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Case report

Pemphigus vulgaris and complications of systemic corticosteroid therapy: a case report

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Abstract: Pemphigus refers to a group of diseases characterized by painful lesions caused by intraepidermal acantholytic structures in the skin and mucous membrane. The exact nature of the disease remains unknown. Pemphigus is a rare chronic mucocutaneous disease characterized by intra-epithelial bulla formation, due to autoantibodies directed against proteins of the desmosome-tonofilament complex between keratinocytes. The bullous lesions are painful, slow to heal and with a tendency to become invasive. Any part of the oral cavity may be affected, with the soft palate, buccal mucosa and lips being the most common sites. The high doses and prolonged administration of corticosteroids often required to control the disease result in several side effects, many of which are serious or life-threatening. In the present case, steroid treatment was begun at 180 mg/day and subsequently increased to 250 mg/day and 350mg/day Oral lesions were treated locally with 0.2% chlorhexidine gluconate in addition to systemic corticosteroids containing an immunosuppressive. Oral lesions were observed to recur without healing completely. Respiratory problems occured, necessitating direct lung radiographs and computerised tomography. Pulmonary embolism was diagnosed and the patient was transferred to the vascular surgery department. Unfortunately the patient died due to pulmonary embolism on the seventh day. Pemphigus vulgaris (PV) is a chronic autoimmune mucocutaneous disease that often primarily involves the oral cavity. Therefore, early diagnosis of oral symptoms is crucial for the successful treatment of PV. Although there is no consensus regarding the initial steroid dosage needed to induce remission, it is suggested that high doses of corticosteriods may cause fatal complications. (J. Oral Sci. 45, 165-169, 2003)

Key words: pemphigus vulgaris; oral lesions; complications; treatment.

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Introduction

Pemphigus refers to a group of rare chronic mucocutaneous diseases characterized by painful lesions caused by intraepidermal acantholytic structures in the skin and mucous membrane. The exact nature of the disease remains unknown (1). Pemphigus is characterized by intra-epithelial bulla formation, due to autoantibodies directed against proteins of the desmosome-tonofilament complex between keratinocytes (1,2).

The literature reveals similar prevelancy between the sexes. The disease has two known main types-pemphigus vulgaris (PV) and pemphigus foliaceus. Although there have been reports of children with this condition, it is usually seen between 5- to 7-years of age (2-7).

The mucosal lesions of PV are located most frequently in the oral and pharyngeal mucosa; however, the conjuctiva, larynx, nasal mucosa, vulva, vagina, cervix and ano-rectal mucosa may also be involved (8). The bullous lesions are painful, slow to heal and show a tendency to become invasive. Although any part of the oral cavity may be affected, the soft palate, buccal mucosa and lips are the

most common sites (9). However, it is generally accepted that diseases such as lichen planus and pemphigoid lesions sometimes show similiar clinical appearance (8,9). In the literature, there have also been reports of several other disorders manifesting DG including psoriasis, dermatitis herpetiformis, chronic ulcerative stomatitis, erythema multiforme, epidermolysis bullosa and Kindler Syndrome (10-12). Similar appearances may be seen in reaction to dental materials, mouth washes and medications, and in lupus erythematosis, Crohn's disease, sarcoidosis and leukemias (13-15). Oral lesions are a hallmark of PV and occur in almost all cases, and present the preliminary symptom in more than half of patients. Clinically, the oral lesions are characterized by blisters that rapidly rupture, resulting in painful erosions (13).

Definitive diagnosis cannot be achieved with clinical examination alone, as several other vesiculobullous and ulcerative lesions have a similiar appearance (6,7,16-19). Incisional biopsies are required (1).

In the absence of systemic treatment, oral lesions are almost invariably followed by involvement of the skin, on and occasionally other epithelial surfaces such as the esophagus (9,20). Unless there are only localized oral lesions, in which case treatment with topical corticosteriods suffices for a time, systemic corticosteriods (e.g prednisolone) are essential, sometimes administered intravenously. Once the condition is under control, the dosage of prednisolone can be reduced (7,21,22). Adjuncts or alternatives include azathioprine, cyclosporin, cyclophosphamide, dapsone, levamisole, prostaglandin E_2, chlorambucil and immunoglobulins (22-24).

Unfotunately the high doses and prolonged administrations of corticosteroids that are often needed to control the disease result in several side effects, many of which are serious or life-threatening (25).

In this case, the patient died as a result of pulmonary emboli in the second year of corticosteroid therapy. This is the fifth reported patient to have died as a result of complications of corticosteroid therapy.

Case report

A 43-year-old man was admitted to our department in March 1999 with various skin and oral mucosal lesions. His dermatologist stated that he had been treated for PV for two years.

