Pemphigus Vulgaris: A Case Report with Review of Literature

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ABSTRACT

Pemphigus is a group of autoimmune diseases of the skin and/or mucous membranes characterized histologically by intraepidermal blister, tombstone appearance of basal cells and immunopathologically by the finding of circulating immunoglobulin G (IgG) antibody directed against the cell surface of keratinocytes. Here, we report, case of pemphigus vulgaris, lesions in oral mucosa without any skin lesions. The condition improved with systemic corticosteroids along with adjuvant therapy. The purpose of this article is to emphasize the importance of early diagnosis of pemphigus, thereby decreasing the chances of fatality and improving the quality of life by various treatment modalities.

Keywords: Autoimmune, Corticosteroid, Nikolsky’s sign, Pemphigus.

INTRODUCTION

Pemphigus is a group of potentially life-threatening autoimmune diseases characterized by cutaneous and/or mucosal blistering. Pemphigus vulgaris (PV) is a chronic mucocutaneous disease which usually manifests first in the oral cavity, which later may spread to the skin or the other mucous membrane. As it is a life-threatening disease condition, it is important that the dentist is able to recognize oral manifestations of PV and treat or refer appropriately. The most common variant of pemphigus, is characterized by circulating IgG antibodies directed against desmoglein 3 (Dsg3), with about half of the patients also having Dsg1 autoantibodies. Oral lesions are initially vesiculobullous but readily rupture, new bullae developing as the older ones rupture and ulcerate. Biopsy of perilesional tissue, with histological and immunostaining examination are essential to confirm the diagnosis. Serum autoantibodies to either Dsg1 or Dsg3 are best detected using normal human skin by enzyme-linked immunosorbent assay. Current treatment is largely based on systemic immunosuppressant’s using corticosteroids (CS), with azathioprine or other adjuvant or alternatives but newer therapies with potentially fewer adverse effects, also appear promising.

CASE REPORT

A 23-year-old female reported to the hospital with a chief complaint of painful ulcerations in the mouth of 3 months duration. It started initially as small fluid-filled vesicles on the gums which later ruptured spontaneously forming painful ulcers in the gums and gradually it spread to the inner surface of cheeks and lips. One week back, the pain became severe, lancinating type and continuous in nature. Bleeding occurs while brushing and on spitting. A detailed family history was obtained but was not contributory.

On general examination, there were no signs of cutaneous involvement but multiple superficial ulcerations and erosions were present on the upper and lower lip appearing fiery with bloody crusting (Fig. 1). The lesion was soft in consistency and tender on palpation and bleeding was evident. Peeling of mucosa was also present.

On intraoral examination, there were multiple diffuse erosions and ulcerations present in the entire oral cavity (Figs 2 and 3). The most affected area of the oral cavity was the dorsal aspect of tongue and gingiva. The surface of the lesion was erythematous with peeling of mucosa. Gingiva appeared glossy, erythematous and edematous with generalized desquamation (Fig. 4). Multifocal erythematous areas in dorsal and lateral surface of tongue were present (Fig. 5).

Nikolsky’s sign was positive. By correlating the chronic nature of multiple diffuse ulcerations and erosions, typically accompanied by pain of 3 months duration with positive Nikolsky’s sign, this case was provisionally diagnosed as pemphigus and the patient was further investigated.
The incisional biopsy was taken on the right side of buccal mucosa in relation to 44 region for histopathological examination, which showed intraepithelial separation just above the basal layer of epithelium and acantholytic cells in the intraepithelial separation (Fig. 6) and immunofluorescence features (Figs 7 and 8) show intercellular fluorescence seen in mucosa and submucosal junction were consistent with PV.

After confirmation of diagnosis the patient was prescribed tablet ranitidine 150 mg twice daily before meals–tablet prednisolone–5 mg, four times daily after food for 2 months, then with improvement the dose was tapered to 5 mg twice daily for 2 months along with chlorhexidine mouthwash once daily. Complete remissions of erosions were seen after 5 months (Figs 9 and 10). Maintenance dose of 5 mg was prescribed once daily for 1 month. There was no recurrence of the condition for 1 year after stopping the steroids.

DISCUSSION

‘Pemphix’ in Greek means ‘bubbles or blisters’ and ‘vulgaris’ in Latin means ‘common’.1 The term pemphigus was originally named by Wichman in 1791. It is mediated by circulating autoantibodies directed against keratinocyte cell surface. 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. Today, with treatment, it is approximately 5 to 15%.2 Oral lesions often represent the first clinical manifestation. It is thus important that the dentist is able to recognize oral manifestations of PV and treat or refer appropriately.1 In our case report there was oral lesions without any skin lesions. There is damage to desmosomes by antibodies directed against the extracellular domains of cadherin-type epithelial cell adhesion molecule—the Dsg with immune deposits intraepithelially, and loss of cell-cell contact (acantholysis), leading to intraepithelial vesiculation.4

In our case histopathological examination revealed intraepithelial split with loss of cell-cell contact. On direct and indirect immunofluorescence, Dsg3 index value was 33 while Dsg1 index value was negative with C3 as 105 mg/dl. The main antigen in PV is Dsg3 but 50% of patients also have autoantibodies to Dsg1. The proportion of Dsg1 and Dsg3 antibodies appears to be related to the clinical
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Fig. 8: Intercellular fluorescence seen in mucosa and sub-mucosal junction

