A Rare Case of Pemphigus Vulgaris, Mucocutaneous Type in a 26-year Old Female

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Pemphigus is an autoimmune blistering disease of the skin, mucous membrane, or both. There are two main categories: pemphigus foliaceus (PF) and pemphigus vilgaris (PV) based on clinical, histopathologic and serologic features. PV The mean age of onset of the disease is approximately 40 to 60 years of age. We report a case that clinically showed blisters and erosions in the skin and mucous membrane in a 26 years old female patient. Histologic examination of the cutaneous lesions demonstrated suprabasilar acantholysis. Direct immunofluorescence showed intercellular deposition of IgG (+2) and C3 (+2). Prednisone and a steroid sparing agent- Azathioprine were given and significant improvement was observed after just three weeks.

Abbreviation used.
PV: Pemphigus vulgaris
PF: Pemphigus foliaceus
Dsg: Desmogleins

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Pemphigus is an autoimmune blistering disease of the skin, mucous membrane, or both. There are two main categories: pemphigus foliaceus (PF) and pemphigus vulgaris (PV) based on clinical, histopathologic and serologic features. PF is characterized clinically by the presence of shallow erosions, with evident scaling and crusts on the skin, without mucosal involvement. PV is characterized clinically by mucosal erosions mainly on the oral cavity with minimal skin involvement. PV is further subdivided into mucosal and mucocutaneous type, according to the extent of cutaneous lesions.[7] The mean age of onset of the disease is approximately 40 to 60 years of age, with equal men and women involvement. It has a worldwide incidence of 0.5-3.2 cases per 100,000.[10] In our institution, there were only 11 cases of PV seen since 2001 up to present and the patients were mostly female in their 40's to 60's. This is the first case of PV reported in a 26 years old female.

CASE REPORT

We report a case of 26 year old female, with a 1 ½ year history of recurrent painful erosions on the lower lip. No fever nor lymphadenopathy was noted. Over time patient noted fluid-filled lesions that would easily rupture on the abdominal area. No history of trauma prior to appearance of lesions. Blisters spontaneously rupture forming erythematous plaques with erosions which healed with hyperpigmentation. New lesions appeared on her face, back, neck, breasts and lower extremities. Patien self-medicated with Amoxicillin 500mg three times a day for 1 week and applied topical fluocinonide ointment irregularly on the lesions but only afforded temporary relief. Hence, she decided to consult in our institution.

Past medical history was unremarkable. Patient is single, unemployed, with no history of illicit drug use, no intake and topical application of herbal medications nor any other medications and no history of chronic sun exposure. She is non-alcoholic beverage drinker and non-smoker.

On physical examination, there was a solitary, erythematous erosion on right side of soft palate. Lesions on the genitalia. Dermatologic examination revealed multiple erythematous plaques, some with erosions on the scalp, forehead, neck, chest, back and few on the lower extremities. Few flaccid bullae containing clear fluid also noted on the trunk. Positive for Nikolsky and Asboe-Hansen signs.

Basing on the clinical findings, the initial impression was Pemphigus vulgaris. Punch biopsy of a bulla revealed an intraepidermal vesicle filled with red blood cells and few acantholytic cells. Focal areas of the base of the vesicle show a suprabasal tombstoning acantholytic pattern. The dermis shows moderately severe inflammatory infiltration consisting of lymphocytes (predominantly) and histiocytes. Few melanophages are also seen in the upper dermis (*Fig 1*). Punch biopsy of the normal skin adjacent a bulla was done and was sent for direct immunofluorescence which showed intercellular deposition of IgG (+2) and C3 (+2) (*Fig 2*). Other laboratory work up were normal, which included complete blood count, erythrocyte sedimentation rate, urinalysis, stool examination with occult blood, chest xray, SGPT, SGOT, BUN, serum creatinine, sodium, potassium, calcium, random blood sugar and lipid panel. Final clinicohistopathologic diagnosis is Pemphigus Vulgaris.

Patient was started on Prednisone 1 mg/kg/day decreasing the dose by 10 mg weekly. On the second week of treatment, Azathioprine 50mg/day was added. Both medications continued up to 3 months. Dramatic improvement was observed starting at the third week of treatment (*Fig 4*). No new lesions appeared and the old lesions healed with hyperpigmentation.

DISCUSSION

PV occurs worldwide, but is more common in Jews and in people of Mediterranean descent.[1] It affects men and women equally and is considered an organ-specific autoimmune disease.[2] The mean age of onset of disease is approximately 40 to 60 years of age; however, the range is broad, and disease may start in the elderly and in children. There was no report of PV occurring in young adults.

