Mr. L.F. is a 53yr old gentleman who initially presented to his family doctor with mouth ulcers, hoarseness and odynophagia. He was given various treatments including antibiotics, anti-virals, non-steroidal anti-inflammatory drugs (NSAIDs) and oral steroids with no effect. His condition worsened and was associated with a 5kg weight loss. He subsequently developed skin blisters and erosions and was referred to the dermatology department. A clinical diagnosis of pemphigus vulgaris was made and he was started on high dose oral steroids. A skin biopsy sent for histology and immunofluorescence confirmed the diagnosis. On confirmation he was admitted for rituximab therapy and started on azathioprine.

**Fact File on Pemphigus Vulgaris**

Pemphigus vulgaris is a potentially life-threatening autoimmune disease with a number of clinical variants. This blistering disorder affects the mucosa and the skin. In up to 50% of cases, it initially presents with intra-oral lesions, and may remain so for about a year (Becker, et al., 2009). This emphasizes the need for dentists to be aware of this condition as it is most likely to present first in their practice. This is particularly important as early recognition results in a better prognosis (Shafer, et al., 2008). The age of presentation is often between 30-50 years, with a male predominance of 2:1. Pemphigus vulgaris is estimated to affect only 1-5 patients per million populations per year (Shamim, et al., 2008).

The aetiology of the disease is still largely unknown, however, it is characterized by the production of autoantibodies against desmosomes, particularly targeting desmoglein 3. Desmoglein 3 is predominantly expressed in the oral mucosa, hence explaining the reason why initial presentation is often with oral lesions. The loss of adhesion between these structural units gives rise to the manifestation of intraepidermal bullae (Robinson, et al., 2004).

Characteristically the oral blisters are prone to rupture, with ensuing painful erosions. There is a predilection for soft-palate, buccal mucosa and lip involvement but any site in the oral cavity can be affected (Neville, et al., 2008).

Initially pemphigus vulgaris presents with a positive Nikolsky’s sign, which is a pressure-induced wrinkling of seemingly healthy skin. Clear-fluid containing bullae, occurring over both normal as well as erythematous skin, are the primary lesions. These bullae increase in size on application of pressure, with the fluid spreading to the surrounding epidermis (indirect Nikolsky’s sign). Scarring is not a feature, though the healing process is slow (Pradeep, et al., 2010).

A lesional biopsy is necessary to confirm diagnosis of pemphigus vulgaris. On histology, intraepidermal clefting with acantholysis and Tzanck cells in the prickle cell layer is characteristic. Direct and indirect immunofluorescence can be used to further confirm the diagnosis of pemphigus vulgaris. On indirect immunofluorescence IgG antibodies are seen circulating in the serum whilst on direct immunofluorescence, intercellular IgG antibodies can be seen (Tamgadge, et al., 2010).

Pharmacological therapy is aimed at reducing the autoantibody production and the accompanying inflammatory response. Corticosteroids and immunosuppressants often make up the treatment regimen. Overall mortality has improved significantly with corticosteroid therapy. Despite this, steroid use is limited due to their significant side-effect profile which contributes to morbidity. Thus, steroid-sparing immunosuppressive drugs such as rituximab, are nowadays considered early on in treatment. Therapy is tailor to the patient’s clinical picture, taking into consideration any other co-morbidities (Bassam, et al., 2015).

**Case Report on Pemphigus Vulgaris**

**Presenting Complaint**

The patient initially complained of discomfort whilst eating accompanied with nausea for a few weeks. He was reviewed by an E.N.T. specialist and was found to have an oedematous and erythematous uvula which resolved following a short course of prednisolone. On stopping the steroids, he developed mouth ulcers and hoarseness, resulting in odynophagia and troublesome eating. A few days later, he noted a single skin lesion in the supraclavicular region which bled after showering, however the patient...
thought nothing of it. In the ensuing
days, the number of mouth ulcers 
increased. After seeking the advice of his 
general practitioner, he was diagnosed 
with herpes zoster and started on a five-
day course of acyclovir. Despite this, the 
mouth ulcers continued to increase in 
number together with the appearance of 
skin erosions on his chest, prompting him 
to attend the E.N.T. clinic. The patient was 
prescribed metronidazole, clarithromycin 
and diclofenac; however, his symptoms 
did not improve. He had also visited his 
dentist who had prescribed mouth gurgles 
with little effect. At a subsequent dental 
appointment, a mucosal biopsy was taken 
for histology due to worsening mouth 
ulcers. Throughout the course of this 
history, he noted a five-kilogram weight 
loss with no associated loss of appetite. 
The following morning, he visited his 
general practitioner in view of worsening 
mouth ulceration and skin erosions. This 
prompted his general practitioner to refer 
him to Boffa Hospital for dermatological 
review and investigation.

