

Case Report

Pemphigus Vulgaris as Oral Mucosal Ulcer Progressive to Skin Lesion:

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ABSTRACT

Among all the life threatening diseases, autoimmune diseases are among most notorious and complicated diseases. As these diseases have no specific cause or responsible organism, it is therefore very difficult to distinguish and diagnose and thus stands as a major threat for public health. It is assumed that the reason for these diseases may be from genetic to environmental factors, from stress to idiopathic origin. Pemphigus Vulgaris(PV) is such an autoimmune blistering disease that frequently affects the mucous membrane and skin. Very often it starts from oral cavity and Dentists therefore the first to recognize. This paper describes the case of a patient presenting with a one-year history of painful ulcerated gingiva, tongue, floor of the mouth and even on GIT who is finally diagnosed as having PV spreading to generalized skin.

Introduction:

Pemphigus Vulgaris (PV) is an autoimmune intraepithelial blistering disease involving the skin and mucous membrane¹. PV is characterized by acantholysis in the epithelium¹. It affects both sexes almost equally and is more common in middle-aged and elderly patients^{2,3}. Systemic corticosteroid therapy is associated with a dramatic improvement of the condition; however, complications of medical therapy still remain a concern. In many PV patients, the oral lesions are followed by the development of skin lesions^{3,5}. Consequently, if oral PV can be recognized in its early stages, treatment may be initiated to prevent progression of the disease to skin involvement. Early oral lesions of PV are,

however, often regarded as difficult to diagnose, since the initial oral lesions may be relatively nonspecific, manifesting as superficial erosions or ulcerations and rarely presenting with the formation of intact bullae^{2,4,5,6}. Diagnostic delays of greater than 6 months are common in patients with oral PV⁴. The average interval from the onset to confirmation of the diagnosis of PV has been reported to be 6.8 months⁶ or 27.2 weeks². Historically, studies of autoimmune responses had been conducted by analyzing the presence and/or concentration of single antibodies in biological fluids using conventional immunoassays, such as ELISA, radioimmunoassay, immunoblot, and others. More recently, antigen microarrays have been constructed and validated for over a dozen autoimmune diseases⁷. This paper describes the case of a patient presenting with a one-year history of painful ulcerated gingiva, tongue, floor of the mouth and even on GIT who is finally diagnosed as having PV spreading to generalized skin.

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Casereport:

In 2011, a 63-year-old woman was referred with a one-year history of painful ulcerated gingiva, tongue, soft and hard palate, angle and floor of the mouth. The patient noticed peeling out of the gingival epithelium while she brushed her teeth. She had initially received periodontal treatment, including scaling, periodontal treatment and oral hygiene instructions, from a general dentist; however, she had noted no improvement of the burning sensation and peeling away of her mucosa. She also reported an increased salivation with sticky discharge. Her condition was getting worsen and consequently she developed skin lesion all over her body within weeks. She had no history of hypertension, diabetes or any other systemic diseases. On examination, bullous lesions were found in oral mucosa, gingiva, tongue, angle and floor of mouth (fig 1, 2 & 3). The bullae were seen to rupture with discharge of sticky fluids. Nikolsky's sign showed a positive reaction, and the epithelium could be peeled away easily by slightly scratching the surface of the mucosa and skin. Endoscopy of GIT confirmed the involvement of ulcer on GIT. However patient was admitted to the hospital and systemic corticosteroids were given and she responded quickly with disappearance of lesions in oral cavity, angle of mouth and skin (fig 4 & 5).

The cytological smear was collected before obtaining biopsy specimens. Smears were prepared by exfoliating from the labial gingiva using a cytobrush (Medscand Medical AB, Malmo, Sweden). In the cytological smear, collective acantholytic cells (Tzank cells) were recognized. These cells enabled a presumptive diagnosis of PV to be made. A gingival biopsy was obtained from the perilesional site and submitted for routine histopathology and the direct immunofluorescence (DIF) test. DIF was performed using conjugates for IgG, IgA, IgM, C3, and fibrinogen, and it revealed deposition of IgG and C3 between the epithelial cells. A definitive diagnosis of PV was made based on these clinical and histopathological and immunofluorescent findings.



