Considerations in Complications Arising from the Management of Pemphigus Vulgaris: A Case Report

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ABSTRACT

Background: This paper reports a case of pemphigus vulgaris in a middle-aged male with oral lesions and skin eruptions

Objective: To highlight the complications of prolonged steroid therapy.

Case Report

A 48-year old male presented with an eight-month history of recurrent mouth ulcers. There was positive history of cutaneous ulcers on the upper extremities, back and genital areas. Patient had been placed on long term steroid therapy prescribed by general practitioners. General examination showed bilateral pitting pedal oedema, moon face and low blood pressure. Intra-oral examination revealed multiple irregular shaped ulcers and erosions with erythematous floor on the buccal mucosa, labial mucosa, floor of the mouth, soft palate and anterior pillar fauces. The dorsum of the tongue had areas of ulcerations with necrotic slough. An impression of pemphigus vulgaris was made based on high index of clinical suspicion and patient was commenced on azathioprine 50mg and prednisolone 40mg daily for a week. Topical use of clobetasol ointment (0.05%) was also commenced to be applied twice daily. There was improvement with the oral lesions on a one-week review. The dose of prednisolone was then stepped down to 20mg daily for one week and 0.2% chlorhexidine mouth rinse twice daily was introduced.

Punch biopsy of an intact labial mucosa was done on a subsequent visit and histopathology examination confirmed the diagnosis of pemphigus vulgaris. Patient was referred to the cardiologist on account of the hypotension and bilateral pedal oedema which was suggestive of complications of long-standing steroid use.

Patient was placed on maintenance dose of prednisolone 10mg and azathioprine 50mg daily, and topical steroid oral rinse.

Conclusion: This study reports a case of pemphigus vulgaris with oral and skin lesions in a middle-aged male. Patient developed some complications due to the prolonged duration of steroid therapy. Regular patient monitoring, adjustment of steroid therapy combined with adjuncts like steroid-sparing drugs are essential to minimizing the steroid-induced adverse effect

Keywords: pemphigus vulgaris, complications, prolong steroid therapy

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INTRODUCTION

Pemphigus is a rare, chronic, autoimmune, intra-epithelial blistering disease with skin and mucous membrane affectations (soft linings of the eyes, nose, mouth, throat and genitals) [1,2]. Major variants of pemphigus are pemphigus vulgaris, pemphigus vegetans, pemphigus erythematosus, pemphigus foliaceous, drug-induced pemphigus, and paraneoplastic pemphigus [3].

Pemphigus vulgaris (PV) is the most common of these diseases accounting for about 80% of cases [4]. Blisters essentially always affect the mouth and oral lesions may be seen as an initial manifestation in 50% of cases before the appearance of skin lesions [5]. The oral lesions may occur with or without cutaneous involvement [6].

The incidence of PV varies worldwide [6]. The condition has been reported to be common in people of Jewish descent and people from Middle East, India, Southeast-Europe are at an increased risk of developing pemphigus [7,8]. The disease may develop at any age [9,10], however the average age of onset is between fourth and sixth decades of life [11]. Pemphigus has been reported to affect more women than men [12] while an equal sex distribution has also been reported [11,13].

The exact cause of pemphigus vulgaris is unknown but genetic predisposition has been identified [14] with no indication the disease is hereditary. Other possible triggers include thermal burns, ultra-violent rays, drugs, diet, infections, endocrine diseases and emotional stress [6]. Diagnosis of pemphigus vulgaris can be made via clinical assessment, biopsy showing suprabasal vesicle formation and blood test to detect serum autoantibodies to desmoglein 1 or desmoglein 3 [6,11,14].

The main stay of treatment is steroid therapy often in combination with adjunt medication like steroid-sparing agents [7,11]. This condition was considered fatal before the advent of steroid therapy mainly from dehydration or secondary systemic infections [14]. The high doses and prolonged use of steroid therapy which are often needed to control the disease may mask the signs and symptoms of inflammation and thus contribute to death in patients[15]. The combination of steroid and steroid-sparing drugs can minimize or delay the onset of the adverse effects of prolonged steroid therapy[11].

