Rom J Morphol Embryol 2020, 61(2):563–567 ISSN (print) 1220–0522, ISSN (online) 2066–8279 doi: 10.47162/RJME.61.2.28

CASE REPORT

RJME Romanian Journal of Morphology & Embryology http://www.rjme.ro/

Oral lichen planus – case report

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Abstract

This paper presents the case of a 58-year-old heavy smoker female who came to our clinic with acute pain, as well as mastication and feeding difficulties. The macroscopic examination revealed oral erosive lesions and ulcerations. The polymorphic aspect of the lesions required the differential diagnosis of oral erythroplakia or carcinoma, which were excluded by biopsy. At the same time, we assessed the expression of S100 protein, Ki67 and the cluster of differentiation (CD) 4, CD8 (T-cell) and CD20 (B-cell) immune cell markers by immuno-histochemical analysis. As a result, after the clinical and pathological assessment, the diagnosis of oral lichen planus was established, and a therapy plan was conducted. We observed a favorable clinical evolution after the administration of corticosteroids and immunomodulatory agents.

Keywords: oral lichen planus, B- and T-cell markers, Ki67, S100 protein.

Introduction

Oral lichen planus (OLP) belongs to inflammatory chronic skin and/or oral pathology [1]. Studies have revealed the malignant potential of the OLP lesions, but the results are controversial, since the reported rate of OLP malignant transformation varies between 0% and 10% [2]. Microscopically, OLP lesions are characterized by the presence of hyaline bodies and chronic inflammatory infiltrate in the basal epithelial layer and the adjacent areas, the alteration of the basement membrane structure and integrity and the obliteration of the conjunctival epithelial line and the epithelial crests [1]. Keratinocyte apoptosis and basement membrane disruption are considered to be involved in OLP pathogenesis, since apoptotic keratinocytes are unable to synthesize the basement membrane components. Keratinocyte apoptosis induced by cluster of differentiation 8 (CD8)-positive cytotoxic T-cells can cause basement membrane disruption, which allows the non-specific T-lymphocytes migration to the epithelium [3]. Although the immune mediated reaction is recognized in OLP pathogenesis, an exact etiology is yet unknown. The disease affects mostly middle-aged females but is less common in children. The atrophic and erosive forms are rare. The malignant potential of OLP is controversial. Consequently, dentists should treat all intra-oral lichenoid lesions as suspicious and monitor the patients on a regular basis [4].

Aim

This paper reports a case of tongue leukoplakia, right and left jugal lichen planus in a female patient, laying emphasis on the histopathological (HP) aspects and the B- and T-lymphocyte subpopulations.

Case presentation

A 58-year-old Caucasian female with smoking history was referred to Dentissimo Dental Care Clinic, Timişoara, Romania, for acute pain and mastication and feeding difficulties. Fatigue, insomnia, and anxiety disorders were associated with these local symptoms. The macroscopic examination of the oral cavity revealed an aberrant granular layer on the jugal mucosa, both on the gums and the tongue area, of a mother-of-pearl whiteness and with central ulcerations characteristic of lichen leukoplakia (Figures 1 and 2). At the same time, white intercrossed streaks of web-like aspect were found on the jugal mucosa (chiefly on the dental occlusion line), typical of the Wickham striae (Figures 3 and 4). Initially, the leukoplakia was asymptomatic, but it became painful with the oral erosions. It is important to specify that the patient presented the same modifications in the genital area as well. The erosive and ulcerative lesions produced by the epithelial necrosis in the oral cavity caused acute pain in contact with food or fluids, which made feeding difficult.

The lesions worsened in time and the asymptomatic evolution caused the patient's both mental and physical debilitation, especially regarding her nutritional status. The clinical examination revealed the presence of small, polygonal and umbilicated purple papules with a slightly shiny surface and a fine web of white pruritic lines (Wickham striae) on the upper and lower limbs. The aspect of the lesions and the accompanying symptoms supported the diagnosis of lichen planus.

