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Vesicular lesion of gingiva diagnosed as bullous lichen planus: Management with combination therapy

Khushboo Goel, Ashish Shrestha, Vinay Marla, Iccha Maharjan

ABSTRACT

Introduction: Oral lichen planus is a T cell mediated autoimmune disease which often affects middle-aged adults. Amongst the reticular, atrophic and erosive types, bullous form of lichen planus is rarely observed. Case Report: A case of 60-year-old male complaining of discomfort in lower front gingiva with occasional fluid filled vesicles in same area and buccal mucosa. Based on clinical and histopathological findings the case was diagnosed as bullous lichen planus. Management of bullous form of oral lichen planus is challenging and there is no reliable effective treatment. The mainstay of therapy remains topical and oral corticosteroids but there are limited data on the potential efficacy of newer agents. Here we report a case which was managed with low dose corticosteroids (betamethasone) combined with an immunomodulator (pentoxifylline) which achieved clinical success with no recurrence and minimal side effects during one year follow-up. Conclusion: This case provides evidence that low dose corticosteroids combined with immunomodulator improved clinical outcome in bullous form of disease. Early diagnosis and treatment can help prevent the complication and reduce morbidity in this rare entity.

Keywords: Autoimmune disease, Betamethasone, Bullous lichen planus, Pentoxifylline

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INTRODUCTION

Oral lichen planus is relatively common immunologically mediated mucocutaneous disease of unknown etiology. The characteristic feature of oral lichen planus is its chronicity, symmetrical appearance and multi-site involvement [1]. Oral lichen planus may manifest in the reticular, erythematous (atrophic) and erosive (ulcerated, bullous) clinical subtypes. Amongst them the reticular form is the most commonly observed while the bullous form of lichen planus is the rarest with

only few cases reported till date [2, 3]. Bullous lichen planus (BLP) is commonly seen on buccal mucosa but are quiet uncommon on the gingiva. Vesicles or blisters that appear in BLP are generally short lived and leave an ulcerated lesion on rupturing. More than one clinical subtype can coexist and vesicles can develop in direct connection to previous areas or present patches of lichen planus [2]. The clinical identification of disease is difficult and histopathological evaluation may be necessary to establish a definitive diagnosis and avoid an erroneous identification to implement a proper treatment plan.

CASE REPORT

A 60-year-old male was referred to the department of periodontology and oral implantology, with chief complaint of discomfort in lower anterior gingiva since one year with burning sensation. He had sometimes noticed few vesicles/blisters in the same area and in buccal mucosa that use to burst within few seconds. There was no history of smoking, alcohol or drug intake. No history of use of allergic related components of chewing gums, dentifrices or any specific diet components. The patient's medical history was unremarkable and cutaneous or any other mucosal surfaces were not involved. On intra-oral examination, there was minimal plaque accumulation with absence of bleeding on probing. Diffuse white linear striae with areas of erythema was seen in lower anterior region extending from free to attached gingiva (Figure 1A). White striae arranged in a reticular pattern were also observed in attached gingiva of posterior aspect and buccal mucosa bilaterally (Figure 1A). There was absence of any local exacerbating factors in areas of erythema. Considering the history, provisional diagnosis of BLP was made with differential diagnosis of pemphigus vulgaris and bullous pemphigoid. An incisional biopsy for histopathological examination was therefore planned to be taken from attached gingiva and buccal mucosa for a confirmatory diagnosis (Figure 1B). After two weeks the patient reported with vesicle formation. Vesicles were two in number and present in areas of white striae in left buccal mucosa with ≤10 mm in diameter (Figure 1D). The vesicles were short lived, had tendency to rupture spontaneously and healed quickly.

Histopathological Findings

Microscopic examination of the formalin fixed specimen revealed hyperplastic parakeratotic stratified squamous epithelium with the stroma revealing a dense band of lymphocytic infiltration along with few plasma cells. The epithelium also revealed detachment from the underlying connective tissue is focal areas (Figure 1C). These findings along with the clinical correlation were suggestive of bullous lichen planus.

