

Pemphigus Vulgaris: Application of Occlusal Soft Splint with Topical Steroid in the Treatment

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ABSTRACT

Pemphigus vulgaris (PV) is a rare autoimmune bullous dermatosis with a high mortality rate if untreated. It is characterized by the binding of IgG autoantibodies to desmogleins 3 (DSG 3), a transmembrane glycoprotein adhesion molecule present on desmosomes. This glycoprotein strengthens the intercellular connection, and loss of this connection due to the antigen-antibody reaction weakens and finally breaks the connection between epithelial cells resulting in blisters and desquamation. Patients with PV mainly involving the mucosa have antibodies directed against DSG 3, but patients with PV involving both the skin and mucosa will have antibodies against both DSG 3 and DSG 1. Most patients are initially misdiagnosed and improperly treated for many months or even years. Dental professionals must be sufficiently familiar with the clinical manifestations of PV to ensure early diagnosis and treatment, since this in turn determines the prognosis and course of the disease.

Keywords: Pemphigus, Autoimmune, Desmoglein, Desmosome.

INTRODUCTION

'Pemphix' in Greek means 'bubbles or blisters'^{1,3} and 'vulgaris' in Latin means 'common'.^{2,3} Though pemphigus is a rare disease, PV is the commonest of all, comprising of 80% of the disease entity.³ The term pemphigus was originally named by Wichman in 1791.^{1,3} PV is a serious, chronic autoimmune mucocutaneous disease characterized by the appearance of vesicles and bullae, small or large fluid-filled blisters that develop in cycles.¹ Pemphigus includes a group of autoimmune blistering diseases of the skin and mucous membrane characterized histologically by intradermal blisters and immunologically by the finding of circulating immunoglobulin G (IgG) antibody directed against the cell surface of the keratinocytes.¹ The common autoimmune mucocutaneous diseases affecting the oral mucosa are pemphigus and mucous membrane pemphigoid.

Here, we are presenting a case report of pemphigus vulgaris with a follow-up period of 8 months reported to the Department of Oral Medicine and Radiology, SVS Institute of Dental Sciences, Mahabubnagar.

CASE REPORT

A 35-year-old female patient (Fig. 1) reported to our department with a chief complaint of oral and skin lesions since 2 months.

Patient gave a history of small fluid-filled blisters that burst after sometime resulting in erosion and ulcers. These oral erosions and ulcerations caused discomfort to the patient and significantly affected her normal oral function.



Fig. 1: Clinical picture of the patient

On general examination, patient was moderately built, moderately nourished, conscious, coherent and vital signs within normal limits.

On extraoral examination, there are multiple bullae seen on the back (Fig. 2), nape of the neck, chest, abdomen and on right thigh. Intraoral examination revealed multiple small- medium irregular areas of intense erythema involving particularly the gingiva, right buccal mucosa (Fig. 3) and hard palate. The site most severely affected was labial marginal and attached gingiva of maxillary and mandibular anterior teeth. Multiple small-medium size ulcers were seen on left buccal mucosa.

The provisional diagnosis of PV was made. Incisional biopsy was performed on perilesional sites of the right side of the buccal mucosa. This specimen was submitted for immunofluorescence studies and conventional histopathology.

Histopathological examination revealed detached stratified squamous epithelium, basal layer with tombstone appearance and focal regeneration. Underlying subepithelial tissue shows

moderate lymphoplasmocytic infiltrate with perivascular accentuations (Fig. 5).

Direct immunofluorescence with fluorescence isothiocyanate (FITC) labeled antibodies show intercellular deposits of IgG and weak deposits of IgM and IgA. With this the diagnosis of PV was confirmed (Fig. 6).

The patient was commenced on systemic prednisolone (wysolone) at an initial dose of 30 mg/day (20 mg morning and 10 mg at night) along with topical corticosteroid clobetasol propionate 0.05% (Tenovate 3 times/day) with occlusal soft splint for 1 week. After 1 week of the treatment, there is complete regression of the lesions on left side of the buccal mucosa with reduction in the size of the erosions on hard palate and right side of the buccal mucosa. Regression in desquamative gingivitis is also seen on maxillary and mandibular anterior gingiva. Next week, the patient was put through periodontal sessions, which include oral hygiene instructions and quadrant scaling. As the initial dose failed to reduce the disease signs and symptoms completely, the systemic corticosteroid prednisolone (Wysolone) dosage was increased to 40 mg/day (20 mg twice daily) for next 2 weeks along with topical steroid application. As the desquamative gingivitis persists without much regression, the systemic corticosteroid dosage was increased to 50 mg (30 mg morning and 20 mg at night) along with topical steroid application for next 1 week. There is decrease in the symptoms of oral lesions with completely healed bullae on the skin without scar formation.

