



## Unique Journal of Medical and Dental Sciences

Available online: [www.ujconline.net](http://www.ujconline.net)

### Case Report

## GRINSPAN'S SYNDROME: A VARIANT

Nilima TS<sup>1\*</sup>, Senthil Kumar S<sup>2</sup>, Arun RT<sup>3</sup>, Rajasekar S<sup>4</sup>

<sup>1</sup>Post graduate, Department of Periodontics, Rajah Muthiah Dental College, Tamilnadu, India

<sup>2</sup>Professor and Head, Department of Periodontics, Rajah Muthiah Dental College, Tamilnadu, India

<sup>3</sup>Professor, Department of Periodontics, Rajah Muthiah Dental College, Tamilnadu, India

<sup>4</sup>Professor, Department of Periodontics, Rajah Muthiah Dental College, Tamilnadu, India

Received: 31-07-2016; Revised: 29-08-2016; Accepted: 25-09-2016

\*Corresponding Author: **Dr. T.S. Nilima,**

Post graduate, Department of Periodontics, Rajah Muthiah Dental College and Hospital, Annamalai Nagar, Chidambaram, Tamilnadu.

### ABSTRACT

Grinspan's syndrome, a rare clinical entity reported by Grinspan in 1966 is a symptomatic triad including Diabetes mellitus, Hypertension and oral lichen planus common in elderly. The definitive diagnosis of this condition is established by correlating the medical history and clinical examination along with histopathologic interpretation of the lesion. We present a case report of a clinical variant of Grinspan's syndrome of a 72 year old male patient with significant ulceroproliferative lesion on the palate along with the clinical triad of Grinspan's syndrome.

**Keywords:** Diabetes mellitus, Grinspan's syndrome, Hypertension, Squamous cell carcinoma, Oral lichen planus

### INTRODUCTION

Lichen planus is a relatively common and fairly distinctive mucocutaneous disorder which affect skin and/or oral mucosa. Oral lichen planus is estimated to be present in 0.1-5% of individuals with prevalence possibly varying in different races. In 25 % of cases oral lesions may precede the appearance of skin lesions. Although the exact cause of Oral Lichen Planus (OLP) is unknown, experimental evidence suggests that it is an inflammatory T-cell mediated immune response<sup>1</sup>.

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<sup>2</sup>.

One of the most controversial aspects of oral lichen planus is its malignant potential. Various studies have suggested that OLP has potential for malignant transformation, although there is consensus that the probability of such transformation is low<sup>3</sup>.

Here we present a rare case of oral lichen planus in a patient with the medical history of Diabetes and hypertension presenting with the histologic evidence of oral squamous cell carcinoma.

### CASE REPORT

A 72 year old male patient reported to the department of periodontics, Rajah Muthiah Dental College and Hospital,

Chidambaram with the chief complaint of an asymptomatic growth in the palatal region noticed since 15 days. Patient gave a history of burning sensation in mouth for the past 15 days with severity increasing while taking spicy food substances.



a



b



c

Figure 1: (a & b) Clinical photograph of buccal and palatal lesions, (c) Surgical excision of the palatal lesions.

Medical history revealed the patient to be type II diabetic for duration of 15 years and a hypertensive for past 2 years. He was on medical treatment for both diabetes and hypertension. On general physical examination, the patient was found to be well nourished and moderately built without any deleterious habits.

Extraoral clinical examination revealed the right and left submandibular lymphnode to be palpable, non-tender measuring approximately 0.8 x 1 cm, roughly oval in shape, mobile and firm in consistency.

On intraoral examination, Oral hygiene status was found to be poor. A diffuse gingival lesion was seen buccally extending from distal aspect of 12 to the mesial aspect of 18, involving the marginal and attached gingiva, which was erythematous, with interspersed areas of hyperkeratosis, soft and edematous in consistency, non-tender, exhibiting bleeding on probing and with a distinct white linear pattern at its apical extent.

An isolated ulcero-proliferative lesion was also seen palatally in 12,13 region involving the marginal gingiva, attached gingiva and the interdental papilla which was sessile, rough surfaced, erythematous with areas of hyperkeratosis, soft and edematous in consistency, tender, friable, measuring approximately 10 x 14 mm and exhibiting bleeding on probing. And a similar asymptomatic sessile growth with corrugated surface, pigmented, non-tender, involving the marginal gingiva, attached gingival and interdental papilla, measuring approximately 7 x 10mm was also present palatally in 16,17 region.

