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Case Report

Self - Limiting Cutaneous Pemphigus Preceding the Oral Lesions - A Case Report

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Abstract

Pemphigus is a group of potentially fatal autoimmune, muco-cutaneous disease, characterized by appearance of vesicle or bullae that rupture to form large ulcers. The oral manifestations often precedes the skin lesions by many months, or may remain as the only symptoms of the disease. It is therefore, important that its manifestations to be detected early to make a proper diagnosis, and initiate timely treatment This care report presents an uncommon case of female patient reporting to our dental hospital with skin lesions preceding the oral lesions of Pemphigus Vulgaris. This case emphasises on pivotal role of the dentist in the early detection and following multidisciplinary treatment approach for better management of Pemphigus Vulgaris.

Keywords: Pemphigus Vulgaris; Skin Lesions; Bullous Lesions; Nikolsky's Sign; Autoimmune Disorders

Abbreviation

PV: Pemphigus vulgaris

Introduction

Pemphigus is a rare, chronic, potentially life-threatening, autoimmune bullous disease of the skin and the mucous membranes. The two major subtypes of pemphigus are pemphigus vulgaris (PV) and pemphigus foliaceus [1]. It is a rare disease reported in 0.1-0.5/100,000 population/year [2], with peak incidence in the fifth or sixth decade of life [1,2]. Pemphigus vulgaris (PV) is the most common type affecting the oral cavity, and sometimes with lesions on skin as pemphigus vegetans. Oral lesions usually precede skin lesions in 60% of the cases, and skin involvement may not be seen at all [3,4]. Oral lesions appear as flaccid bullae, which easily rupture leaving behind painful erosions. These lesions occur on lips, tongue, buccal mucosa, palate, and often along with desquamative gingivitis [5]. The skin involvement can be seen similar to oral lesions on normal or erythematous skin of neck, abdomen and back commonly.

Pemphigus is diagnosed based on clinical appearance, positive nikolsky's sign, tzank cells and supra-basilar split in histopathology, and demonstration of immunoglobulins in the spinous cell junctions in immunofluroscence [5]. Management of Pemphigus has to be vigorous including oral and systemic corticosteroids, and other steroid sparing drugs like methotrexate, cyclophosphamide, etc. Patient with skin involvement are treated in hospital, as extensive lesions can be life threatening due to dehydration, loss of protein or secondary infection [2].

Before the introduction of corticosteroids, around 75% of patients died within the first year of appearance of lesion. Although, Matinez., *et al.* had reported a drastic fall in mortality to less than 10% currently [2]. Precise and early diagnosis increases the efficiency and efficacy of treatment strategy [6].

As the oral presentation of the disease is often the first indicator, it is very critical for the dental practitioner to recognize the lesions at a sufficiently early stage to initiate further investigations and treatment. This case report presents a rather unusual case of PV, reporting of self-limiting skin lesions preceding the oral lesions.

Case Report

A 53-year-old female farmer reported to, with a complaint of ulcers and bleeding from mouth for 3 days. These ulcers were

preceded by bullae formation, which bled on rupturing. She also complaint of soreness of her entire gingiva and difficulty in swallowing. On further history taking, she also admitted of having similar lesions on her neck from past 2 weeks. However, that was not her primary concern, as no new lesions had formed in past 5 days. Her medical history was unremarkable. Patient was not taking any medication. Her family history and past medical history was non-contributory. She had no known oral abusive habits.

On general examination, the patient was lean built with signs of pallor. The extra- oral examination revealed a wide spread lesion on her neck anteriorly, starting from below the chin superiorly to mid neck inferiorly, and extending to submandibular space bilaterally (Figure 1). The irregular area was pinkish red, inflamed, tender and covered with dried brownish scab superiorly. A recently ruptured bulla was present just below the chin. There was bloody frustration on her lower lip and dried blood on both her lips (Figure 2). There was no involvement of the eyes or any other part of the skin.