Fig. 9: Complete remission of erosions in labial mucosa after treatment of pemphigus

Fig. 10: Complete remission of erosions after treatment pemphigus

severity of PV. Those with only Dsg3 antibodies have oral lesions predominantly. In PV mainly IgG antibodies are deposited intercellularly directed against the extracellular domains particularly of Dsg3 and as oral epithelium expresses largely Dsg3 (skin expresses Dsg1 as well as Dsg3), oral lesions appear at an early stage.\(^2,4\)

Biopsy of perilesional tissue, with histological and immunostaining examination, are essential to the diagnosis. ELISA has been proved to be helpful even for PV. With appropriate dilution, ELISA detection of autoantibodies to Dsg3 and Dsg1 can provide useful information for assessing disease activity.\(^2\)

The principle aim of treatment is to reduce inflammatory response and autoantibody production, thereby achieving disease remission. A positive clinical response is associated with a decrease in the circulating autoantibodies in the serum and absence of bound autoantibodies in the skin. This is followed by a period of maintenance treatment using the minimum drug doses required to achieve disease control and minimize their side effects. Management mainly comprises of CS with/without adjuvant drugs. Systemic CS are effective and the mainstay of treatment with PV, even if confined to the oral mucosa.\(^6,7\) Adjuvant drugs are commonly used in combination with the aims of increasing efficacy and of having a steroid-sparing action, thereby allowing reduced maintenance CS doses and reduced CS side effects. The oral lesions of PV may respond partially to topical CS (creams, pastes), but some form of systemic immunosuppression is needed to control the level of circulating autoantibodies. Patients with mild disease are treated with initial prednisolone doses of 40 to 60 mg per day and in more severe cases, 60 to 100 mg per day. If there is no response within 5 to 7 days, the dose should be increased in 50 to 100% increments until there is disease control, i.e. no new lesions and healing of existing ones. If doses above 100 mg per day are required, pulsed intravenous CS should be considered. Once remission is induced and maintained with healing of the majority of lesions, the dose of CS should be cautiously tapered. A 50% reduction every 2 weeks has been suggested.

In our case, tablet prednisolone (5 mg) four times daily after food for 4 months, dose was tapered after 2 months 5 mg two times daily for 2 months. Chlorhexidine mouth was once daily for 2 months and tablet ranitidine 150 mg twice daily before meals. Maintenance dose of 5 mg was prescribed once daily for 1 month duration. Patient has no clinical remissions till now.

Pulsed intravenous CS refers to the intermittent administration of high doses of intravenous CS, usually methyl prednisolone (250-1,000 mg) or equivalent doses of dexamethasone given on 1 to 5 consecutive days. The theoretical aims of pulsing are to achieve more rapid and effective disease control compared with conventional oral dosing, thus allowing a reduction in long-term maintenance CS doses and CS side effects. Pulsed CS could be considered in severe or recalcitrant PV to induce remission, particularly if there has been no response to high oral doses. Patient should be informed about risk of acute adrenal insufficiency\(^8\) caused due to CS regimen.

Azathioprine\(^9\) is a commonly prescribed adjuvant drug in PV. Azathioprine doses of 1 to 3 mg/kg have been used but ideally should be titrated according to the individual activity of TPMT (thiopurine methyltransferase). Oral cyclophosphamide could be considered as an alternative to azathioprine. Pulsed intravenous cyclophosphamide with dexamethasone or methylprednisolone refers to the intermittent administration of high doses of intravenous CS and cyclophosphamide, usually three daily doses of dexamethasone (100 mg) or methylprednisolone (500-1,000 mg) and a single dose of cyclophosphamide (500 mg) given monthly. Mycophenolate mofetil (MMF) is a relatively new agent in PV therapy. Total daily doses of 2 to 2.5 gm are typically given in two divided doses with prednisolone. MMF could be considered in recalcitrant cases or when azathioprine and cyclophosphamide cannot be used. Intravenous immunoglobulin (IVIG) doses of 1.2-2 gm/kg divided over 3 to 5 days were infused every 2 to 4 weeks
for 1 to 34 cycles. It was beneficial and steroid-sparing. Plasma exchange (PE) was combined with both CS and immunosuppressive drugs and it is thought that the latter is necessary for clinical effect in order to prevent the rebound production of autoantibodies stimulated by PE. Extracorporeal photopheresis (ECP), 2-day cycles given every 2 to 4 weeks for a minimum of two cycles. There was clinical improvement and it was possible to taper the concurrent doses of prednisolone and immunosuppressant drugs. ECP could be considered in recalcitrant cases of PV where there has been failure to improve with more conventional therapy.

CONCLUSION

PV is a chronic mucocutaneous disease with formation of painful ulcers, vesicles and bulla, usually manifesting first in the oral cavity which later may spread to the skin or the other mucous membrane. Oral ulceration is rarely caused by PV but the mouth may be the only site of involvement for several months which may lead to delayed diagnosis and treatment of this potentially fatal disorder. Hence, early diagnosis and treatment stops the progression, leading to lasting remission and good prognosis.

REFERENCES


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