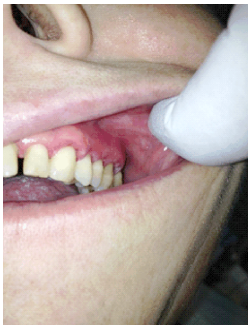

Figure 1 – ***Erosive gingivitis on the left upper arch.***

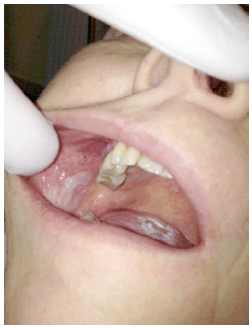

Figure 2 – ***Leukoplakia plaque on inside of the right cheek.***

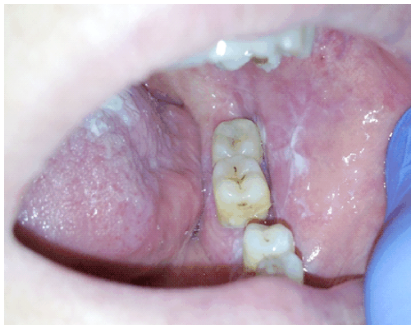

Figure 3 – ***Wickham striae on inside of the right cheek.***

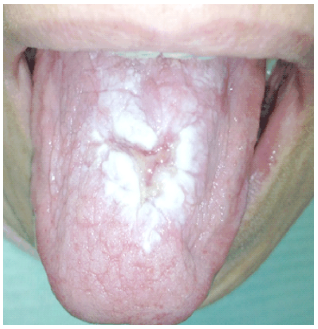

Figure 4 – ***Leukoplakia patches on the anterior side of the tongue.***

Histopathology

The lesions were biopsied, tissue samples being harvested after local anesthesia, fixed in 10% neutral buffered formalin, sent to Service of Pathology, and processed with the standard paraffin-embedding technique. The 5 μm thick sections were cut with a Leica RM2235 rotary microtome and stained with Hematoxylin–Eosin (HE), in order to obtain a HP diagnosis. Additional immunohistochemical (IHC) reactions were done for CD4, CD8, CD20, S100 protein, and Ki67.

The microscopic examination of the biopsy revealed fragments of oral mucosa covered by a thickened squamous stratified epithelium with irregular acanthosis, hypergranulosis and hyperparakeratosis with the formation of parakeratin lamellae detached from the epithelium. Between the epithelial cells of the basal layer there were observed apoptotic keratinocytes. Rich band-like inflammatory infiltrate consisting of lymphocytes, macrophages, neutrophils, and eosinophils were identified in the connective tissue of lamina propria, just beneath the epithelium. The inflammatory cells have a tendency toward exocytosis, with the perturbation of the basement membrane integrity and the presence of inflammatory cells within stratified epithelium. Moreover, in the lamina propria was observed elastotic degeneration of the collagen fibers (Figures 5 and 6) and capillaries hyperemia (Figure 7).

IHC examination

The analysis of the B- and T-cell subpopulations distribution in the erosive oral lesions revealed the absence of the CD4 immunolabelling (Figure 8) of the lymphocytes. Instead, 35% of the inflammatory cells were CD8-positive T-cells and 5% were CD20-positive B-cells (Figures 9 and 10). S100 protein was negative in the inflammatory infiltrate, although the immunomarker was positive on the non-epithelial cells as Langerhans cells and melanocytes, in the squamous epithelium and on the dendritic cells cytoplasm in the connective tissue of lamina propria (Figure 11). The number of positive Langerhans cells was not increased compared to the normal epithelium. Ki67 cell proliferation immunomarker was expressed in 5% of inflammatory cells (Figure 12).

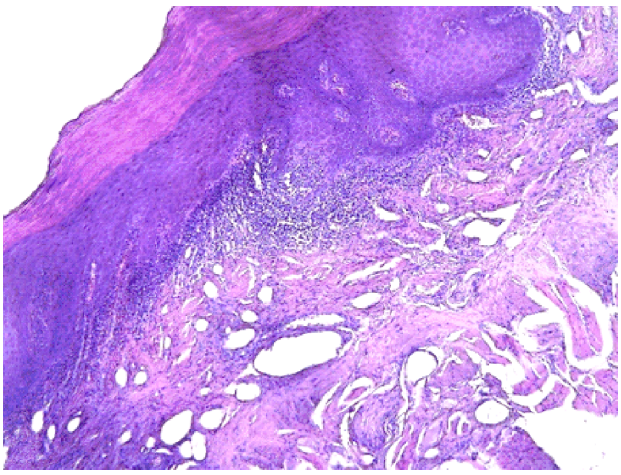

Figure 5 – ***Labial mucosa, thickened epithelium with irregular acanthosis, hypergranulosis and hyperparakeratosis. HE staining, ×100.***