Clinical examination revealed wide, painful, erythematous, ulcerative areas on the buccal mucosa, tongue and lips (Figs. 1 and 2). Periodontal pockets that were deeper than 4 mm were also found proximal to the molar teeth. The gingiva was characterized by redness, bleeding and desquamation. Erosive lesions were observed around his chin and back (Fig. 3). Bullous lesions (0.5 × 0.8 cm) were also observed in these areas. Skin and oral mucosal biopsies were taken for pathological examination under hematoxylin-eosin stain, which confirmed a diagnosis of PV (Fig. 4).

Liver function parameters were found increased in serum. The patient was experiencing femoral pain for which Cataflam was prescribed. MR findings were normal. Blood gas pressures were PCO_2 22 mmHg and PO_2 2 mmHg. The leucocyte count was low at 3700 per microliter.

Systemic steroid treatment was begun at 180 mg/day and this dose was subsequently increased to 250 mg/day and 350 mg/day. No healing of the skin lesions was observed. Therefore, an oral immunosuppressive (Endoxan) was added to the treatment. For oral lesions, local treatment of 0.2% chlorhexidine gluconate was used. The patient had been treated by a periodontist for 15 days with oxygenating agents, and metronidazole (Flagyl) had been prescibed (1500 mg/day for 7 days). The oral lesions were observed to be in remission rather than healing (Fig. 5).

Respiratory problems appeared, and direct lung radiographs and computerised tomography were undertaken. Pulmonary embolism was diagnosed and the patient was transferred to the vascular surgery department. Ig G (Octagam 5 g) was given for 5 days/intravenously, and the steroid dose was decreased to 120 mg/day. On the fifth day serious diarrhea occurred, and the patient died due to pulmonary embolism on the seventh day.

Discussion

In PV, acantholysis occurs deep in the stratum spinosum, creating a suprabasal cleft, whereas in pemphigus foliaceus the bulla formation occurs at a higher level (26). In PV, the oral mucosa is the first site to be involved (up to 70% of cases) and it is the only site affected in over 50% of patients (7). In the present case, ruptured erosive and bullous lesions were seen on the lips, commissures and the chin as well as the oral mucosa and gingiva.

Distal extension from the oral cavity can occur in PV, affecting the pharynx, larynx and esophagus producing dysphagia (7,9).

In the literature, the gingival lesions of PV have been described as severe desquamative and erosive gingivitis where bullae have ruptured to leave flaps of healing tissues with red erosions or deep ulcerative craters mainly in the attached gingiva (27,28). In the present case, although the gingival desquamative was present, there were no erosive lesions or bullous lesions on either the attached or free gingiva. However, the patient's oral hygiene was very poor and he had severe generalized periodontitis.

Systemic oral corticosteroids are the treatment of choice

in patients with PV (20,29). Topical steroid therapy alone is insufficient for sustained control of the disease because of the systemic autoimmune characteristics of PV. There is no consensus regarding the initial steroid dosage needed to induce remission and its effect on the subsequent course of the disease, but it is generally agreed that low doses (below 60 mg/day) usually do not suffice to induce initial control. In the present case, oral corticosteroid treatment was begun with a high dose (180 mg/day) and then increased higher to 250 mg/day and then 350 mg/day. At the first oral dose, the lesions did not respond. Consequently, the corticosteroid dose was increased and an immunosuppressive (Endoxan) was added to this therapy. At present most patients who die of PV do so as a result of complications of therapy (< 10%). Four recent studies show that sepsis and lung embolism are the main causes of death resulting from steroid use (20,30,31). This has led

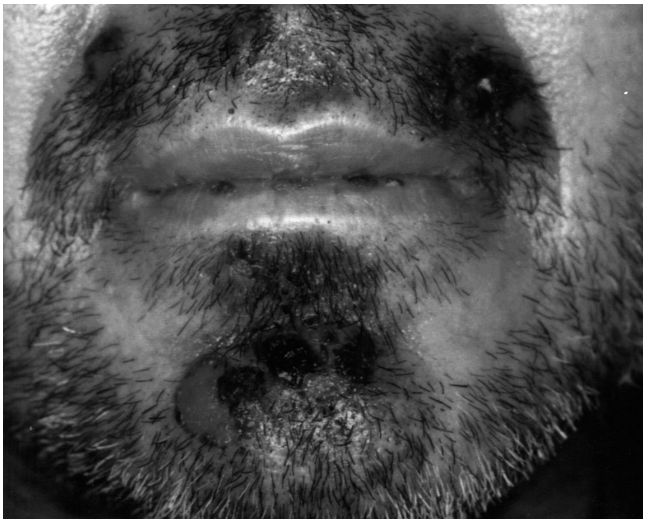

Fig. 3 Pemphigus vulgaris skin lesions on lip, chin and commissures.