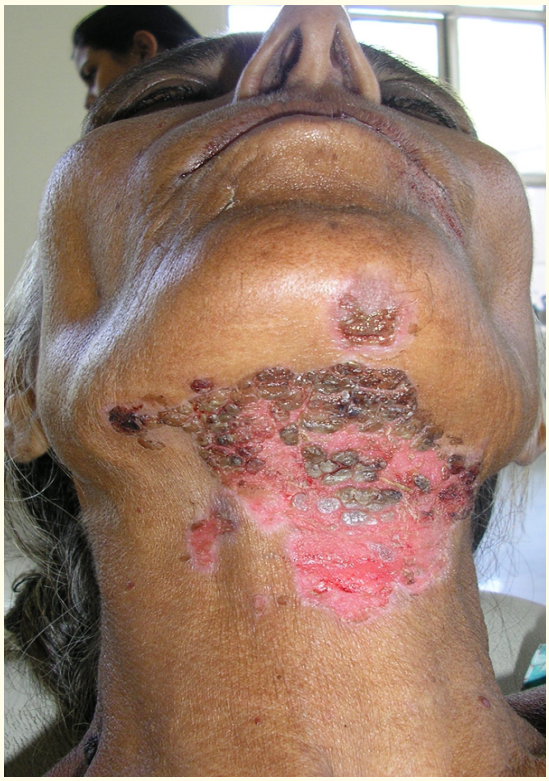

Figure 1: Skin Lesions.

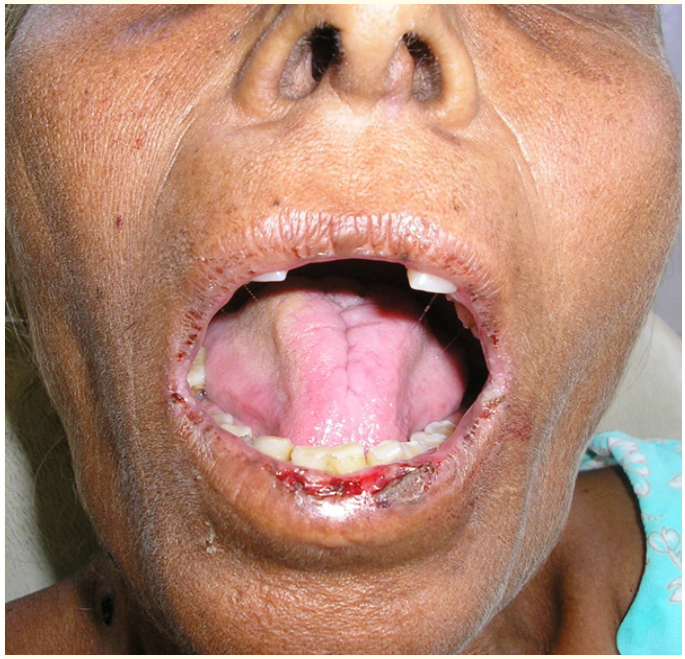

Figure 2: Blood on the lips.

Intraorally, ruptured linear erosions with irregular borders, and macerated tissue tags were present in bilateral posterior buccal mucosa along the line of occlusion, and lower labial mucosa (Figure 3-5). Desquamative gingivitis was seen confined to both upper and lower anterior gingiva (Figure 6). Nikolsky's sign was positive in buccal mucosa. General oral hygiene of the patient was poor with extensive deposits of calculus.

Based on history and clinical appearance a provisional diagnosis of pemphigus vulgaris involving skin and mucosa was drawn. A differential diagnosis of para-neoplastic pemphigus was given. Patient was advised to get a biopsy done for confirmation of the diagnosis, but patient refused to undergo the same. She was put on soft diet and topical steroid ointment (0.1% triamcinolone acetonide) and topical analgesic (mucopain) for oral use.

She was referred to a hospital for evaluation and further management by a dermatologist. She was admitted and started on IV dexamethasone 100 mg for 3 days along with 500 mg of cyclophosphamide (Pulse therapy). Before that, biopsy from both skin and oral lesions was taken. Histopathology confirmed diagnosis of PV for both the specimens. Two more cycles of this regime at intervals of 4 weeks each were repeated. The patient was prescribed prednisolone 30 mg/day during the interim 4-week period. Patient had undergone complete remission by the end of therapy.

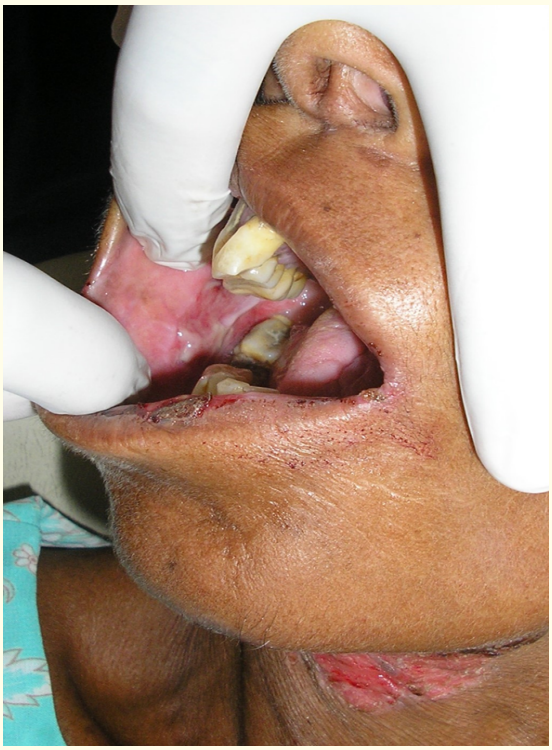

Figure 3: Ruptured Bulla on right buccal mucosa.

