Pemphigus Foliaceous: A Rare Case Report

Patel Krina N\textsuperscript{1}, Deepak bhavsar\textsuperscript{2}, Maharaul Mashrutee S\textsuperscript{3}, Agrawal Vama M\textsuperscript{4}, Patel Ankitkumar B\textsuperscript{5}

\textsuperscript{1,3,4}Final MBBS Student, 5Junior Resident - Department of Paediatrics, G.M.E.R.S. Medical College and Hospital, Gotri, Baroda, Gujarat, India
\textsuperscript{2}Consulting dermatologist, Skin care clinic, 2\textsuperscript{nd} floor lohana building, Tower

ABSTRACT:
BACKGROUND: Pemphigus foliaceus (PF) which is a rare autoimmune blistering disease, presents in endemic and sporadic forms with the typical presentation of seborrheic distribution of recurrent shallow erosions. Here we present a case of a 62-years-old male with PF who was successfully treated with a combination of oral corticosteroids and azathioprine.

Key Words: Pemphigus foliaceous, Prednisolone, Azathioprine, Immunofluorescence, ELISA

INTRODUCTION
The term pemphigus is derived from the Greek word pemphix meaning blister or bubble. The incidence of pemphigus ranges from 0.76 to 5 cases per one million per year\textsuperscript{1}. Pemphigus is further divided into 2 major forms on the basis of blister location: pemphigus vulgaris (PV) and pemphigus foliaceus (PF). A variant of PV is Pemphigus vegetans and variants of PF are pemphigus erythematous (PE) and fogo selvagem. Uncommon forms of pemphigus have been described during past 3 decades, which includes pemphigus herpetiformis, immunoglobulin A (IgA) pemphigus, and paraneoplastic pemphigus\textsuperscript{2}.

CASE REPORT
A 62-year-old male presented with a 4-month history of superficial erosions on the upper back in 2011. He denied any photosensitivity, and his medical history was otherwise unremarkable. On examination, the erosions were in the form of painless vesicles, which bursted in 2 days discharging clear watery fluid. The patient was started on low dose Prednisolone (20 mg) for 1 month but he did not improve; rather the lesions spread on the entire body from scalp to legs. Two punch biopsies (one lesional and one perilesional) were performed. Routine histology results showed intraepidermal vesicles in the upper granular layer containing acantholytic cells. Results of direct immunofluorescence demonstrated IgG and complement 3 (C3) in the intercellular spaces in the epidermal cell surface. Also, antinuclear antibody and anti–double-stranded DNA were negative. These findings were consistent with our clinical diagnosis of Pemphigus Foliaceous. The patient was then started on high dose Prednisolone(40 mg) for 4 weeks when new lesions ceased to appear; then the medication was slowly tapered off. Azathioprine(50 mg) was also added to his regimen. Shelcal in a single morning dose containing 500 mg calcium and 250 IU vitamin D3 also was added to the regimen. He was seen at regular follow-up visits every month. As the patient improved clinically, oral prednisone taper continued slowly over a total of 18 months. No lesions were present for the last 5 monthly visits.

CASE DISCUSSION
Pemphigus is a blistering disease affecting the skin and mucous membrane. The disease is characterized by acantholysis; which means loss of adhesion between keratinocytes histologically, and immunopathologically characterised by the
presence of antibodies directed towards the cell surface of keratinocytes. Indirect immunofluorescence study revealed that circulating antibodies are mainly IgG1 and IgG4 in pemphigus foliaceous and the deposited antibodies are mainly IgG type, with predominantly IgG1 and IgG4 types of antibodies.