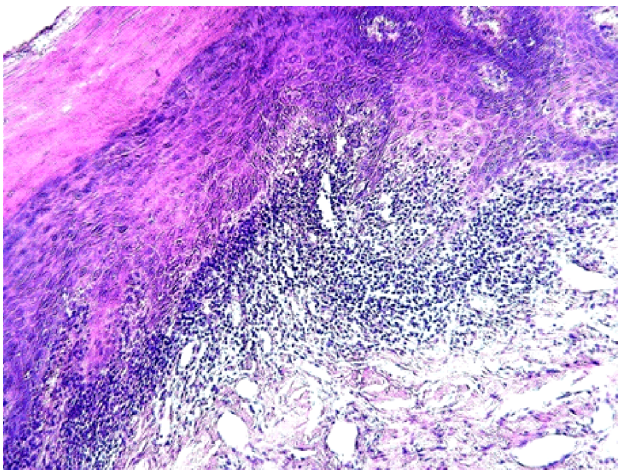

Figure 6 – ***Labial mucosa, band-like infiltrate of inflammatory cells beneath the squamous cell epithelium. HE staining, ×200.***

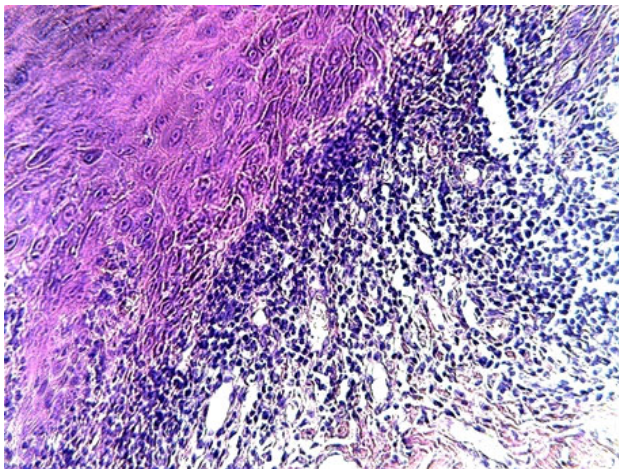

Figure 7 – ***Labial mucosa, exocytosis of inflammatory cells, with perturbation of basement membrane integrity. HE staining, ×400.***

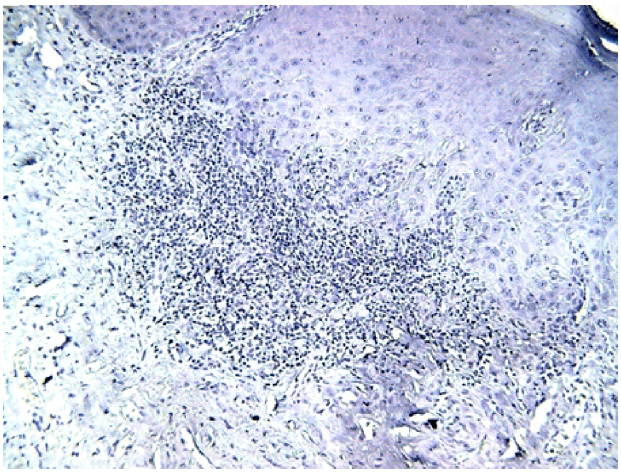

Figure 8 – ***Labial mucosa: negative immunohistochemical reaction for CD4. Immunostaining with anti-CD4 antibody, ×200. CD4: Cluster of differentiation 4.***

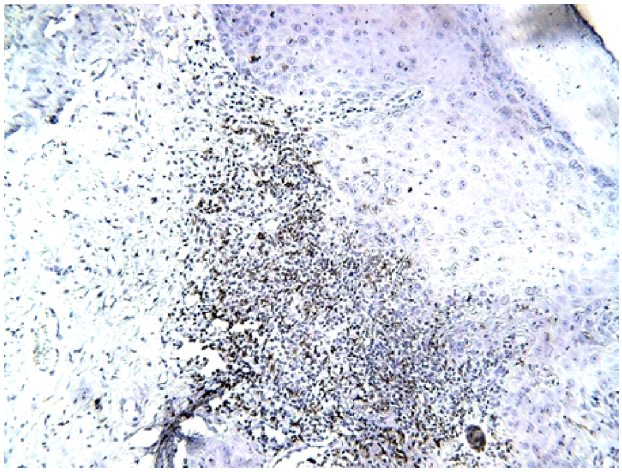

Figure 9 – ***Labial mucosa: positive immunohistochemical reaction for CD8 in 35% of inflammatory infiltrate cells, with the presence of some positive T-cells between epithelial cells. Immunostaining with anti-CD8 antibody, ×200. CD8: Cluster of differentiation 8.***