This paper reports a case of pemphigus vulgaris in a middle aged male. Patient had been on steroid therapy for the condition about a year prior to presentation at the Oral Medicine clinic of the University of Benin Teaching Hospital. He presented with painful oral lesions, and some complications of prolonged steroid therapy: 'moon face', hoarsness of voice, bilateral pitting pedal oedema, and low blood pressure.

CASE REPORT

A 48 years old male patient who was referred to the Oral Medicine clinic of the University of Benin Teaching Hospital (UBTH), on account of mutiple ulcers in the mouth of 8 months duration. The oral lesions have been recurrent over that last 2 years. The lesions were preceded by complaints of sore throat and dysphagia. There was no history of use of sulphur-containing drugs prior to appearance of the oral lesions. The oral lesions appeared about 8 months after he stopped smoking. There was a positive history of skin eruptions on the upper extremities, back, and genital areas which appeared about a year after the on-set of the oral lesions and they ruptured leaving areas of hyperpigmentation. The skin lesions cleared rapidly with treatment. There were associated symptoms like pain, odynophagia, voice change (hoarse voice) and limitation in mouth opening.

Intra-oral examination revealed multiple irregular shaped ulcers and erosions with erythematous floor on the buccal mucosa, labial mucosa, floor of the mouth, soft palate, and anterior pillar fauces (figure 1). The dorsum of the tongue had areas of ulcerations with whitish slough. Oral hygiene was poor with marked halitosis. There were associated bilateral enlarged, mobile and non tender submandibular lymphnodes. Patient also had bilateral pitting oedema of the ankles and a low blood pressure of 90/60mmHg. An initial impression of pemphigus vulgaris was made based on high index of clinical suspicion. The results of blood tests (full blood count, electrolytes, retroviral screening and fasting blood sugar) were normal. Perilesional punch biopsy of the oral mucosa was done and sent for histopathological examination. Hematoxylin and eosin stained sections showed a keratinizing stratified squamous epithelium with prominent rete ridges overlying a fibrocellular connective tissue stroma. There was presence of suprabasal layer cleft and within the clefts were extravasated red cells. Section also showed numerous sub-epithelial chronic inflammatory cells infiltrates and vascular spaces. Deep within the tissues were aggregates of adipocytes, striated muscle bundles and thick walled vascular spaces (figure 2). A definitive diagnosis of pemphigus vulgaris was made.

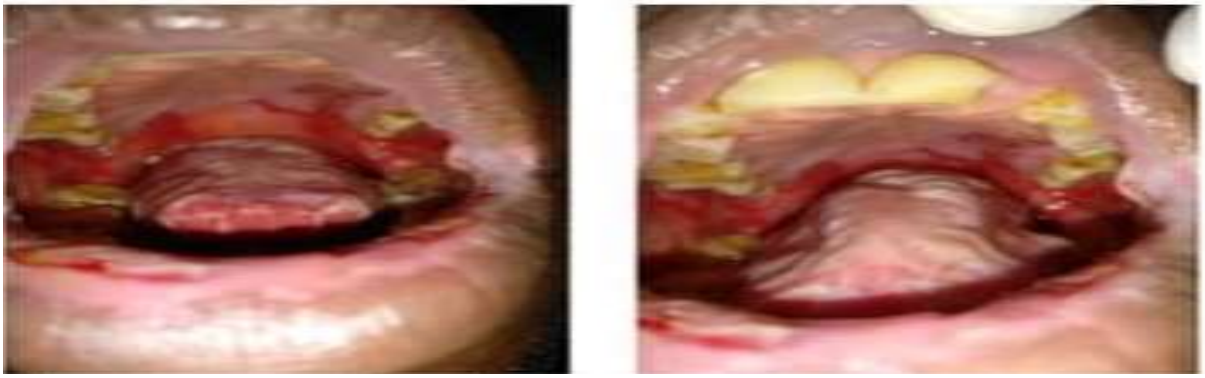

Figure 1: Intra oral view showing wide spread erosions and ulcerations on the buccal mucosa, labial mucosa, and soft palate and whitish slough on the tongue.

