Case Report

PEMPHIGUS VULGARIS: A case report and literature review

Okoh M, [1] **Omoregie OF,** [1] **Otakhoigbogie U** [2]

[1]Department of Oral Surgery and Pathology, Faculty of Dentistry, College of Medical Sciences, University of Benin, Benin City, Nigeria. [2] Department of Oral Pathology and Medicine, University of Benin Teaching Hospital, Benin City

ABSTRACT

OBJECTIVE: This paper reports a case of pemphigus vulgaris (PV) in a young adult male affecting the oral mucosa to highlight the importance of early diagnosis and treatment of this lesion

CASE REPORT: A 33 years old student presented with a six week history of multiple ulcers in the oral cavity. Intra-oral examination revealed multiple irregular shaped ulcers with erythematous floor on the soft palate, buccal mucosa, anterior pillar of fauces, ventral surface of the tongue and floor of the mouth. An initial diagnosis of erythema multiforme was made. Investigations with full blood count, retroviral screening and fasting blood sugar showed normal findings. A definitive diagnosis of pemphigus vulgaris was made following histopathological examination.

The initial treatment administered were Prednisolone tablets 60mg/day for one week, then the dose was stepped down to 40mg daily for a week. Triamcinolone dental paste was applied topically twice daily for 2 weeks. The oral lesion improved drastically and the dose of prednisolone was further stepped down to 20mg daily in 2 weeks. There was an exacerbation of the oral lesions at a dose of 20mg daily of prednisolone, hence the daily dose was adjusted to 60mg daily for 4 weeks at which the oral lesions started improving. The patient has been on maintenance dose of prednisolone of 30 mg/day and Dexamethasone 1 mg dissolved in 10 ml of water as mouth rinse daily for 5 months.

CONCLUSION: This study reported a case of PV involving the oral mucosa found in a young adult male. Early diagnosis and treatment of the oral lesions with local and systemic steroid resulted in remission within 6 months.

Correspondence address:

Mercy Okoh
Department of Oral Surgery and Pathology, Faculty of Dentistry, College of Medical Sciences, University of Benin, Benin City, Nigeria
drmerccy@yahoo.com
+2348077082732

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INTRODUCTION

Pemphigus is a rare chronic mucocutaneous disease characterized by intra-epithelial bulla formation, due to autoantibodies directed against proteins of the desmosome-tonofilament complex between keratinocytes. [1] Pemphigus can be classified into six types namely: pemphigus vulgaris, pemphigus vegetans, pemphigus erythematosis, pemphigus foliaceus, paraneoplastic pemphigus and IgA pemphigus. [2]

Pemphigus vulgaris (PV) is the most common variant showing oral lesions as an initial manifestation in 50% of case. [3] It is caused by autoantibodies directed against the epidermal keratinocytes desmosomal cadherin desmoglein 3 or desmoglein 3 and desmoglein 1, resulting in loss of adhesion between the keratinocytes and blister formation. [4] Pemphigus vulgaris affects women more than men, [5, 6] although some authorities claim an equal prevalence in both sexes. [7] The average age at the onset is between the fourth and sixth decades of life, [7] but can also arise in children and older people. [8, 9] PV is a rare condition, with a reported incidence ranging from 0.75–5 cases per million per year to 0.5–3.2 cases per 100,000 per year, depending on the population, with an increased incidence among people of Jewish and Mediterranean descent.[10, 11]

Clinically, the oral lesions are characterized by blisters that rapidly rupture, resulting in painful erosions. While any area in the oral cavity can be involved, soft palate, buccal mucosa, and lips are predominantly affected. [1] The diagnosis depends on biopsy confirmation of intraepithelial vesicle formation, acantholysis and presence of Tzank cells. [12] Demonstration of immunoglobins especially IgG and complement in the intracellular space by direct immunofluoresence (DIF) is a very reliable test for pemphigus vulgaris. Indirect immunofluorescent studies enable a search for circulating autoantibodies in the patient's serum and are usually performed after direct immunofluorescence studies reveal antibody deposits in the mucosa or skin. [12] The treatment consists of systemic corticosteroids and corticosteroid-sparing agents. [7]

If PV is not promptly treated, the disease has a high morbidity rate, and it may be fatal in 5% to 10% [13] of cases. This study reports a case of pemphigus vulgaris in a young adult male affecting the oral mucosa to highlight the importance of early diagnosis and treatment of the lesion.

CASE REPORT

This was a case of a 33 years old male student in a tertiary institution who presented with a six-week history of multiple ulcers in the oral cavity. The lesions were preceded by vesicles that ruptured to become ulcers. There was no history of use of sulphur-containing drugs prior to presentation, no history of prodromal symptoms and no skin and genital involvement. There were associated symptoms like pain, odynophagia, headache and limitation in mouth opening.

Intra-oral examination revealed multiple irregular shaped ulcers with erythematous floor on the soft palate, buccal mucosa, anterior pillar of fauces, ventral surface of the tongue and floor of the mouth (Figure 1). Light pressure on the intact mucosa did not provoke the formation of bullae (negative Nikolsky's sign). There were associated bilateral enlarged and tender submental and submandibular lymph nodes. An initial diagnosis of erythema multiforme was made.