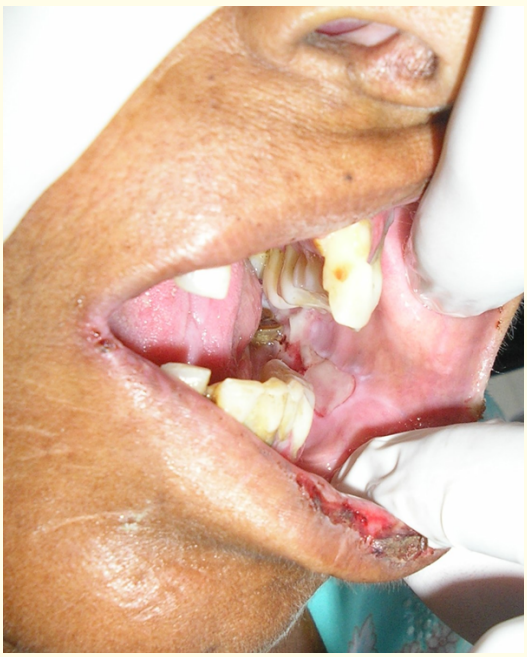

Figure 4: Ruptured Bulla on left buccal mucosa.

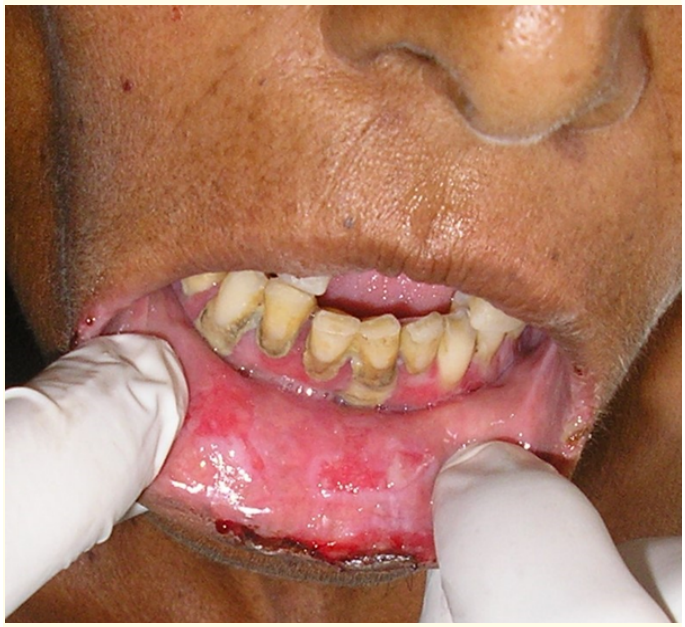

Figure 5: Erosions on lower labial mucosa.

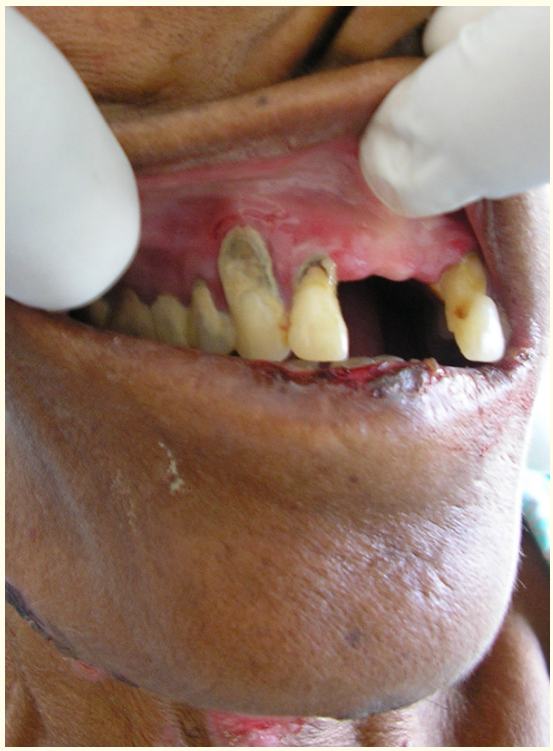

Figure 6: Ruptured Bulla on right buccal mucosa.