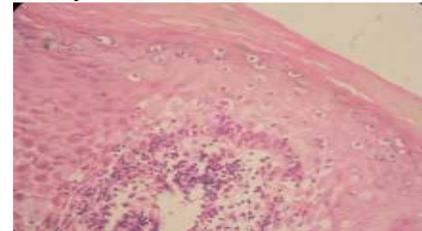
Periodontal examination revealed generalized bleeding on probing, a generalized probing pocket depth of 7 mm with grade I mobility in 31,41. Radiographic evaluation revealed a horizontal bone loss of 4-5 mm between 11 to 13 and a crestal bone loss extending from 15 to 18. Periodontal ligament space widening was seen in relation to 12,13,15,16. An excisional biopsy of the palatal lesions was made under LA and subjected to histopathological evaluation.

Histopathologic examination of the lesion on buccal side confirmed the lesion to be lichen planus. The epithelium exhibited hyperorthokeratosis, hypergranulosis and acantholysis. There was considerable basal cell degeneration and subepithelial inflammatory cell infiltration. Connective tissue showed abundant vascularity and dense chronic inflammatory cell infiltration.

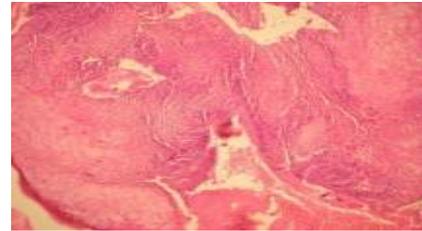
In addition, the palatal lesion revealed hyperplastic epithelia with hyperorthokeratosis, intraepithelial keratin pearls and focal areas of cellular atypia. Numerous mitotic figures and koilocytes were seen. Connective tissue was seen with superficial epithelial invasion and dense chronic inflammatory cell invasion suggestive of early invasive carcinoma.

Correlating the patient's systemic background of diabetes and hypertension with the histopathologic finding suggestive of lichen planus, a clinical diagnosis of Grinspan's syndrome was made. Topical corticosteroids and vitamin supplementation were prescribed to alleviate the symptoms of oral lichen planus and patient was disposed with an instruction to come for periodic review to assess the progression of the lesion. Patient was kept under regular

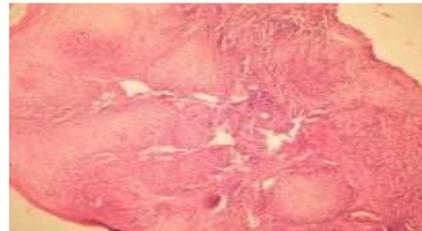
follow up, until he returned after 3 months with a recurrence of the palatal lesion. Patient was explained about the nature of the lesion following which he underwent a hemimaxillectomy.



a



b



c

Figure 2: (a) Epithelium with hyperorthokeratosis, hypergranulosis, acantholysis, basal cell degeneration and subepithelial inflammatory cell infiltration.

(b & c) Hyperplastic epithelia with hyperorthokeratosis, intraepithelial keratin pearls, cellular atypia, mitotic figures and connective tissue exhibiting superficial epithelial invasion.

## DISCUSSION

The association of erosive oral lichen planus with diabetes mellitus and arterial hypertension was first reported by Grinspan<sup>4</sup>. The results of their research were exposed at the Congress on Dermatology in Buenos Aires, 1963. In 1965 in a repetitive study Grupper & Avul seemed confirm the existence of this symptomatological triad; therefore the authors defined this complex as "Grinspan's syndrome". Further researches conducted by other authors confirmed the association between hypertension-diabetes-"erosive" lichen planus.



Figure 3: 2months after surgical excision

The exact etiology behind 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 co-morbidities with a lethal risk<sup>4</sup>. It is also suggested to be an oral lichenoid reaction as an adverse effect for the drug therapy for diabetes mellitus and hypertension<sup>5,7</sup>. Factors that predispose to pharmacological adverse drug reactions include dose, drug formulation, pharmacokinetic or pharmacodynamic abnormalities, and drug interactions. The metabolic conversion of drugs to chemically reactive products is now established as a prerequisite for many idiosyncratic drug reactions. Increased levels of reactive drug metabolites, their impaired detoxification, or decreased cellular defense against reactive drug products appears to be an important initiating factor<sup>6</sup>. There have been a number of reports suggesting that antihypertensive agents and oral hypoglycemic agents may induce Oral Lichenoid Reaction (OLR). Captopril and glybenclamide are recognized as being capable of producing such an oral lichenoid reaction<sup>7</sup>. Oral lichenoid reactions maybe regarded as a disease by itself or as an exacerbation of an existing OLP, by the presence of medication<sup>8</sup>.

