

Grinspan's syndrome : a case of the triad of oral lichen planus, hypertension, and diabetes mellitus

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Abstract

The triad of oral lichen planus, hypertension and diabetes mellitus has been described before and is known as Grinspan's syndrome. Drug therapy for diabetes mellitus and hypertension is capable of producing lichenoid reactions of the oral mucosa. We reported a case of a 73-year old woman suffering from oral erosive lesion who received antidiabetic and antihypertensive agents. Topical steroids, antiseptic mouth rinse, and supportive multivitamin were prescribed. She was advised to modify her diet and was also referred to her physician who changes her medication. Her condition improved slightly and he is still under follow up. It appears that proper identification of the causative drug together with its immediate withdrawal and adjunctive topical therapy is an effective method for treating drug-induced lichenoid reactions in this case. It's concluded that based on clinical features and medical history, the patient was diagnosed Grinspan's syndrome, and the ultimate confirmation of oral lichenoid reaction is resolution of the condition following withdrawal of the drugs. By taking an active role in the diagnosis and treatment of oral conditions association with systemic disease, dentist may contribute to the maintenance of optimum health.

Key words: Oral lichen planus, diabetes mellitus, hypertension.

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Introduction

Grinspan's syndrome as originally described is a triad of conditions, namely essential vascular hypertension, diabetes mellitus and lichen planus of the oral mucosa (oral lichen planus or OLP).¹ Grinspan & his co-workers observed this syndrome. 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 hypertension-diabetes-"erosive" lichen.²

Oral lichen planus is a chronic inflammatory oral mucosal disease whose etiopathogenesis has not been completely disclosed.³⁻⁵ Cell mediated immune dysregulation has been associated with the pathogenesis of OLP. T-cell mediated immune response in which basal epithelial cells are recognized as foreign because of changes in antigenicity of their cell surface.⁴ Current data suggest that OLP is a T-cell-mediated autoimmune disease in which

autocytotoxic CD8+ T cells trigger the apoptosis of oral epithelial cells.⁶ The cause of this immune-mediated cell damaged is unknown.^{4,6} However, several predisposing factors have been implicated in the pathogenesis of OLP such as systemic medications (several drugs), certain dental materials, stress, genetic background, tobacco chewing, Graft-versus-host disease, and infectious agents (hepatitis C virus).^{5,6} Oral lichenoid reactions (OLR) are considered variants of OLP.⁶ Oral lichenoid reactions may follow the administration of systemic drugs, with a variable lag periode which is called lichenoid drugs reactions or lichenoid eruptions. Drugs that have been implicated in OLR include antimalarial drugs, non-steroidal anti-inflammatory (NSAIDs) drugs, anti-hypertensive agents, oral hypoglycaemic agents, diuretics, beta-blockers, although there are many others.^{3,6-8}

It is likely that Grinspan's syndrome represents a drug induced disorder.¹ The oral lichenoid lesion in Grinspan syndrome is may be a reaction to the drugs used to treat diabetes mellitus and/or hypertension. However, the precise relationship is not clear. We describe a clinical case observed at the Clinic of Oral Medicine, Dental Hospital of Padjadjaran University, characterized by three simultaneous symptoms which are hypertension, diabetes mellitus, and oral erosive lesions.

Case report

A 73-year-old woman was referred by her own general dental practitioner to the Oral Medicine Clinic, Dental Hospital of Padjadjaran University, Bandung in July 2008, with a history of burning sensation, painful ulceration on the tongue and bilateral buccal mucosa. The lesions had been present for over 1 year. She complained of impaired oral function, such as inability to wear her partial denture, dysphagia, and the resultant reduction in food intake and subsequent fall in body weight. Prior to referral, the patient had visited her general medical practitioner and dental practitioner, neither of whom had been able to offer a specific diagnosis or management.