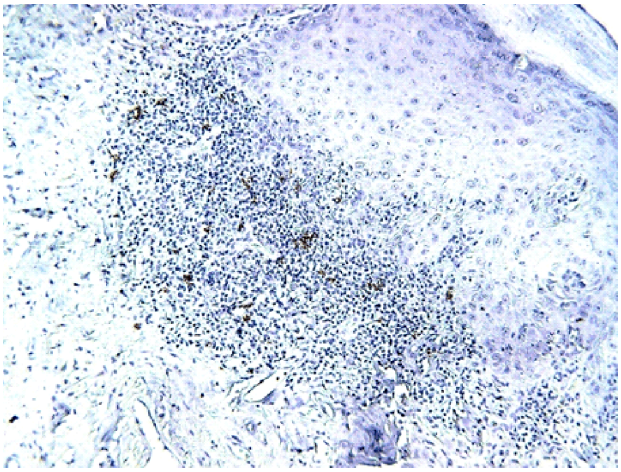

Figure 10 – ***Labial mucosa: positive immunohistochemical reaction for CD20 in 5% of inflammatory cells. Immunostaining with anti-CD20 antibody, ×200. CD20: Cluster of differentiation 20.***

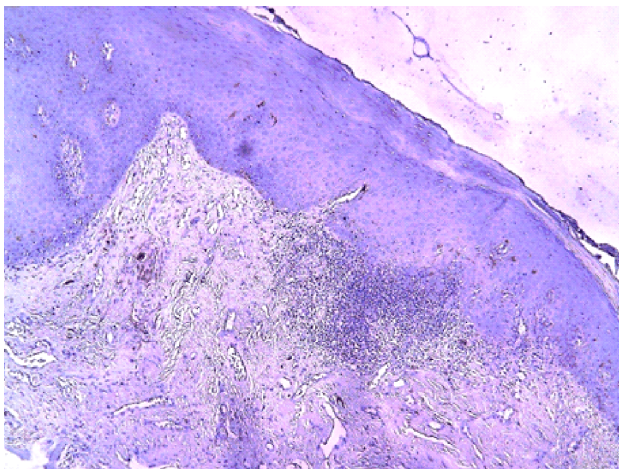

Figure 11 – ***Labial mucosa: positive immunostaining for S100 protein in some Langerhans cells. Immunostaining with anti-S100 antibody, ×100.***

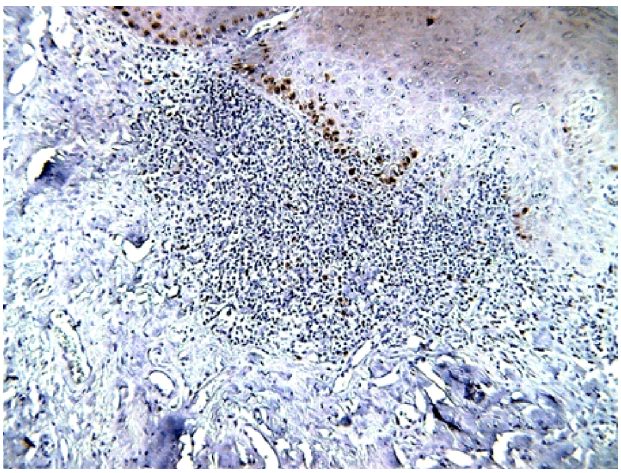

Figure 12 – ***Labial mucosa: immunostaining for anti-Ki67 antibody restricted to the basal layer keratinocytes. Immunostaining with anti-Ki67 antibody, ×200.***

Discussions

Lichen planus is an autoimmune inflammatory condition [5]. It is the most frequent non-infectious disease of the oral mucosa in adult patients. Of the affected patients, only 17% make a full recovery, although remissions have been reported in 39% of cases with OLP lesions. The exact etiology of this disease is not yet known, but stress, drugs, dental fillings, genetic factors, immunity, and hypersensitivity reactions can contribute to its pathogenesis. OLP is mediated by T-cells, chiefly CD8-positive T-cells that release various cytokines like tumor necrosis factor alpha (TNFα) and interleukin-12 (IL-12), which causes the perturbation of the basement membrane integrity [6]. OLP patients can develop additional lesions that affect their skin or other sites of their mucosa. About 5% of OLP patients will develop cutaneous lesions. The most common lesion site is the flexor region of the forearm, but such lesions can also occur frequently on the legs, the back, and the chest. The cutaneous lesions are polygonal, violaceous, flat-topped, erythematous papules covered with a web of fine lines (Wickham striae), usually occurring several months after the oral lesions [7].