Fig-1 shows multiple blistering lesions involving gingiva and buccal mucosa



Fig-2. shows blistering lesions involving angle of the mouth



Fig-3 shows the lesions on hand skin



Fig-4 shows disappearance of lesions in angle of mouth after treatment



Fig-5 shows disappearance of lesions from hand skin

In this patient, although it took only two weeks from her first visit to our hospital until a definitive diagnosis of PV was made, one year had elapsed from the onset of the oral lesions to the definitive diagnosis. However, after the remission of her skin lesions, she was given prednisolone 1.1mg/kg/body wt., 100 mg azathioprine/day, calcium supplement and omeprazole. The prednisolone was in tapered mode at the rate of 2.5 mg decreasing in every two weeks. Finally, it stopped at 5 mg in every alternative day for six months. After two years she was instructed to lower the dose of azathioprine from 100 mg /day to 50 mg/day and prednisolone was completely stopped. However, she had not reported the recurrence of the lesions till now.

Discussion:

The term pemphigus was originally named by Wichman in 1971⁸. Pemphigus is a group of potentially life threatening autoimmune mucocutaneous disease characterized by epithelial blistering affecting cutaneous and/or mucosal surfaces, the term being derived from the Greek word pempix (bubble or blister). Although vulgaris means common in Latin, the worldwide incidence of PV is very low and has been reported to be 0.1-0.5 per 100,000 persons per year. PV appears to occur in males and females in an equal ratio and is most frequently reported in patients between fourth and sixth decades of life^{9,10}.

PV is an autoimmune disease that is characterized by acantholysis in the epithelium¹. The main antigen in PV is desmoglein (Dsg) 3, a

protein constituent of the desmosomes¹¹. Most patients with PV have circulating IgG autoantibodies against Dsg3^{11,12}. These antibodies bind to the Dsg3 on the epithelial cell membrane and may evoke acantholysis^{11,12}. Acantholytic cells are often found in intraepithelial blisters. These cells show degenerative changes, including round, swollen hyper chromatic nuclei with a clear perinuclear halo in cytoplasm. Acantholytic cells can be confirmed in the cytological smear obtained by exfoliating from the oral mucosa¹³. In general, autoimmune diseases are characterized by the presence of multiple types of autoantibodies mediating a coordinated immunological attack against a fraction of the tissue proteome. Multiplex analysis of autoantibody responses against a spectrum of candidate antigens represents a powerful screening tool to delineate biomarker signatures in autoimmunity, allowing elucidation of the overall autoimmune process rather than individual components¹⁴. The availability of multiplex technologies has made possible the simultaneous detection of several different autoantibodies overcoming some of the limitations of conventional methods¹⁵. For instance, antigen arrays proved to be 4- to 8-fold more sensitive than conventional ELISA analyses for detection of autoantibodies specific for some autoantigens¹⁶. In this report, we recognized acantholytic cells in the cytological smear, also a DIF which enabled a presumptive diagnosis of PV to be made. However, it is necessary to perform a biopsy since the appearance of acantholytic cells alone does not allow a definitive diagnosis, but only permits a presumptive diagnosis of PV. This is because acantholytic cells may also appear in other diseases such as impetigo, Darier's disease, transient acantholytic dermatosis, viral infections, and carcinoma¹⁷. PV often be bewildered by pemphigoid or DG (Desquamatie Gingiitis), but DG is a clinical manifestation of the gingiva that is characterized by desquamation of the gingival epithelium, chronic redness, ulceration, and/or blister formation^{6,18,19,20}. Nisengard and Levine¹⁰ cited the following as the standard in making a clinical diagnosis of DG: (1) gingival erythema not resulting from plaque, (2) gingival desquamation, (3) other intraoral and sometimes

extra oral lesions, and (4) complaint of sore mouth, particularly with spicy foods. It is reported that most cases of DG are caused by several mucocutaneous diseases^{6,18,19}. Mucous membranepemphigoid and erosive lichen planus are the most frequent causes of DG, accounting for 48.9% and 23.6%, respectively, of all cases of DG²¹ while Pemphigoid lesions are widespread tense blisters, bullae can occur on normal-appearing, as well as erythematous, skin surfaces. The bullae usually heal without scarring or milia formation. There are mild clinical difference in between Pemphigus and pemphigoid.

Conclusion:

PV is a potentially fatal disease if not treated timely and perfectly. As it is very difficult to diagnose except the confirmatory test, it can be convoluted with the many other oral lesions like Erosive Lichen Planus, Systemic Lupus Erythematosus, Pemphigoid, Desquamative Gingivitis etc. Many often physicians fail to diagnose it at its early stage and patients often may not receive the appropriate treatment. Therefore physicians should be more aware regarding the ulcers especially oral ulcers. And since dentists' foreplay the role in treating with oral diseases, therefore they must be familiar with all these potentially fatal diseases.

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