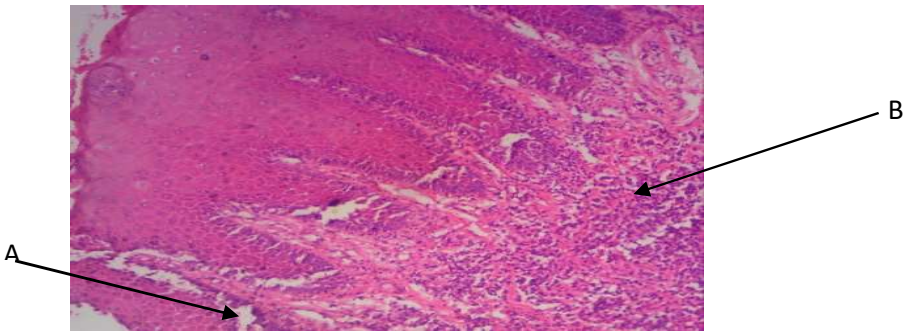

Figure 2: Photomicrograph showing stratified squamous epithelium with prominent rete ridges and suprabasal cleft (A) and dense sub-epithelial inflammatory cell infiltrates (B) (H&E stain, x100)

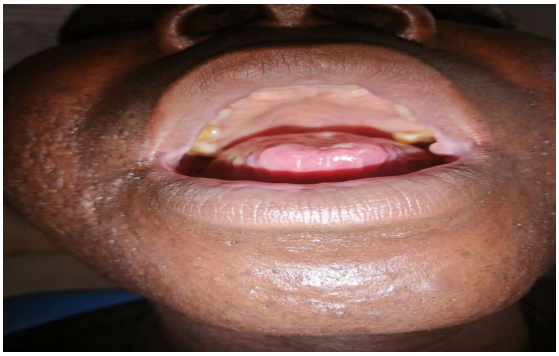

Figure 3: intra-oral view showing healing oral lesions

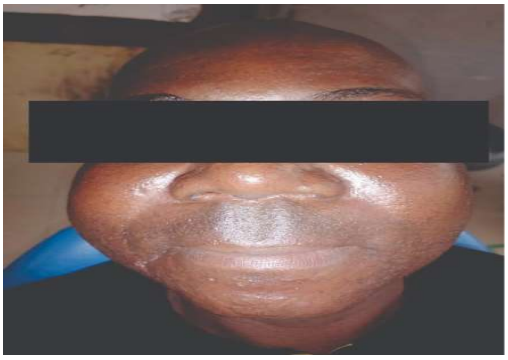

Figure 4: Cushingnoid appearance 'moon-facies'

The initial treatment administered was Prednisolone tablets 40mg/day for one week, Azathioprine 50mg daily for one week, clobetasol ointment 0.05% twice daily for one week. Patient was referred to the Cardiologist on account of the low blood pressure and pedal oedema. A one week review revealed improving oral lesions, however new areas of ulceration with erythematous floor were observed on the lower lip. The patient was continually placed on prednisolone 40mg daily for three weeks, azathioprine 50mg for three weeks, topical clobetasol twice daily for three weeks. After three weeks of treatment with prednisolone, the oral lesions showed improving condition, the dose of

prednisolone was then stepped down to 20mg/day for one week, azathioprine maintained at 50mg daily, chlorhexidene 0.2% oral rinse twice daily for one week was introduced. The clobetasol ointment was substituted with dexamethasone (2mg in 10ml of water) oral rinse for one week. At this time patient had been placed on Torsinex 10mg daily by the cardiologist on account of the pedal oedema. A two week review revealed oral lesions were healing, and the medications were maintained at prednisolone 20mg/day, azathioprine 50mg/day, dexamethasone (2mg in 10ml of water) oral rinse daily, and nystatin oral rinse three times daily, all for another two weeks, with the chlorhexidine discontinued.

