GRINSPLAN SYNDROME: THE TRIAD
Dr Seema M¹, Dr Shruti Srinivasan²
1 MDS, Senior Lecturer, Oxford Dental College
2 MDS, Senior Lecturer, Oxford Dental College
Corresponding author: Dr Seema M
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Abstract:
Lichen Planus is a chronic immunologically mediated mucocutaneous disorder with varied clinical manifestations. The condition might be associated with multiple causative or exacerbation factors. An interesting association of Oral Lichen Planus with Diabetes Mellitus and vascular hypertension is called as Grinspan’s syndrome. Since its inception has been an arena of interest. It has appeared very lucrative to many researchers as it lacks clarity and enhanced ambiguity. A 65 year female patient came with a complaint of burning mouth and difficulty in swallowing since 1 year with H/O Diabetes Mellitus since 8 years and hypertension since 2 years. Malignant transformation is the most significant complication of long standing and non healing Lichen Planus. Repeated follow up and biopsies are mandatory for prevention and early detection of malignant transformation.

Keywords: Grinspan Syndrome, Hypertrophic Lichen Planus, Esophageal Lichen Planus

Introduction:
Lichen planus is a chronic immunologically mediated mucocutaneous disorder with varied clinical manifestations affecting the skin, oral mucosa, nail, genital mucosa, and the scalp. The condition is T cell mediated, where the CD8⁺ T cells trigger the apoptosis of oral epithelial cells at the basal layer. It has a well established clinical features and histopathological features that aid in the diagnosis. The condition might be associated with multiple causative or exacerbation factors such as chronic infection, allergies, systemic conditions, endocrine disorders, tobacco chewing habit, psychological stress, graft versus host diseases and genetics. Grinspan Syndrome, since its inception has been an arena of interest. It has appeared very lucrative to many researchers as it lacks clarity and enhanced ambiguity.

Case Report:
A 65 year female patient came with a complaint of burning mouth and difficulty in swallowing since 1 year. H/O Diabetes Mellitus since 8 years and hypertension since 2 years. Patient was on medication for the above since the time of onset of the systemic condition. On clinical examination showed skin lesions involving both the elbows, knees and ankles. Lesions were pruritic, with multiple bleeding spots and scarring. On oral examination, showed pigmentation of lips and labial mucosa. Buccal mucosa on both the sides showed dark pigments with focal areas of white striae. Moderately maintained oral hygiene and chronic periodontitis was evident. Based on the above features a clinical diagnosis of Hypertrophic Lichen Planus of the skin was rendered along with Grinspan Syndrome (Oral lichen Planus, Diabetes Mellitus and Hypertension) involving esophagus.

An exfoliative cytology was performed as the patient denied for a biopsy. Smears were taken from both the sides of buccal mucosa and labial mucosa and were stained for PAP and PAS. On cytological examination showed, PAS positive smear suggestive of oral Candidiasis with evident Candidal hyphae. PAP test showed numerous parabasal and superficial exfoliated epithelial squames with altered nuclear and cytoplasmatic ratio, hyperchromatic nucleus and increased micro nuclei.

Figure 1: Hyperpigmented lesions on both the elbows noted
Figure 2a: (Left ankle) and 2b: (Right Ankle): Lesions noted with areas of healing

Figure 3a: (Right Knee) and 3b: (Left knee): Lesions with bleeding spots noted

Figure 4: Lesions noted on the lower lip

Figure 5: Lesions noted on the lower labial mucosa

Figure 6a: (Right Buccal Mucosa) and 6b: (Left Buccal Mucosa): Lesions involving both the sides of buccal mucosa with thin white striae.

Figure 7: PAP stained Exfoliative Cytology smears show numerous parabasal (green) and superficial (Orange) exfoliated epithelial squames with altered nuclear and cytoplasmic ratio(a), hyperchromatic nucleus(b) and increased micro nuclei (c).
Lichen planus is characterized by violaceous, shiny, flat topped polygonal papules. Multiple variants of lichen planus are recognized. The most common variants being hypertrophic, linear, mucosal, actinic, follicular, pigmented, annular, atrophic and guttate lichen planus. Hypertrophic lichen planus generally develops during the course of a sub acute attack but infrequently only hypertrophic or warty lesions are found. It most commonly involves the lower limbs, particularly around the ankles. These lesions may persist for many years. When such lesions eventually heal, an area of pigmentation and scarring may remain and there is often some degree of atrophy. Similar lesions were noted in our case suggestive of Hypertrophic Lichen Planus.

Oral lichen planus (OLP) may be associated with several other systemic conditions. Grinspan et al. in 1963 found an interesting association of OLP with Diabetes Mellitus (DM) and vascular hypertension (blood pressure) and hence named Grinspan's syndrome.

OLP is mediated by T cells through secretion of inflammatory mediators including TNF-α and IL-6. IL-6 is considered as a pro inflammatory cytokine, that was originally considered to mediate adverse metabolic effects. Further contributing to insulin resistance and deteriorating glucose homeostasis. Binding of IL-6/IL-6R, the dimerization of gp130 results in activation of three gp130 pathways including JAK/ STAT, SPH1/ MAPK, and PI3K/ AKT. This subsequently leads to reduce insulin sensitivity in the liver.

A drug induced disorder and the oral lichenoid lesion, a variant of OLP may be a response to the antihypertensive and/or antidiabetic drugs . Several other systemic medications are known to produce reactions in oral mucosa that are clinically and histopathologically similar to lichen planus. Such lesions possibly be considered as a disease itself or as an exacerbation of an existing OLP but these lesions are usually unilateral, and either erythematous and ulcerative variant.

Esophageal lichen planus is a rare condition however its exact incidence is not known. Literature shows esophageal involvement in about a quarter of the patients diagnosed with lichen planus. It is characteristically seen in the age group 44-79 years and all the reported cases were females. All patients had showed buccal involvement and symptomatic patients presented with progressively increasing dysphagia similar to our case.

It is been suggested that extended hyperglycemia in DM can lead to an exaggerated response including inflammatory and immune related. This can lead to added periodontal breakdown. Literature also supports that formation of advanced glycation end products that results in greater breakdown of collagen fibers and show the accelerated destruction of the bone leading to periodontitis as seen in our case. Further evidence also suggests that poor control in blood pressure is noted in patients suffering from periodontitis. OLP with chronic periodontitis also show higher serum interleukin 17 (IL 17) expression signifying its role in the immuno pathogenesis of both diseases. Superficial Candida infections may also occur in combination with Lichen planus as seen in our case.

Conclusion:
Malignant transformation is the most significant complication of long standing and non healing Lichen Planus. Repeated follow up and biopsies are mandatory for prevention and early detection of malignant transformation. It is still controversial that Grinspan syndrome, The Triad involving OLP, DM and Hypertension are accompanying OLP or medication related to DM and hypertension leads to oral lichenoid lesions. The case was further transferred to Dermatologist and Gastroenterologist for further investigations and treatment.

References:
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