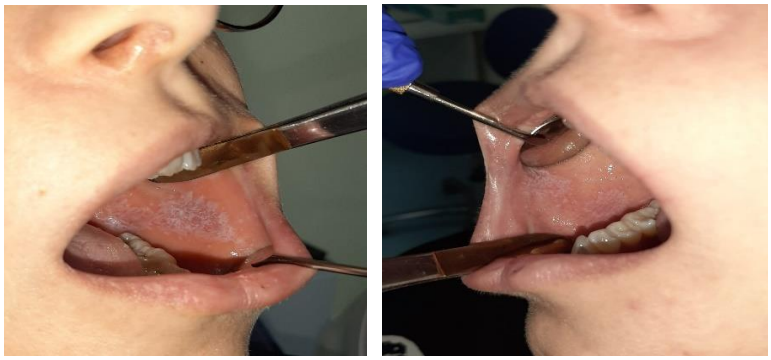

Figure 1. Classical clinical aspect of a reticular oral lichen planus

The role of genetic factors in the etiology of OLP is still under investigation and is an intriguing hypothesis. The literature contains several studies on familial cases of OLP, whose observations suggest a genetic predisposition. A case report published in 2005 tracking 3 patients with OLP from successive generations within the same family suggested an autosomal dominant transmission, with each patient having an affected parent (30).

Wang et al. reported a case of a Chinese family in which 5 members were diagnosed with OLP. At diagnosis, they presented with multiple, associated keratotic and erosive lesions, and 2 of the patients progressed to oral cancer. This raised the discussion of a genetic susceptibility and genotyping was performed on these patients. Results identified chromosome 3p14-3q13 as the region associated with the gene responsible for OLP. This research represented an initial step towards further studies that will provide important evidence regarding the role of genetic factors in the etiology of OLP (31).

Conclusions

Although the role of genetic factors in OLP is not yet fully clarified, the existence of familial OLP cases highlights the possibility of genetic transmission of this condition. This is particularly relevant given that published studies have reported atypical clinical patterns and an earlier age of onset compared to non-familial cases. Additionally, the reported risk of progression to oral mucosa carcinoma has been higher. All these factors may provide arguments for future research directions focusing on the involvement of genetic factors in the etiology of OLP.

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