Medical history revealed that the patient had diabetes mellitus, diagnosed more than 10 years ago. She also has hypertension approximately 6 years ago. She was on medical treatment for diabetic and hypertension. Her diabetes was controlled with glibenclamide 5 mg daily. The patient also had been taking captopril 25 mg twice daily previously, and the medication was changed to Adalat for the last 6 months up to now.

On extraoral clinical examination, There was no cervical lymphadenopathy and no extraoral lesions. Intraorally, ulcerations (yellowish areas) with irregular margins surrounded by red areas were presence on the left (Figures 1a) and right buccal mucosa (Figures 1b), palatum (Figures 1c), and the dorsum of the tongue extending from the anterior third to the tip of the tongue (Figures 1d).

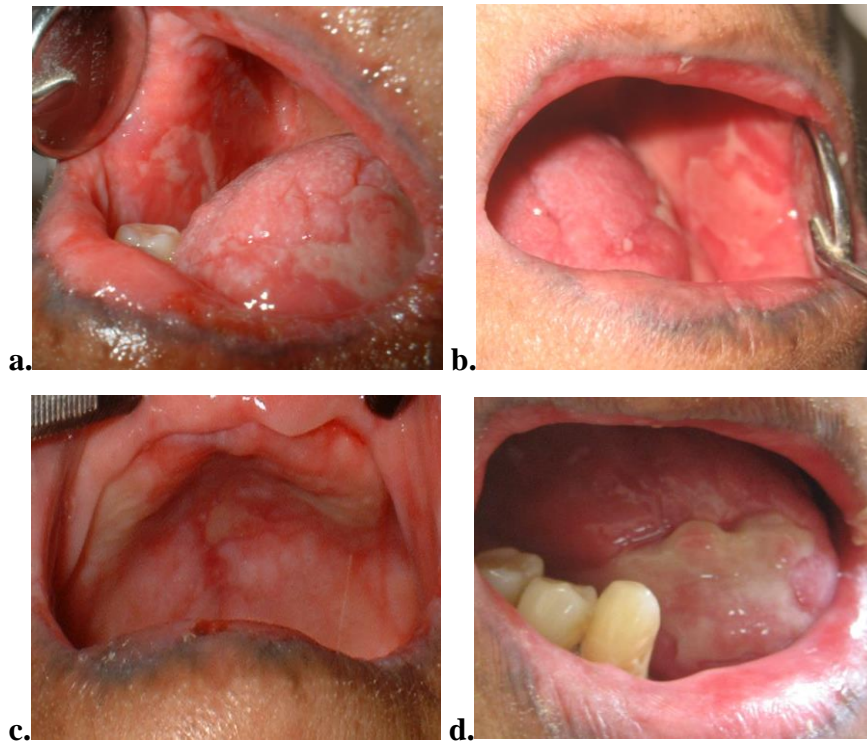


Figure1. Initial visit. Clinical photograph showing ulcerations (yellowish areas) with irregular margins surrounded by red areas were presence on the left (buccal and right (b) buccal mucosa, palatum (Figures c), and the dorsum of the tongue extending from the anterior third to the tip of the tongue (Figures d).

The investigation undertaken included routine hematology, blood glucose level and at two-hour postprandial. A biopsy of the lesion was not taken immediately due to the severity of the lesion on initial presentation and because of the patient's poor general health.

She was advised to modify her diet and improved his oral hygiene. Prednisone 5 mg tablets as mouth rinse 3 times daily, benzydamine hydrochloride 0.15% oral rinse 3 times daily, and multivitamin were prescribed. She was also referred to his physician, who changes his medication. At the last review appointment, eight weeks later, improvement in signs and symptoms were found. The patient had minimal oral complaints, there was marked

improvement in mastication, swallowing, and speech. Clinically, there are appear improved lesions on the oral mucosal (Figure 2). The patient has regular follow-up and to date.