A one month review showed oral lesions were improving (figure 3). Patient was thus placed on maintenance dose of prednisolone 10mg/day, azathioprine 50mg daily, dexamethasone (2mg in 10ml of water) oral rinse daily. Subsequent reviews over the past 6 months revealed considerably progress with the oral lesions healing satisfactorily, the moon facie was observed to be subsiding and the pedal oedema had cleared completely. The hoarse voice has however not abated.

DISCUSSION

Pemphigus is a potentially life-threatening, autoimmune condition characterized by intraepithelial blisters on the skin and mucous memebrane (e.g eyes, nose, mouth, throat and genitals) [1,14]. The oral lesions are quite recalcitrant in nature [7] and are often the first manifestation of the disease [7,16]. This patient developed oral lesions first before appearance of skin eruptions about a year later. The final diagnosis was based on histological features.

The main stay of treatment for pemphigus is use of local and systemic corticosteroid therapy [1,11,17]. Use of only topical steroid therapy is insufficient for sustained control of the condition as a result of the autoimmune characteristics of the disease [1]. Treatment is often quite prolonged and can last many years with a mean of 5-10years [6]. This is often associated with complications from long term steroid therapy hence the use of steroid-sparing drugs to delay the onset or minimize these complications[11]. Commonly used steroid-sparing drugs include azathioprine, dapsone, mycophenolate-mofetil [6,17].

Long-term adverse effects of prolonged administration of systemic corticosteroids include osteoporosis and fractures, hyperglycemia/diabetes, adrenal suppression, cardiovascular disease and dylipidemia, cataracts and glaucoma, myopathy, psychiatric disturbance, immunosuppresion, gastrointestinal and dermatologic events, Cushingnoid appearance and weight gain [18] . This patient, having been on prolonged oral steroid therapy, even before presentation at the Oral Medicine clinic of the University of Benin Teaching Hospital developed a 'moon face', (figure 4) and bilteral pitting pedal oedema. The patient also had persistent low blood pressure of 90/60 mmHg. The low blood pressure was not in keeping with the expected complications of prolonged steroid therapy, as a high blood pressure is usually the case. Drops in blood pressure may arise as a result of rapid withdrawal of steroids which causes adrenal insufficiency. Our patient was closely monitored as the steroid dose was gradually reduced, hence the low blood pressure was not expected.

Recommendations for prevention and monitoring of systemic corticosteroid-induced adverse effects include a thorough assessment before initiating long-term systemic corticosteroid therapy [18]. Baseline values for body weight, height, bone mineral density(BMD), and blood pressure , full blood count, lipid profile and blood glucose can also be obtained before commencement of therapy. It is very important to measure the above-mentioned parameters regularly [18].

Modalities for minimizing steroid-induced adverse effects include administering the lowest effective steroid dose for a minimum period of time to achieve treatment goal [18], taking drugs once daily. Morning administration and/or intermittent or alternate-day dosing has been recommended. Other modalities for minimizing steroid -induced adverse events include adopting lifestyle habits to minimize the risk of weight gain. Patients should never discontinue steroid therapy abruptly unless on physician's advice [18]. The use of steroid-sparing drugs should be considered whenever possible as they reduce the dose and duration of treatment with corticosteroid [17]. They can also be used when the condition cannot be controlled with steroid alone, or when there is a clinical contraindication for high dose steroid therapy [6]. The steroid-sparing drugs have also been used to prevent relapses in previously controlled patients [19]. Based on response and clinical judgement, the steroid dose for this patient was gradually tapered to attain the minimum therapeutic dose as a maintenance dose, taken once daily in the morning

along-side a steroid sparing drug to minimize side effects.

CONCLUSION: This study reported a case of pemphigus vulgaris in a middle-aged male with oral and skin involvement. Patient developed bilateral pedal oedema and moon facies due to the prolonged duration of therapy. Regular patient monitoring, adjustment of steroid therapy combined with steroid-sparing drugs were very essential to minimizing the steroid-induced adverse effect.

Source of Support
Nil.

Conflict of interest
None declared

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