The major histologic feature is acantholysis.[3] Direct immunofluorescence of perilesional skin

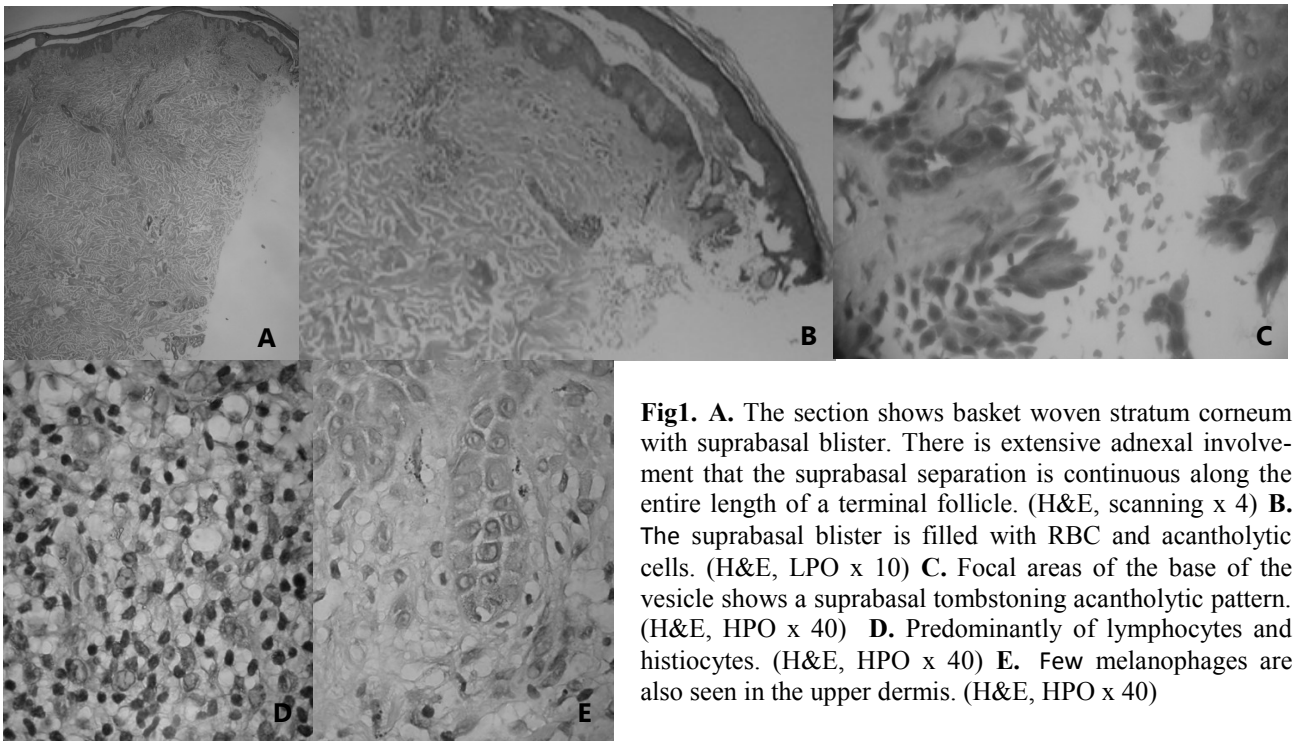

Fig1. A. The section shows basket woven stratum corneum with suprabasal blister. There is extensive adnexal involvement that the suprabasal separation is continuous along the entire length of a terminal follicle. (H&E, scanning x 4) **B.** The suprabasal blister is filled with RBC and acantholytic cells. (H&E, LPO x 10) **C.** Focal areas of the base of the vesicle shows a suprabasal tombstoning acantholytic pattern. (H&E, HPO x 40) **D.** Predominantly of lymphocytes and histiocytes. (H&E, HPO x 40) **E.** Few melanophages are also seen in the upper dermis. (H&E, HPO x 40)

binding of IgG antibodies to the epidermis in an intercellular pattern.[4] Pemphigus antibody is pathogenic and is present in the serum of patients with PV.[5] It is directed against a normal component of the intercellular substance known desmoglein 3.[6] The clinical and histologic sites of blister formation in pemphigus are now logically explained by desmoglein compensation theory. Dsg1 and Dsg3 have distinct intraepithelial expression patterns in the skin and mucous membranes. In the superficial layers. Dsg3 is expressed in the lower part of the epidermis, mainly in the basal and parabasal layers. In contrast, in the mucous membranes, Dsg1 and Dsg3 are expressed throughout the squamous mucosal epithelia, but the expression level of Dsg1 is much lower than that of Dsg3.[7]

Pemphigus vulgaris, once a fatal disease, now has a mortality rate below 10% with the introduction of corticosteroids and adjuvant therapy with immunosuppressive drugs. Currently, the mainstay of treatment is corticosteroids. Before the availability of corticosteroids, approximately 75% of patients died of pemphigus, usually within 1 year. The use of corticosteroids in the 1950s reduced the mortality to approximately 25% to 45%. However, the use of long-term glucocorticosteroids is linked to severe and life-threatening complications. Side effects from corticosteroids can be the major cause of death in patients with pemphigus.[8]