Past Medical & Surgical History

The patient is a known case of 
hypothyroidism (diagnosed five years ago) 
and borderline hypercholesterolaemia. 
He wears dentures as a consequence of 
an extensive history of periodontal gum 
disease. Surgical history included two 

Drug History & Allergies

The patient has no known drug allergies. 
Drug history is listed in Table 1.

Family History

The patient’s father had a history of 
type II diabetes mellitus (T2DM), and 
hypertension. He had a stroke aged 48 
and died of natural causes. His mother 
had a history of ischaemic heart disease, 
heart failure, deep vein thrombosis, 
and died aged 81. He has five siblings. 
One of his brothers suffers from T2DM 
and hypercholesterolaemia. His sister 
developed hypertension at 34 years and 
also suffers from hypercholesterolaemia.

Upon dermatological consultation, the 
patient’s lesions were examined (Figures 
1 and 2).

Differential Diagnoses

1. Pemphigus vulgaris;
2. Pemphigus foliaceus;
3. IgA pemphigus;
4. Pemphigus erythematosus;
5. Bullous pemphigoid.

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Diagnostic Investigations

Requested investigations: Liver function 
tests & hepatitis screen;

Justification for procedure: Possible 
deterioration of liver function on 
rituximab, and the use of rituximab in 
the presence of chronic viral hepatitis.
may lead to worsening of pre-existing hepatitis;

**Result:** Normal.

**Conclusion:** No contraindication to rituximab therapy with respect to liver function.

**Requested investigations:** Tuberculosis (TB) Quantiferon test & Chest X-Ray (CXR);

**Justification for procedure:** To investigate for latent TB as rituximab therapy needed to treat pemphigus vulgaris may reactivate latent TB;

**Result:** CXR and Quantiferon test both normal.

**Conclusion:** No evidence of previous infection with TB.

**Requested investigations:** Anti-nuclear antibody (ANA), extractable nuclear antigens (ENA) antibody and immunoglobulin tests;

**Justification for procedure:** Possible other associated autoimmune disorders apart from pemphigus vulgaris;

**Result:** Normal.

**Conclusion:** Other associated autoimmune disorders highly unlikely.

**Requested investigations:** Skin incisional biopsy for histology and direct immunofluorescence;

**Justification for procedure:** Necessary for definite diagnosis of pemphigus vulgaris

**Result:**

Histology: Intraepidermal clefting with acantholysis in the prickle cell layer. A sparse chronic inflammatory cell infiltrate, which includes scattered eosinophils, is present in the papillary dermis. A perivascular lymphocytic infiltrate involves the superficial plexus and vessels in the mid dermis.

Direct Immunofluorescence: Intercellular deposition of IgG and of C3 within the epidermis, outlining the cell membranes of keratinocytes in the prickle cell layer.

**Conclusion:** Diagnosis of pemphigus vulgaris confirmed.

**Diagnosis**

The characteristic nature of the skin lesions, coupled with the definite findings on histology and direct immunofluorescence, confirmed the diagnosis of pemphigus vulgaris. The investigations conducted revealed no contraindications to treatment with rituximab and high-dose steroids, thus, the patient was started on these two medications.

**Management**

**Pharmacological Therapy**

Following investigations, the patient was started on the following:

**Follow Up**

The patient received his weekly dose of intravenous (IV) rituximab for four weeks, with routine bloods and glucose monitoring. There was a partial response to treatment with some improvement but he was still getting new mouth ulcers. He will be followed up regularly at the outpatient department and will be continued on oral steroids and an increasing dose of azathioprine. Further courses of rituximab are planned in view of active disease.

**References**