As there was gradual reduction in the size of oral erosions (right side of buccal mucosa, palate, desquamative gingivitis) systemic prednisolone (wysolone) dosage has been tapered down to 40 mg/day (20 mg twice daily) for one week followed by 30 mg/day (20 mg morning and 10 mg at night) for 1 week, 20 mg/day (10 mg twice daily) for next 3 weeks followed by 10 mg/day (5 mg twice daily) for 15 days and then by 5 mg/day (once daily in the morning) for 1 month. The patient was advised to stop systemic prednisolone and is currently on the topical corticosteroid therapy with occlusal splint (Fig. 4) as the desquamative gingivitis persists. To date, no other sites are



Fig. 2: Blisters on the back



Fig. 3: Irregular shallow ulcer with erosion and intense erythema is seen on right side of the buccal mucosa



Fig. 4: Intraoral picture with mandibular occlusal soft splint

involved. The plan was to wean the patient off the topical corticosteroids gradually while maintaining the clinical remission.

DISCUSSION

Pemphigus has two major subtypes: Pemphigus foliaceus (PF) and pemphigus vulgaris (PV), based on clinical, histopathologic and serologic features. PV is further subdivided into the mucosal dominant type and the mucocutaneous type. Pemphigus erythematosus is a localized variant of PF, and pemphigus vegetans is a rare vegetative variant of PV. Mucosal dominant PV is characterized clinically by mucosal erosions mainly in the oral cavity with minimal skin involvement, histologically by blister formation just above the basal layers or suprabasilar acantholysis, and serologically by detection of anti-DSG3 IgG

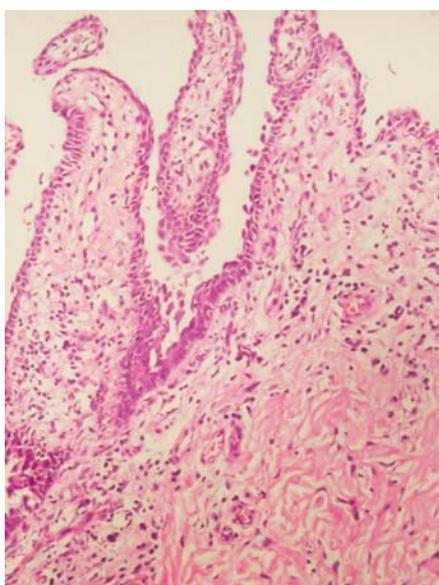


Fig. 5: High power photomicrograph showing TZANCK cells

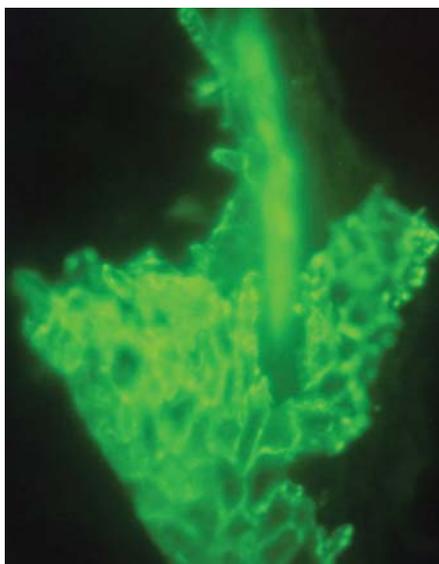


Fig. 6: Chicken mesh pattern of deposition of IgG

autoantibodies alone. Mucocutaneous PV is characterized clinically by extensive skin blisters and erosions in addition to the mucosal erosions. Histologic classification is by suprabasilar acantholysis and serologic classification by detection of both anti-DSG1 and anti-DSG3 IgG autoantibodies.⁵ Mortality from PV before the development of effective therapies was as high as 90% and was often fatal mainly from dehydration or secondary systemic infection. Furthermore, oral lesions are often the first sign of the disease, and they are the most difficult to resolve with therapy. This has prompted the description of oral lesions as 'the first to show and last to go'.^{2,3}