The addition of adjuvant therapy with a "steroid sparing" effect has reduced the mortality of pemphigus to less than 10%.[7] Adjuvant therapies for pemphigus can be divided according to the mechanism of action. Immunosuppressive drugs include cyclophosphamide, azathioprine, chlorambucil, cyclosporine, methotrexate, and mycophenolate mofetil. Antiinflammatory drugs include antimalarials, dapsone, and gold. Immunomodulatory procedures include plasmapheresis and photopheresis.[9] dapsone, and gold. Immunomodulatory procedures include plasmapheresis and photopheresis.[9]

The most efficacious cytotoxic drug to reduce steroid was found to be azathioprine, followed by cyclophosphamide (pulse therapy), and mycophenolate mofetil.[11] Azathioprine (1-2 mg/kg/day) and corticosteroid treatment of pemphigus is highly effective and safe; it leads to long-term remissions in most patients and possibly to a cure in some.[12]

It is possible to eventually induce complete and durable remissions in most patients with pemphigus that permit systemic therapy to be safely discontinued without a flare in disease activity. The induction of complete remission was related to the initial severity and extent of disease and to early response to treatment.[13]

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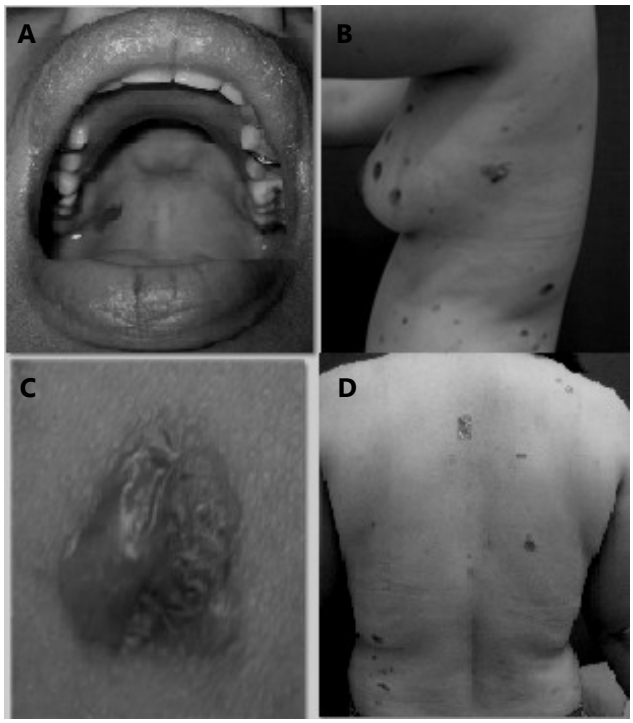

Fig 3. Patient before treatment . **A,** solitary erosion on right side of soft palate. **B and D,** multiple hyperpigmented plaques some with erosions on trunk. **C,** few bullae with clear fluid

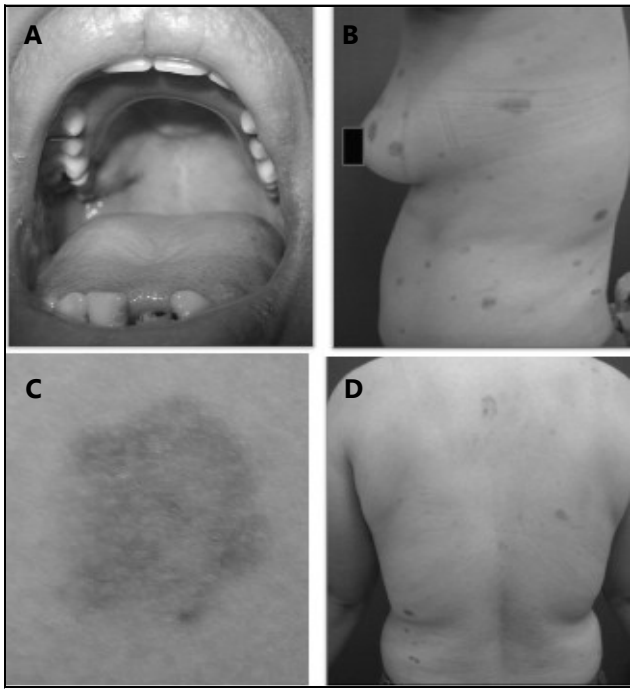

Fig 4. Patient after 7 weeks of treatment with Prednisone and Azathioprine. **A**, smaller erosion on the soft palate. **B and D**, multiple hyperpigmented patches on trunk. **C**, resolution of