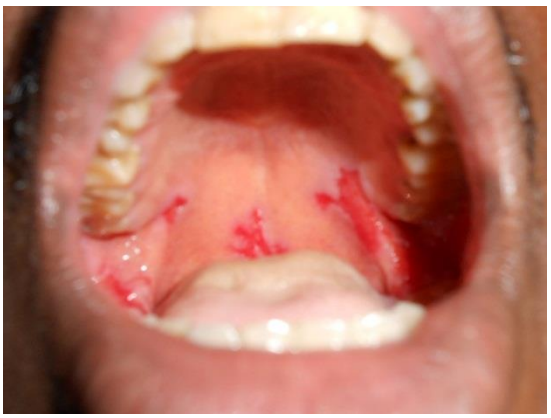

Figure 1: Ulcerative and erosive lesions in the soft palate and retromolar sites

The results of blood tests (full blood count, retroviral screening and fasting blood sugar) were normal. Perilesional cutaneous biopsy of the oral tissue was carried out and sent for

histopathological examination. Hematoxylin and eosin stained sections showed a reactive lesion with a covering parakeratinized stratified squamous epithelium, undergoing intraepithelial degeneration to form suprabasal clefts and focal epithelial ulceration. There was marked acute and chronic inflammatory cell infiltration of the bulla and submucosa. The ulcer base consists of granulation tissue with small vascular spaces (figure 2). A definitive diagnosis of pemphigus vulgaris was made.

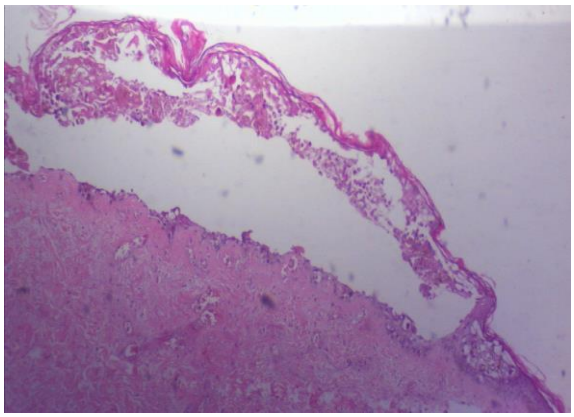

Figure 2: Photomicrograph of the lesion showing intraepithelial degeneration to form suprabasal bulla(H&E X40)

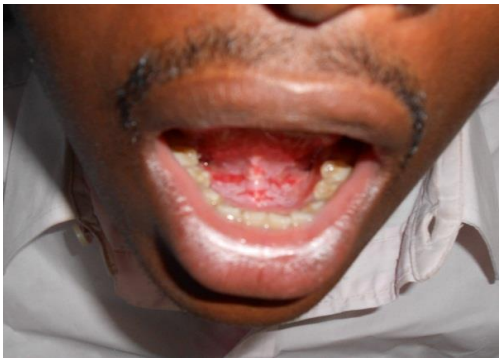

Figure 2: Ulcerative and erosive lesions in the ventral surface of the tongue and the floor of the mouth

The initial treatment administered were Prednisolone tablets 60mg/day for one week, then the dose was stepped down to 40mg daily in a week. Triamcinolone dental paste was applied topically twice daily for 2 weeks. Metronidazole tablets (400mg, 8 hourly) and Amoxycillin capsule (500mg, 8 hourly) were administered for five days to treat secondary infection. After two weeks of treatment with corticosteroid, the oral lesion improved drastically. The dose of prednisolone was further stepped down to 30mg daily for a week; then to 20mg daily for one week. There was an exacerbation of the oral lesions at a dose of 20mg daily of prednisolone, hence the daily dose was adjusted to 60mg daily for 4 weeks at which the oral lesions started improving.

After 2 months of treatment, patient presented with burning sensation in the epigastrium. Patient was then placed on omeprazole 20mg daily; prednisolone was reduced to 40mg daily, Dexamethasone 1mg dissolved in 10 ml of water as mouth rinse daily was added. There was constant monitoring of the patient's blood pressure which was within the normal range. Six months after the initial diagnosis, the corticosteroid therapy had been reduced to 30 mg/day, and almost all the lesions had disappeared except for a small lesion in the soft palate (Figures 3 and 4). After 9 months of treatment, the corticosteroid therapy was maintained at 30 mg/day and Dexamethasone 1 mg dissolved in 10 ml of water as mouth rinse daily.

Figure 3: Almost oral lesions have resolved except for a small lesion on the soft palate

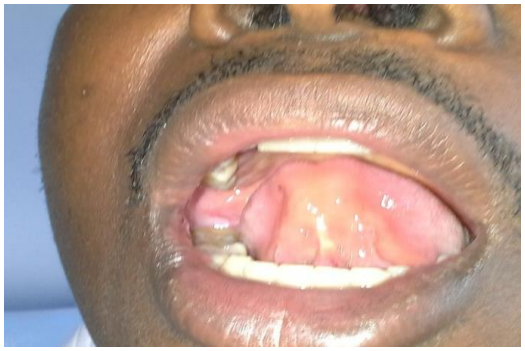

Figure 4: Healed ulcers at the floor of the mouth at 6 months.

