

## Case Report

### Grinspan's Syndrome -Affecting A 46 Year Old Male

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#### ABSTRACT

**Aim** Oral lichen planus is a chronic inflammatory condition, etiologically obscure, affecting 0.1-4% of the general population. The erosive form of oral lichen planus is most severe, often unresponsive to systemic and topical therapies. A rare association between this form, diabetes mellitus and hypertension was first reported by Grinspan in 1966. The increased prevalence of diabetes mellitus and carbohydrate intolerance observed in patients with oral lichen planus suggests a possible pathogenic role of the metabolic disorder.

Case report A 46 years old male, presented with eroded and ulcerated extremely painful lesions all over the oral mucosa, but predominantly localized on the palate, buccal mucosa and attached gingiva, associated with white patches. He was also suffering

of type 2 diabetes mellitus and hypertension. Histopathological findings sustained the clinical diagnosis of erosive oral lichen planus. Laboratory data revealed high plasma levels of glucose. The treatment we chose was topical tacrolimus 0.1% ointment twice a day and triamcinolone 0.1% oral paste once a day with satisfactory results after 2 weeks.

**Keywords :** Lichen planus, white lesions

**Discussion:** Oral lichen planus represents a cell-mediated immune response with infiltrating T4 and T8 lymphocytes. The exact nature of the correlation between erosive oral lichen planus, diabetes mellitus and hypertension is not yet clarified but it is very well known that systemic inflammation is a contributor to atheromatosis.

**Conclusion:** All patients with oral lichen planus and particularly those with the erosive form should be examined in order to identify a metabolic syndrome and to initiate an early treatment to avoid future cardiovascular problems. The prognostic of our case correlates with the response of oral lesions to treatment (these lesions should be periodically clinically and histopathologically monitored for the malignant transformation risk).

### Introduction

Oral lichen planus is a chronic inflammatory condition of unknown etiology, with a prevalence of 0.1 -4%. Oral lesions of lichen occur in 70-77% of patients with cutaneous manifestations, but oral mucosa may also represent the only site of the disease.<sup>1</sup> The disease mainly occurs in patients of medium age and in females. In regard to the physiopathology, it is considered to be the result of an immune response to antigens in the oral epithelium that are still unidentified. Oral lichen planus may be associated with several other diseases. A rare association between the most severe form of oral lichen planus – the erosive form – diabetes mellitus and arterial hypertension is Grinspan's syndrome.

### Case report

A 46 year old male patient presents with extremely painful, erosive, ulcerative and leucoplaziform lesions all over the oral mucosa with a progressive and persistent evolution of approximately one year. The treatment he underwent for the last one year with topical corticosteroids and antimycotic resulted in a

partial and transitory effect for the oral lesions. The patient had been diagnosed arterial hypertension in 2002, type 2 diabetes mellitus in 2006 being treated with Enalapril 10 mg/day, Metoprolol 50 mg/day, Gliclazid 80 mg/day. Intraoral examination revealed multiple erosive and ulcerative lesions with fibrin deposits intermixed with leucoplaziform patches located on buccal mucosa, hard palate and attached gingival (fig. 1, 2), accompanied by marked pain that was accentuated by speaking, mastication, deglutition that severely impaired the patient's quality of life. Histopathological examination of a biopsy from the lesional buccal mucosa revealed an atrophic scuamous epithelium with a profound ulceration partially replaced by granulation tissue with numerous neoformation capillaries and microabcesses and a dense lymphocytic inflammatory infiltrate with a lichenoid aspect lateral to the ulceration, that remodeled the basement membrane (fig. 3, 4). Laboratory investigations revealed the following pathological data: hyperglycemia (156 mg/dl). Considering the general biological status of the patient, topical treatment with Tacrolimus ointment 0.1%, 1-2 applications per day and triamcinolone 0.1% oral paste was initiated. The evolution of the oral lesions after two weeks with this treatment was favourable with partial epithelisation and alleviation of functional symptoms. The patient needs further periodical clinical monitoring because of the risk of conversion to an invasive squamous cell carcinoma.