Discussion

Vesico - bullous lesions have varied presentation, with autoimmune aetiology in most cases. Pemphigus is an autoimmune mucocutaneous disease characterized by intra-epidermal bulla formation with reported incidence of 0.1-0.5/100,000 population/year [2], to 0.42 to 1.62 cases per 100,000 [6]. The word Pemphigus is derived from the Greek word "pemphix", meaning bubble or blister. It predominantly affects adults of both genders equally, with a mean age of 50 years [6]. Pemphigus is common amongst certain races like Ashkenazi Jews, Mediterranean's, and Asians (especially Indians and Japanese) [2]. A relationship has been found with HLA, especially with certain HLA class II alleles, with implication of HLA-DR4 (DRB1*0402) in Ashkenazi Jews and of HLA-DRw14 (DRB1*1041) and HLA-DQB1*0503 in Mediterranean and Asiatic peoples [2,6].

Pemphigus has many variants like Pemphigus Vulgaris, Pemphigus Foliaceous, Pemphigus Vegetans, Pemphigus Erythematoses, and rarely Paraneoplastic Pemphigus. PV is the most common form (80%) seen affecting the oral cavity and sometimes, it occurs in conjunction with Pemphigus Vegetans on the skin [3]. Mucosal lesions may be the sole sign for months before skin lesions develop, or they may be the sole manifestation of the disease [3,7]. In our case, the skin lesions had preceded the oral lesions by 2 weeks. Altun E., *et al*. had reported of skin lesions preceding oral lesions in 18.4% of 49 of their patients, and both mucosal and skin involvements in 38 (77.6%) patients [8].

The autoimmune response may be triggered in susceptible individuals due to various medicines (especially thiol-containing drugs, e.g., penicillamine and ACE-inhibitors), diet, stress, physical or viral agents, vaccines or neoplasms [2,6,7,9]. In our case, use of fertilizers or excessive sun exposure in her work place may have triggered PV. The blisters occur in the epithelium where the IgG autoantibodies are produced in response to triggering factors target desmoglein 3, which leads to epithelial cell separation, by triggering complement activity or plasminogen plasmin system. Thin separation at the desmosomal region triggers the acantholysis and suprabasal spilt. D Kuriachan*., et al*. have reported of new pemphigus antigen Desmoglein 4 and other non-Desmoglein antigens like human α-9-acetylcholine receptor that regulates keratinocyte adhesion and keratinocyte annexin like molecules binding acetylcholine termed pemphaxin and catenin that are thought to play a role in its etio-pathogenesis [5].

Oral lesions can range from superficial ulcers, to small vesicles, or flaccid bullae. The primary lesion is usually a thin-walled or flaccid bulla, several centimetres in size, containing clear fluid. The most common sites of oral involvement include the buccal mucosa, soft palate, labial mucosa, and gingiva, although any oral site may be affected [6]. Nikolsky's phenomenon- detachment of a large area of the surface with the formation of blisters can occur by exerting a slight pressure on the apparently normal epithelium of these patients, is the key to clinical diagnosis [2,7]. The oral lesions of PV are extremely painful, resulting in hyper salivation, halitosis, difficulty in swallowing and difficulty in phonation [6,7]. Healing is very slow but without scars formation (which is typical of bullous pemphigoid).

Pemphigus skin lesions can arise as simple rashes to erosions, vesicles, blisters, or ulcers, affecting predominantly the trunk and the limbs, especially large areas of bending folds such as the neck [9], as seen in our case. The other mucosae covered by pavement epithelium, e.g., oropharyngeal, genital or conjunctival mucosae, can also be affected [7].

The diagnosis of PV is based on clinical features, histology, and positive immunological tests. For a definitive diagnosis, an incisional biopsy of a peri-lesional tissue should be performed. Histopathological examination typically shows acantholysis, which is the loss of coherence of epidermal cells and their subsequent detachment. This further leads to, intra-epithelial vesicle above the basal cell layer causing supra – basilar split. On cytological examination, typical acantholytic cells contains detached rounded keratinocytes with swollen hyperchromatic nuclei called Tzanck cells are seen [6,7]. Direct Immunofluorescence study shows the typical "fish-net" pattern of IgG and complement C3 deposits in the spinous layer [5]. The most frequent differential diagnoses of PV with oral lesions are recurrent aphthous stomatitis, Bullous pemphigoid, Behçet disease, erythema multiforme, erosive lichen planus, and oral candidiasis [2].