The OLP diagnosis is based on the clinical symptomatology and the HP aspects. Clinically, the lesions are usually multiple and bilateral and appear on various sites of the oral cavity. Classically, OLP distribution is symmetrical, with well-defined white striations on a slightly erythematous background that frequently involves the tongue, and buccal mucosa. Some other clinical studies reported different type of lesions: bullous-like, papular, erosive, and atrophic [8]. The differential diagnosis includes drug-related lichenoid eruptions, lichenoid lesions caused by the contact with restorative dental materials, leukoplakia, lupus erythematous [9]. In our case, the oral lesions were located on the jugal mucosa, the gums, and the tongue area. They were accompanied by lesions on the vaginal mucosa. Generally, HP lesions are characterized by the hydropic degeneration of the basal epidermal layer, keratinocytes apoptosis and the presence of an inflammatory infiltrate, hyperkeratosis, hypergranulosis and acanthosis [10, 11].

Some studies have reported the concurrent occurrence of a known autoimmune disease (systemic lupus erythematosus, primary biliary cholangitis, and Sjögren's syndrome) and OLP, which suggests that at least part of the OLP lesions can be related to autoimmune mechanisms. In OLP, the autoreactivity phenomena have been revealed during the study of the CD4-positive cell subset from the OLP patients' peripheral blood and lesions. In the lesions occurring on the subepithelial region and the lamina propria, CD4-positive T-lymphocytes have been reported as prevalent. CD4-positive T-lymphocytes can be differentiated in distinct types of T-helper (Th) cells. Recent proofs have indicated that the Th1/Th2 imbalance influences the expression of the cytokines involved in OLP immunopathology [12, 13]. Differences have been reported in the distribution of T-lymphocyte subsets between the control groups and the examined groups, and an increased distribution of CD4 and CD8 cells in lamina propria was found. These were located primarily on the sub-basal region of the papillary layer and only rarely on the intraepithelial region [14]. In our case, the CD4 immunoexpression was not revealed in the OLP lesions. Instead, CD8-positive T-lymphocytes and CD20-positive B-lymphocytes were revealed on the membrane level, the CD8-positive cells prevailing over the CD20-positive B-cells, which suggest the T-lymphocytes are preponderant. S100 protein immunoexpression aimed at revealing the Langerhans cells, antigen presenting cells with a role in lymphocyte sensitization. Contrary to the studies published in the English literature, which have reported significant increases in the mean value of Langerhans cells in OLP [14], in the presented case, only a small number of Langerhans cells were identified in the epithelium, similar with the number of Langerhans cells found in normal epithelium. Ki67 nuclear antigen is a cell proliferation marker detected in all the phases of the cell cycle and assessed as a risk factor in oral cancer development from precancerous cells. Although Ki67 has been studied intensively in oral cancerous and precancerous lesions, only a limited number of studies have examined Ki67 expression in inflammatory diseases of oral mucosa. A high index of Ki67-positive cells in the squamous cells epithelium may indicate that some OLP-specific lesions can have malignant potential, which could explain the current controversies over the premalignant nature of OLP lesions [15, 16]. In the presented case, the Ki67 index was similar to normal squamous epithelium, the positive epithelial cells being restricted to the basal layer of keratinocytes.

Consequently, the OLP pathogenesis can involve the B- and T-lymphocytes interdependent mechanisms. It is a complex, difficult to treat pathology. The characterization of the B- and T-cell subpopulations can prove valuable for the application of precision therapeutic strategies with monoclonal antibodies, B- and T-cell specific inhibitors. Ki67 can be useful in selecting patients for regular follow-up in order to prevent malignancy.

Conclusions

OLP is an immune mucocutaneous disease with unknown etiology, therefore a correct diagnosis of lesions by biopsy, followed by HP and IHC analysis may consistently improve the management of this pathology. In this presented case, the clinical evolution was favorable after the administration of corticosteroids and immunomodulatory agents. Further studies are needed to elucidate the etiopathogenesis of this disease and optimize the treatment.

Conflict of interests

The authors declare that they have no conflict of interests.

Authors' contribution

The authors Cristian Sebastian Vlad and Sînziana Luminiţa Istrate contributed equally to the article.

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Received: March 11, 2020

Accepted: October 23, 2020