It is also considered that the high prevalence of diabetes mellitus and hydrocarbonate intolerance in patients with oral lichen planus is suggestive as a possible pathogenic role of these conditions<sup>4</sup>. It has been proposed that the endocrine dysfunction in DM may be related to an immunologic defect that may also contribute to the development of OLP.

Oral lichen planus is a chronic inflammatory oral mucosal disease whose etiopathogenesis has not been completely disclosed<sup>5,9,10</sup>. 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. 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>4</sup>.

Grinspan's syndrome is usually treated symptomatically. Excellent oral hygiene is believed to reduce the severity of the symptoms, though it may be difficult for patients to achieve high levels of hygiene during periods of active disease. Treatment is aimed primarily at reducing the frequency and severity of symptomatic outbreaks. The most widely accepted treatment for lesions of OLP involves topical or systemic corticosteroids to modulate the patient's immune response<sup>4</sup>.

The malignant potential of lichen planus is an area of much controversy. But despite the current uncertainty about the probability of malignant transformation of OLP, the fact that such transformation may occur seems increasingly certain. Hence, it is mandatory in patients with oral lesions of lichen planus, even if asymptomatic or barely symptomatic, to programme scrupulous long-term follow up.

## CONCLUSION

Though lichen planus is seen with several other diseases, one rare association is between the severe form of lichen planus, diabetes mellitus and hypertension termed as Grinspan's syndrome. This case report is unique not only because the patient presented with all three symptoms of the syndrome but also due to the co-existence of an early invasive carcinoma. The association of squamous cell carcinoma along with Grinspan's syndrome is whether malignant transformation of preexisting oral lichen planus or an independent lesion is left unclear. To conclude, any patient presenting with oral lichen planus, especially the erosive form, should be examined in order to identify the metabolic syndrome and should be kept under long term follow up with periodic clinical and histopathological monitoring to prevent the risk of malignant transformation.

## REFERENCES

1. Vaidya SB, et al. Prevalence of oral lichen planus and hypertension in patients with diabetes mellitus. *International Journal of Women Dentists* 2014; 1(1): 18-22
2. Sethi E, Gulati M, Kaushal S, Singh OP, Grinspan's Syndrome -Affecting a 46 Year Old Male. *J Periodontal Med Clin Pract* : 2015; 02: 143-147
3. Gandara-Rey JM et al. Malignant transformation of Oral Lichen Planus on lingual location- report of a case. *Oral Oncology Extra*, 2004; 40: 1-4
4. Tatiana Țăranu, Irina Eșanu, Mirela Grigorovici, Mihaela Paula Toader. Grinspan's Syndrome. *Romanian Journal of Oral Rehabilitation* 2013; 5(4): 22-26
5. Sugeran PB, Savage NW. Oral lichen planus: Causes, diagnosis and management. *Australian Dental Journal* 2002; 47(4): 290-297.
6. Pirmohamed M, Madden S, Park BK. Idiosyncratic drug reactions. Metabolic bioactivation as a pathogenic mechanism. *Clin Pharmacokinet* 1996; 31: 215-230.
7. Lamey PJ, Gibson J, Barclay SC, Miller S. Grinspan's syndrome: A drug-induced phenomenon? *Oral Surg Oral Med Oral Pathol* 1990; 70: 184-5. 2
8. Ismail SB, Kumar SKS, Zain RB. Oral lichen planus and lichenoid reactions: etiopathogenesis, diagnosis, management and malignant transformation. *J. Oral Sci.* 2007; 49: 89-186.
9. Edward PC, Kelsch R. Oral Lichen Planus: Clinical Presentation and Management. *J Can Dent Assoc* 2002; 68(8): 494-9.
10. Seoane J, Romero MA, Varela-Centelles P, Diz-Dios P, Garcia-Pola MJ. Oral Lichen Planus: A Clinical and Morphometric Study of Oral Lesions in Relation to Clinical Presentation. *Braz Dent J* 2004; 15(1): 9-12.