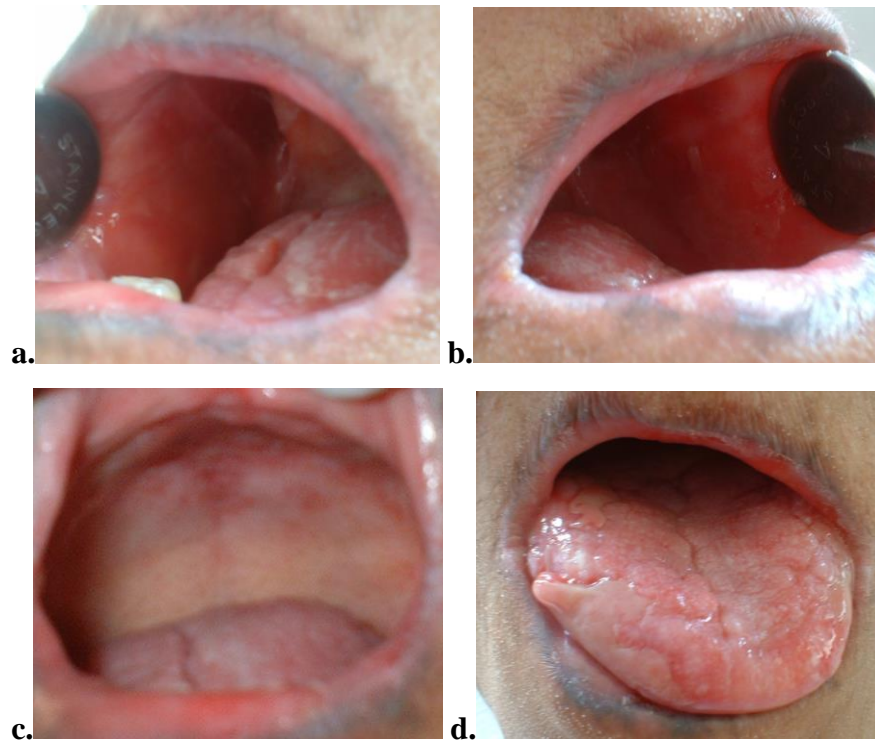


Figure 2. Eight weeks after withdrawal of causative drugs and palliative care. There was complete resolution of her erosive lesions with marked reduction in erythema on the buccal mucosa and palatum (Figures a, b and c). The ulceration on the dorsum of the tongue was also marked improvement.

Discussion

The manifestation of lichen planus, diabetes and hypertension has been reported by Grinspan et al 1963, 1966 and Gruper and Avul 1965. In this case, based on a medical history and clinical examination, the patient may have Grinspan's syndrome. She was diabetic and had hypertension. We have found erosive lesions in her oral mucosa as a clinical sign of erosive lichen planus. These lesions is probably an adverse effect of the drug therapy for her diabetes mellitus and hypertension. Numerous systemic medications have been documented to produce oral mucosal reactions that are similar clinically and microscopically to lichen planus, and this has led to the concept of lichenoid reactions.^{3,6,7} Oral lichenoid reactions (OLR) are considered variants of OLP. They may be regarded as a disease by itself or as an exacerbations of an existing OLP, by the presence of medication.⁶

The pathogenesis of drug-induced reactions, especially the mucosal ones, is largely unknown and appears to involve complex interactions among the drug in question, other medications, the patient's underlying disease, genetics, and life-style factors. Along this line, there is a growing interest in the association between pharmacogenetic polymorphism and adverse drug reactions. 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.^{9,10} Oxidative reactive drug metabolites are found in organs and cells preferentially affected by idiosyncratic drug reactions.¹¹

There have been a number of reports suggesting that antihypertensive agents and oral hypoglycemic agents may induce OLR.^{3,12,13} In this case, the patient was on medical treatment with captopril and glibenclamide. Captopril and glybenclamide are recognized as being capable of producing such a oral lichenoid reaction.¹ The sulphydryl groups of captopril changes enzyme systems. These aberrations may precipitate an immune response to epidermal antigens leading to lichenoid drugs reactions.⁶ Oral lichenoid drug reactions can also be caused by sulfonylurea hypoglycemic agents.^{12,13} However, the exact mechanism is still unknown.