Figure 1. Clinical aspect of the buccal mucosa (ulcerative lesions with fibrin deposits intermixed with white patches)



Figure 2. Erosive, ulcerative lesions on the hard palate

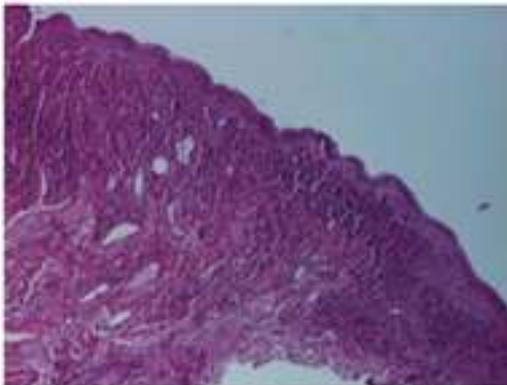


Figure 3. Atrophic epithelium, lichenoid inflammatory infiltrate and numerous capillaries in the dermis

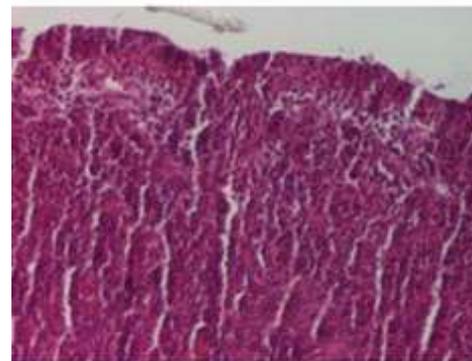


Figure 4. Ulceration, numerous neoformation capillaries in the dermis

## DISCUSSION

The association of erosive oral lichen planus with diabetes mellitus and arterial hypertension was first reported by Grinspan in 1966.<sup>2</sup> The exact nature of the correlation between the elements of this symptomatic triad is unclear. The hypothesis of an iatrogenic origin of the oral lesions has also been stated, considering the inherent multiple drug association due to the two chronic comorbidities with a lethal risk.<sup>3</sup>

Now a days it is considered that the high prevalence of diabetes mellitus and hydrocarbonate intolerance in patients with oral lichen planus is suggestive of a possible pathogenic role of these conditions.<sup>1,4</sup> The etiology of oral lichen planus is not yet completely understood, but immunopathological data sustain the hypothesis of a T cell mediated dysfunction that leads to basal vacuolar change and death of the

basal keratinocytes. Cytokines released from the apoptotic keratinocytes play an important proinflammatory role by selectively recruiting T cells and making up the characteristic subepithelial infiltrate. T cells are in turn the source of high levels of chemokines and cytokines such as IL2, IL6, IL10, TNF $\alpha$ , TGF $\beta$  in the subepithelial infiltrate, that promote inflammation.<sup>5</sup> The systemic chronic inflammatory process is a well known factor that contributes to the pathogenesis of the metabolic syndrome, as well as to atheromatosis.<sup>6,7</sup> Patients with oral lichen planus should therefore be periodically investigated in order to identify and properly treat cardiovascular risk factors.<sup>6</sup> The treatment of choice for the oral lesions in Grinspan's syndrome, is topical. Calcineurin inhibitors (nonantibiotic macrolides: tacrolimus, pimecrolimus), that inhibit the activation of the nuclear factor for activated T cells (NFAT), provide best beneficial effects while having the least adverse side effects when administered for long periods of time (at least 6 months) in order to obtain a significant therapeutic response.<sup>8,9</sup>

### Conclusion

Oral erosive lichen planus is a chronic inflammatory condition with an immune substrate that may be part of morbid associations with a high cardiovascular risk. Grinspan's syndrome is a rare association of a triad of symptoms: erosive oral lichen planus, diabetes mellitus and arterial hypertension. The prognostic of this case correlates with the evolution of the oral lesions that must be clinically and histopathologically monitored because of the risk of malignant transformation (evaluated at 5% in nonsmoking patients with

atrophic, erosive and ulcerative lesions of oral lichen planus), with the evolution of the diabetes mellitus and arterial hypertension.<sup>10</sup>

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