Treatment

Management requires multidisciplinary care. The patient was counseled and reassured about the disease. He received full mouth supragingival scaling with oral hygiene instructions, including use of interdental aids along with modified bass technique for tooth brushing. Currently, there is no reliably effective safe therapy for the long-term management of BLP. Lesions were confined to oral mucosa, therefore, managed with topical corticosteroids initially. The patient was treated with 0.1% triamcinolone with ointment oraplast, topical clotrimazole 1% and 0.15% benzydamine oral rinse for two weeks. After two weeks patient presented with new vesicles in left buccal mucosa and there was only transient improvement in other symptoms. The medications were therefore changed to administration of low dose 0.5 mg betamethasone four times a day for two weeks which was chewed, swish and spat combined with pentoxifylline 400 mg three times a day for one month with proton pump inhibitor once daily for two weeks. Topical fluticasone 0.05% was advised for local application three times a day after drying the area with gauze. At third visit in two months patient had no history of new vesicles but areas of erythema and white striae in the gingiva and buccal mucosa were evident, with no increase in lesions. Betamethasone mouthwash was again repeated for two weeks two times a day for two weeks with pentoxifylline for one month. At six-month, there was resolution in his symptoms with absence of any adverse changes in keratinized tissue and mucosa. Patient is under follow-up

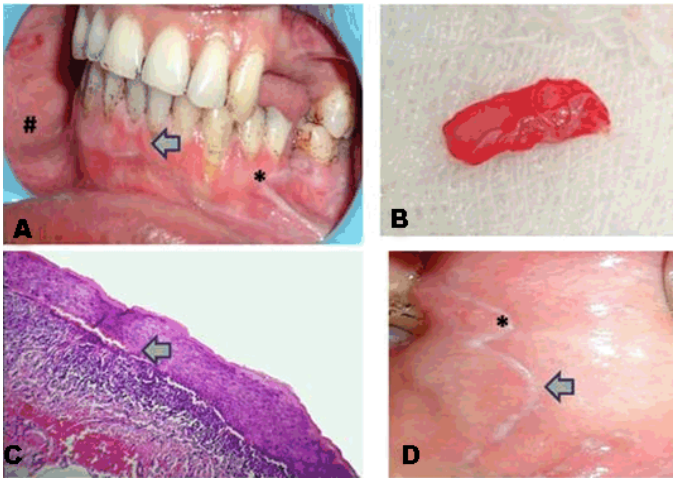

Figure 1: (A) White linear striae with areas of erythema (arrowhead), Wickham's striae in attached gingiva (*) and keratotic circular line with hyperpigmentation (#), (B) Incisional biopsy of attached gingiva, (C) Overlying epithelium is hyperplastic parakeratotic stratified squamous, sub epithelial cleft formation (arrowhead), submucosa comprise of dense aggregate of lymphocytes (H&E stain, x500), and (D) Wickham's striae on left buccal mucosa (arrowhead) and fluid filled vesicle in adjacent area at two weeks (*).

since a year and is free of lesions and symptoms. Patient was satisfied with the results, as the lesions were evident but were asymptomatic and non-progressive with no appearance of new vesicles.

DISCUSSION

Oral lichen planus is a mucosal variant of lichen planus that presents with predominantly white or ulcerative lesion. It develops most commonly in the fifth to sixth decades of life, and twice as more common in women than men but patients of all ages may develop the disorder [4]. The pathology of oral lichen planus was first presented by the English physician Erasmus Wilson in 1869 [5]. Almost after three decades, Louis Frederick Wickham noted the characteristic peculiar striae on the surface of Lichen planus papules, today named Wickham striae [6]. Incidence of oral lichen planus ranges from 0.1–2.2% [7]. Etiopathogenesis is complex with interplay of array of factors such as genetic background, drugs, food allergies, dental materials, immunodeficiency, autoimmunity, stress, malignant neoplasms and some systemic conditions as diabetes and hypertension, and bowel diseases [8]. Current data suggest that oral lichen planus is a T cell-mediated autoimmune disease in which auto-cytotoxic CD8+ T cells trigger apoptosis of oral epithelial cells [9, 10]. It is estimated that 50–70% of adult lichen planus patients have both skin and oral lesions [11] and approximately 25% of patients present with oral lesions alone [12]. In the present case, oral lesion was solely observed. Within the oral cavity, the buccal mucosa is the most common site affected for oral lichen planus (64.3%). However, the gingiva may be involved with a similar frequency (59.8%) [13]. Meanwhile, occurrence of BLP is most unusual clinical form with gingiva as an uncommon site [12].