Oral lesions are challenging, since their response to treatment is much slower in comparison to cutaneous lesions [2]. For local lesions of the oral mucosa, mouthwashes or topical corticosteroids ointments, (0.1% triamcinolone acetonide, 0.05% fluocinolone acetonide, or 0.05% clobetasol propionate) or intralesional injection (triamcinolone acetonide (20 µg/L) or paramethasone every

7-15 days) can be used in focal, refractory lesions2. In patients with extensive oral lesions or skin involvement, a combined therapy consists of administration of corticosteroids (prednisolone, dexamethasone) and systemic immunosuppressant (cyclophosphamide, azathioprine, cyclosporine, etc.) [2,6].

Prednisone is the drug of choice, the maximum daily dose of which is 120 mg (1-2 mg/kg/ day). Khatri ML in his study, compared various drug combination regimens and concluded the superiority of dexamethasone – cyclophosphamide combination, in terms of longer remission periods and least steroid side effects [10]. Pulse therapy (intravenous infusion of very high doses of immunosuppressants for a short time period) was the treatment therapy followed in our patient. Other frequently tried treatment modalities include high doses of intravenous immunoglobulin; plasmapheresis, PUVA, antagonists of TNF α, cholinergic antagonists; and monoclonal antibodies like rituximab [2]. D Temilola., *et al.* have emphasized on promising results showed by low-level laser therapy combined with immunosuppressants [6]. Supportive therapy including, administering local analgesics, maintaining oral hygiene, following a soft diet, maintaining prosthesis, and antifungal therapy in patients on long-term corticosteroid treatments should also be provided [2].

A keen observation of the signs and symptoms can facilitate early diagnosis, management and control of Pemphigus. Finally, a close collaboration between dentists and dermatologists is required to combat this disease as untreated oral lesions may progress to involve other mucosae, or skin. Due to the multi-systemic nature of PV, a multidisciplinary approach for the management of the disease is required, involving dentists, oral medicine specialists, pathologists, dermatologists, ophthalmologists and immunologists.

Conclusion

The appearance of skin lesions of pemphigus prior to oral lesions is rather uncommon. Whenever such a case is seen, referral to an oral medicine specialist or dermatologist should be done without further delay. Early management of pemphigus lesions particularly skin lesions, can have better control of the disease, and save patient from life-threatening dehydration and secondary infections.

Bibliography

1. Scully C., *et al*. "Pemphigus vulgaris: the manifestations and long-term management of 55 patients with oral lesions". *British Journal of Dermatology* 140.1 (1999): 84-89.

2. Bascones-Ilundain C, ., *et al*. "Oral Manifestations of Pemphigus Vulgaris: Clinical Presentation, Differential Diagnosis and Management". *Journal of Clinical and Experimental Dermatology Research* 1 .2 :1000112.

3. Arpita R., *et al*. "Oral Pemphigus Vulgaris: Case Report". *Ethiopian Journal of Health Sciences* 25.4 (2015): 367-372.

4. Pedro EMG., *et al*. "Pemphigus Vulgaris With Oral Mucosa and Skin Involvement: A Case Report". *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology* 120.2 (2015): e57.

5. Kuriachan D., *et al*. "Oral Lesions :The Clue to Diagnosis of Pemphigus Vulgaris". *Case Reports in Dentistry* 2015 (2015): 593940.

6. Temilola D., *et al*. "Oral pemphigus vulgaris with skin and ocular involvement". *The South African Dental Association* 73 (2018).

7. Fassmann A., *et al*. "Manifestation of pemphigus vulgaris in the orofacial region. Case report". *Scripta Medica* 76 (2003): 55-62.

8. Saccucci M., *et al*. "Autoimmune Diseases and Their Manifestations on Oral Cavity: Diagnosis and Clinical Management". *Journal of Immunology Research* (2018): 6061825.

9. Tavakolpour S. "Pemphigus trigger factors: special focus on pemphigus vulgaris and pemphigus foliaceus". *Archives of Dermatological Research* 310.2 (2018): 95-106.

10. Khatri ML. "Pemphigus in North-Western Yemen: A therapeutic study of 75 cases". *Indian Journal of Dermatology, Venereology and leprology* 82 (2016): 359.

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