The underlying mechanism responsible for causing the intraepithelial lesion of PV is the binding of IgG autoantibodies to desmoglein 3 (DSG3), a transmembrane glycoprotein adhesion molecule present on desmosomes. This glycoprotein strengthens the intercellular connection, and the loss of this connection due to the antibody-antigen reaction weakens and finally breaks the connection between epithelial cells, resulting in blisters and desquamation.^{1,2,7} Patients with PV mainly involving the mucosa have antibodies primarily against the DSG3, but the patients with PV involving both the skin and mucosa will have antibodies against both DSG3 and DSG1.^{1-4,6}

CLINICAL FEATURES

PV affects all races, with equal gender distribution among males and females. It usually occurs in middle-aged or elderly patients and is rare in children.^{1,7} PV is characterized by the rapid appearance of vesicles and bullae, varying in diameter from a few millimeters to several centimeters. These lesions contain a thin, watery fluid shortly after development, but this may soon become purulent or sanguigenous.¹ The bulla rapidly breaks but continues to extend peripherally, eventually leaving large areas of denuded skin.⁴ A characteristic sign of this disease is on application of pressure to an intact bulla, the bulla enlarges to the apparently normal skin. This is known as Asboe-Hansen sign.^{4,7} Another characteristic sign of the disease is that pressure to an apparently normal area results in the formation of a new lesion. This phenomenon, called Nikolsky sign, results from the upper layer of the skin pulling away from the basal layer.^{1,2,4,5,7,8}

Oral blisters are fragile and rupture readily, leaving painful erosions that heal with difficulty. In most cases, the disease has a chronic course, with a slowly progressive worsening. Patients complain of pain in the oral cavity, especially while eating spiced or sour foods. Any site in the mouth may be involved, but the soft palate, buccal, gingival, and lower lip mucosa usually predominate. Increased salivary secretion (sialorrhea) and foul breath (halitosis) often occur. Thick brown-blackish hematic crusts unceasingly form at the vermilion border.⁷

In the long run, weakness, loss of weight, malaise, and often fever appear. If left untreated, the disease progresses with an almost always fatal outcome due to uncontrolled fluid and protein loss or opportunistic infection.⁷

Diagnosis of PV is based on clinical signs and laboratory tests. A persistent, stubborn gingivostomatitis should always be considered as suspect PV.⁷

Laboratory examinations encompass the Tzanck cytological test,⁷ useful on oral erosions; standard histology^{1,2,4} on a fresh bulla, which shows suprabasal acantholysis; direct immunofluorescence, which reveals the intercellular deposition of immunoglobulin G (IgG) and C3 in the epidermis of the perilesional skin; indirect immunofluorescence (using monkey esophagus as substrate), the classic method for detecting and titrating intercellular pemphigus antibodies in the serum; ELISA using recombinant human DSG3 and DSG1,^{7,8} a sensitive and specific assay for measuring anti-DSG3 and anti-DSG1 antibodies present in the serum; immunoblotting and immunoprecipitation needed when diagnosis remains uncertain.⁷ Systemic corticosteroids are the most potent therapeutic option for PV. With its use, mortality rate has come down significantly from 60 to 90% to below 10%. When substantial doses of steroids must be used for long periods of time, adjuvant therapy is recommended to reduce the steroid dose and their potential serious complications.^{3,4,10} The most commonly used adjuvants are immunosuppressive drugs like azathioprine, cyclophosphamide, mycophenolate mofetil, dapsone, gold salts, methotrexate, cyclosporine, chlorambucil, dexamethasone plus cyclophosphamide pulse therapy, immunoablative therapy, plasmapheresis and extracorporeal photochemotherapy were used.^{7,9,10} Recently, newer agents, such as intravenous immunoglobulin therapy, 1-5 rituximab (an anti-CD20 chimeric monoclonal antibody), immunoadsorption using the Globaffin adsorber system, and immunoadsorption for rapid removal of desmoglein-reactive autoantibodies have been used.^{8,9} The diversity of these drugs and treatment methods, together with their specific side effects, are indicative of the difficulty involved in choosing a suitable treatment for pemphigus today. In practice, the chosen therapy depends greatly on the experience of experts in different parts of the world.

CONCLUSION

PV is a rare cause of chronic ulceration of the oral mucosa. The mouth may be the only site of involvement for a year or so and this can lead to delayed diagnosis and inappropriate

treatment of a potentially fatal disorder. Newer diagnostic tests and better monitoring of this disease process is achieved with a clear understanding of the role of anti-DSG antibody-keratinocytes binding in blister formation. Treatment by suppressing the circulating autoantibodies, with the use of systemic corticosteroids and adjuvant therapy. Recently, antigen-specific immunotherapy has become an alternative to current conventional treatment modalities.

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