There have been reports of association between LP and diabetes mellitus (DM). The prevalence of DM in patients with OLP has been reported to range from 10% to 85%.¹⁴⁻¹⁶ 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. Petrou-Amerikanou and colleagues (1998)¹⁷ reported that the prevalence of oral lichen planus is significantly higher in patients with type 1 DM and slightly higher in patients with type 2 DM than in control subjects. This may be a side effect of oral hypoglycemic agents or antihypertensive medications.¹⁸ However, others have reported that the prevalence of DM in patients with OLP does not differ from that of DM in the general population.^{19,20} A recent large study found no evidence of increased prevalence of lichen planus in patients with type 1 DM compared with nondiabetic control subjects.²¹

The diagnosis of oral lichen planus and oral lichenoid reactions is based on clinical and histopathologic characteristics.⁶ However, the diagnoses of oral lesions in this case was made on clinical examination only and was not confirmed histologically. A biopsy of the lesion in this patient was not taken due to the severity of the lesion on initial presentation and because of the patient's poor general health. Axell (1987)²² reported that the use of the clinical criteria could be 97% effective. Oral lichenoid reactions, usually have the same clinical features as idiopathic OLP.⁶ The clinical presentation of lichenoid drug reactions are more likely to be unilateral and of the erythematous and ulcerative variety; however, this is not well-substantiated.¹ Lichenoid drug reactions can be identical to lichen planus but have a tendency to produce more full thickness ulceration and more commonly affects sites not frequently affected by lichen planus, such as ventral tongue.⁶ And the ultimate confirmation of oral lichenoid reaction in this case is resolution of the condition following withdrawal of the drugs.

The atrophic-erosive lesions of oral mucosa in this patient cause symptoms ranging from burning sensation to severe pain. Prednisone 5 mg tablets as mouth rinse 3 times a day, benzydamine hydrochloride 0.15% oral rinse 3 times daily, and supportive multivitamin were prescribed. In the symptomatic case, many drugs have been tried including corticosteroids. Topical corticosteroids are the mainstay of medical treatment of OLP and OLR, although rarely, corticosteroids may be administered intralesionally or systemically. Prednisone has been used systemically. However, it can be used as topical corticosteroids, as a mouthwash. Prednisone are usually reversed for severe and more widespread lesions. Maintenance of good oral hygiene can enhance healing and lessen the symptoms. Mechanical trauma (poorly fitting dental prothesa) that can exacerbate was removed. When she was seen again for routine treatment about 3 weeks later, the lesion's clinical appearance had improved, although erosive lesions could still be detected.

After consultation with the patient's medical practitioner, captopril and glybenclamide were discontinued. Resolution of OLR usually follows the removal of causative agent. In some cases, physicians may be reluctant to change patient's medication especially when the drug is being given for potentially life threatening diseases such as cardiovascular diseases. With such situations where the offending drug cannot be withdrawn, the management of OLR would be similar to the management of OLP. Improvement in signs and symptoms was noted

in this patient. Oral lichenoid reactions clear up slowly when the responsible medication is withdrawn.

Any patient suspected of having OLP or OLR should be questioned about systemic medications. It is important for dentist to educate patients about the oral implications of DM and hypertension. A change medication should be considered after consultation with the patient's medical practitioners. Early diagnosis, withdrawal and/or replacement of the causative drug, and appropriate management strategies are essential to improve the quality of life of a patient who was suffering from Grinspans syndrome.

Conclusion

The patient may have the triad of symptoms once described as Grinspans syndrome, possibly due to lichenoid reaction to antidiabetic and antihypertensive drugs. It is important for dentist to be familiar with the medical management of patients with DM and hypertension. By taking an active role in the diagnosis and treatment of oral conditions association with both of these disease, dentist also may contribute to the maintenance of optimum health.

Daftar Pustaka

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