In order to understand the pathogenesis of Pemphigus it is essential to have a basic knowledge of the desmosome. Desmosomes also known as maculae adherens are organelles responsible for cell-to-cell adhesion in keratinocytes. Desmoglea which is the extra cellular part is composed of transmembrane adhesion glycoproteins which belong to the cadherin superfamily, including desmogleins and desmocollins. Desmosomal plaques which are the intracellular part, has two groups of proteins: a) The plakin family (desmoplakins, envoiplakin, periplakin, plectin) which binds to cytokeratin filaments and b) The plakoglobin and plakophilin which binds to the intracellular domain of cadherins. The pemphigus antibodies bind to the antigens in the desmosome which results in acantholysis. PF clinically presents with recurrent shallow erosions associated with erythema, scaling, and crusting. Lesions usually are found in a seborrheic distribution (central face, neck, chest, or upper back). The onset of disease may be slow, starting with only a few transient scattered crusted lesions. In general, patients are not severely ill but often complain of burning and pain associated with the skin lesions. The condition may then stay localized for years or progress into generalized involvement, sometimes resulting in an exfoliative erythroderma. In our case the patient presented with painless superficial erosions first on upper back and later on it gradually spread to other parts of body.

The differential diagnosis of Pemphigus foliaceous are: other forms of pemphigus, bullous impetigo, subcorneal pustular dermatosis, seborrheic dermatitis and linear IgA dermatosis. PF was fatal in about 60% of patients before the advent of glucocorticoid therapy.

The most reliable method of diagnosing pemphigus is Immunofluorescence using both direct and indirect techniques. On the basis of meta-analyses; available ELISAs are found to be highly sensitive and specific, and has a higher diagnostic accuracy as compared to indirect immunofluorescence.

Currently the aim of therapy is to suppress the production of pathogenic antibodies, cessation of the development of new lesions, and to heal old lesions. For the effective management of PF it requires a knowledge of the pharmacologic effects of the agents used, pathophysiology of disease, an ability to make an accurate diagnosis, and also an understanding of the patient’s expectations. The starting dose of prednisone is 1.0 mg/kg and is usually tapered down towards an alternate-day dosage within 1 to 3 months.

Despit of proven benefits, currently no optimal regimen for corticosteroid therapy is available for the treatment of pemphigus. Thus a tailored regime is recommended in routine practice. A starting dose of 0.5 mg/kg prednisolone daily is prudent which may be increased, if new blister formation is observed. Immunosuppressive therapy for pemphigus includes azathioprine, mycophenolate mofetil, methotrexate, cyclophosphamide, cyclosporin and dapsone.

Azathioprine (a purine antimetabolite ) is cleaved to 6-mercaptopurine, which is converted to additional metabolites which in turn inhibits de novo purine synthesis. It inhibits cell proliferation and as a result a variety of lymphocyte functions are impaired. Azathioprine is used to treat pemphigus; a survey of dermatologists in 2003 showed that Azathioprine was the most commonly prescribed adjuvant immunosuppressive agent used to treat Pemphigus. Azathioprine given in combination of Prednisolone reduces the cumulative dose of prednisolone compared with prednisolone alone therapy however remission rates are not reduced. Side effects were also similar between the two group of drugs. In our case the patient...
was prescribed 20 mg Prednisolone but his lesions worsened so the dose was increased to 50 mg Prednisolone and Azathioprine 50mg was also added as an adjuvant therapy; he responded well to this combination. This can be clearly concluded from the pictures of patient’s lesions before and after the treatment. Figure1. Showing lesions before the treatment and Figure 2. Showing healed lesions after the treatment.

**Figure 1: before treatment**

![Image 1](image1)

**Figure 2: after treatment**

![Image 2](image2)

**CONCLUSION**

Pemphigus foliaceous is a potentially life-threatening and debilitating condition thus it is important to promptly recognize the condition clinically and then confirm by characteristic features on histology, direct immunofluorescence and by detection of serum autoantibodies through indirect immunofluorescence or ELISA tests. Corticosteroids remain the mainstay of treatment and starting dose should be of 0.5 mg /kg of oral prednisone per day and is continued until disease control is obtained. An adjuvant agent is added in severe progressing disease. Either azathioprine or mycophenolate mofetil could be utilized as an adjuvant drug. It is recommended to use rituximab for severe cases. If rituximab is unavailable or Contraindicated other biological agents, extracorporeal therapies or cytotoxic agents can be considered.

**REFERENCES**