DISCUSSION

Pemphigus is a rare autoimmune disorder with intraepidermal bullous lesions, which affect the oral, genital or ocular mucosa and the epidermis. [13] The fragile blisters are easily broken, which leaves behind erosions surrounded by epidermal rings. Applying pressure on healthy skin causes either a bulla or erosion; this effect is known as Nikolsky's sign.[14-16] This sign, although highly suggestive of pemphigus, is not specific and may be absent, [13] as in the patient described in this study. Oral lesions are the first manifestation of the disease in 50 to 90% of cases. [12, 13, 17- 19]

Any part of the oral cavity may be affected, especially the soft palate, buccal mucosa and lips.[1] This patient presented with severe ulceration of the soft palate and buccal mucosae. Many patients with PV can be initially misdiagnosed and incorrectly treated for months. The most frequent diagnoses in patients with oral lesions are recurrent aphthous stomatitis, Behçet disease, erythema multiforme, erosive lichen planus, and oral candidiasis. [17, 19] This patient was initially diagnosed as a case of erythema multiforme.

In children and adolescents, PV should be differentiated from erythema multiforme, acute herpetic gingivostomatitis, impetigo, linear IgA disease, epidermolysis bullosa, cicatricial pemphigoid, bullous pemphigus, and paraneoplastic pemphigus [20]. The diagnosis of PV is based on three independent set of criteria: clinical features, histology, and immunological tests.[10,19] Histologic examination is the only reliable tool with which to establish an accurate diagnosis. [21]

The basic treatment for pemphigus consists of either local or systemic corticosteroid therapy.[13, 22] The treatment depends on the prognostic elements of the condition, such as the extent of the lesions and antibody levels. Treatment is administered in 2 phases: a loading phase, to control the disease, and a maintenance phase, which is further divided into consolidation and treatment tapering [13]. As a complement to treatment with local or systemic corticosteroids, the following measures can be taken to improve the wellbeing of patients: administering analgesics, maintaining strict oral hygiene using diluted antiseptic mouthwashes, periodontal treatment, following a soft diet without irritants, checking prosthetic restorations, and applying anti-candida therapy in patients on long-term corticosteroid treatments.[10, 13, 17, 23]

Corticosteroids taken by mouth have many long-term harmful effects, including adrenal atrophy, abnormal sensitivity to infection, high blood pressure, hypertriglyceridemia, hyperglycemia, cortisone myopathy, erosive duodenitis and stress fracture,[13] as was observed in the case presented here, which was treated with omeprazole. To minimize iatrogenic effects, Lever and Schaumburg-Lever [24] recommended a treatment called the "high Lever scheme" with very high loading doses (100–175 mg taken twice daily for 5–10 weeks), followed by the "low Lever scheme," which includes a rapid reduction in dosage over a few weeks. [24]

Depending on the response, the dose is gradually decreased to the minimum therapeutic dose, as maintenance dose taken once a day in the morning to minimize side effects. [13] The patient in this study was placed initially on 60 mg daily of corticosteroid and later tapered to a maintenance dose of 30 mg daily with adjunct topical use of dexamethasone.

Research advances have expanded the therapeutic arsenal against PV, which now includes treatments with: pulse therapy (intravenous infusion of very high doses of immunosuppressants for a short time period); high doses of intravenous immunoglobulin; plasmapheresis; immunospecific immunoadsorption; extracorporeal photopheresis with exposure of serum to psoralens and UVA; antagonists of tumour necrosis factor α (TNFα); cholinergic antagonists; and antiCD20 monoclonal antibodies (e.g., rituximab) [17, 25, 26] However, the use of adjuvant therapy remains controversial. Therefore, it is only used in cases where corticosteroids are contraindicated, and a lower dosage of the corticosteroids is required.[13] However, no treatment has demonstrated

superiority over the others.[27] Furthermore, there is lack of well-designed studies on the efficacy of the numerous new PV treatments and a shortage of evidence-based clinical guidelines.[27]

The prognosis of untreated oral lesions is a progression that involves other mucosae, including the skin. The prognosis is worse when there is an elevated titer of circulating autoantibodies.[10,17] Various authors have reported that the oral lesions can disappear after 2 months to one year,[12,13] although it remains unclear whether the PV completely remits. [23] This study observed almost complete remission of the oral lesions within 6 months of local and systemic steroid therapy. Ocular and genital lesions were not noticed in this patient. Early diagnosis and treatment of the oral lesions may have prevented skin involvement and minimized the level of circulating antibodies.

In conclusion, this study reported a case of PV affecting the oral mucosa in a young adult male. Early diagnosis and treatment of the oral lesions with local and systemic steroid resulted in remission within 6 months.

Conflict of Interest: None declared

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