Clinically, the erosive forms (erosive and bullous) are often accompanied by reticular and erythematous lesion which was seen in our case and these forms are differentiated from other vesiculo-erosive disease, characterized by isolated areas of erosions and/or erythema [14]. Although the presentation was not of a typical bulla, rather a vesicle, a biopsy was recommended to avoid erroneous diagnosis and also establish a proper therapeutic approach for this rare entity. Histopathological findings revealed an accurate diagnosis of BLP and also excluded any dysplastic or malignant changes. There is quiet uncertainty of the premalignant nature of oral lichen planus but risk of malignant transformation is estimated at 0.5–2% during lifetime [15]. A greater malignant potential has been recognized for atrophic, erosive form of oral lichen planus and the plaques form on the back of the tongue [16, 17].

Approximately 17% of cases involving oral lichen planus undergo spontaneous remission [18]. Therefore only the erosive, ulcerative, or symptomatic lesions need to be treated. Limited information is available in literature regarding the treatment of BLP. The main concerns with the current therapies are the local and systemic adverse effects and lesion recurrence after treatment is withdrawn. Recently few studies [19, 20] and case reports [3] have revealed the efficacy of Oral Mini Pulse (OMP) therapy consisting of betamethasone 5 mg orally once daily for two consecutive days in a week for three months in bullous and erosive form of lichen planus. However, the first line of therapy remains high potency topical corticosteroids [21] often co-administered with a topical antifungal to prevent oral candidiasis [15]. The topical steroid mainly triamcinolone acetonide 1%, clobetasol proprionate 0.05%, fluocinonide 0.05% have been used in localized lesion. In multiple mucosal site involvement, mouthwash with betamethasone sodium phosphate 500 μg and fluticasone spray have also been used [22]. In this case, lesions were solely confined to oral mucosa; therefore topical steroid of betamethasone mouthwash was administered to minimize any side effects.

Significant immune alterations are observed in oral lichen planus and therefore topical corticosteroids sometimes are supplemented by immunomodulatory agents [23, 24]. Studies have been done on possible efficacy of agents such as oxpentiphylline [25] but with limited success. There also remains a need to determine the efficacy of other immunomodulatory agents in the treatment of bullous form of lichen planus. Pentoxifylline is a xanthine derivative typically used in the management of peripheral vascular disease, which also has a wide range of immunosuppressive actions, in particular an inhibitory action upon tumor necrosis factor (TNF)-α [26]. TNF-α is a pro-inflammatory cytokine and has also been implicated in the immunopathogenesis of OLP [20, 27]. Therefore, pentoxifylline might be expected to be of some benefit in lessening the signs and symptoms in bullous form of lichen planus. In lack of effective, reliable therapies and to minimize the side effects further, we combined low dose of betamethasone with pentoxifylline in this case that achieved effective clinical results with no signs of side-effects and recurrence of vesicles. There is no absolute cure available yet, but the principal aim of therapy is resolution of painful symptoms, decrease in risk of oral cancer, and maintenance of good oral hygiene. Therefore, it is necessary to follow-up the patient regularly at least annually for a possible neoplastic degeneration. The extreme rarity of oral bullous lichen planus warrants further long term clinical studies to evaluate this treatment modality.

CONCLUSION

Oral lichen planus is a multifactorial disease origin of mucous membranes, skin, nails and scalp. It is imperative that bullous form of lichen planus are identified precisely and followed-up meticulously for detection of dysplastic changes. However, most of the treatment available is non-specific, therefore proper therapy need to be administered

at the earliest. This case provides evidence that low dose corticosteroids combined with immunomodulator improved clinical outcome in bullous form of disease.

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Khushboo Goel – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Ashish Shrestha – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published
Vinay Marla – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published
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Guarantor
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Conflict of Interest
Authors declare no conflict of interest.

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