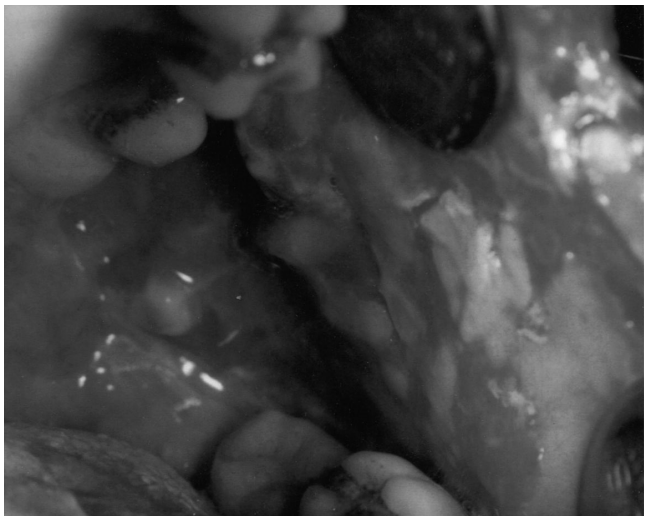

Fig. 1 Pemphigus vulgaris lesions on buccal mucosa.

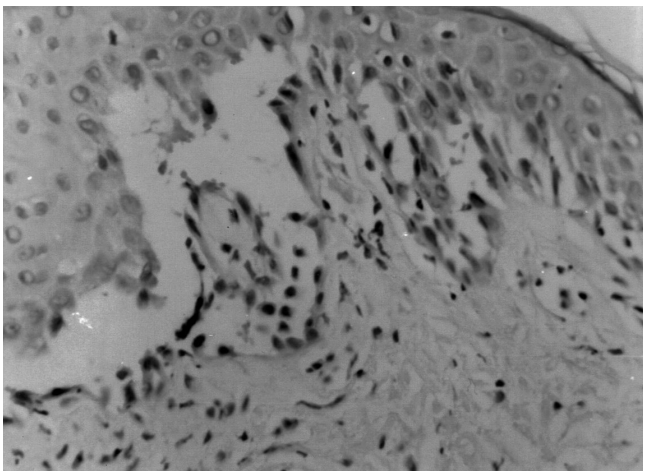

Fig. 4 Microscopic view of skin lesions in pemphigus vulgaris. (H-E × 200)

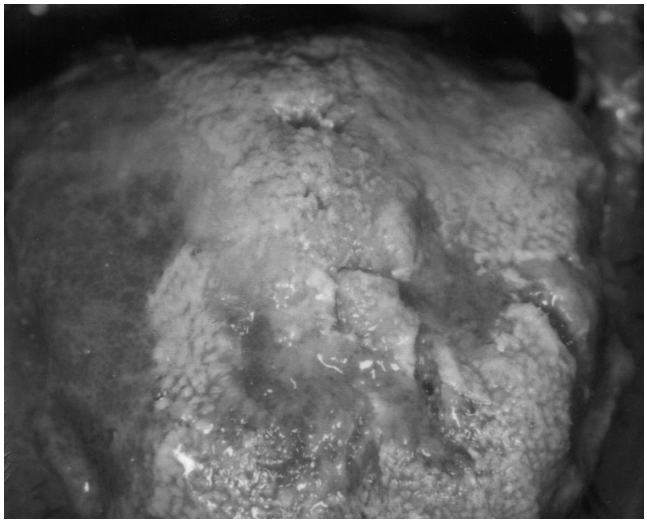

Fig. 2 Erosive lesion of tongue.

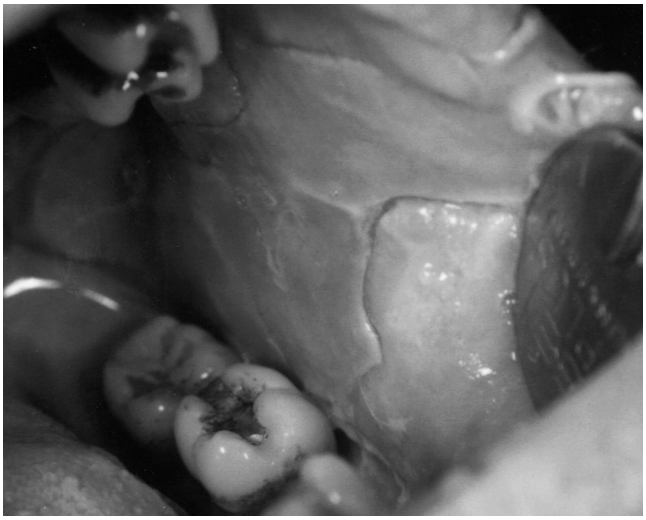

Fig. 5 Healing of oral lesions after therapy.

to a continued search for treatment strategies with low maintanence steroid dosage and adjuvant "steroid-sparing" modalities that may reduce the need for steroids (32,33). Adjuvant therapy is introduced immediately at the start of corticosteroid treatment with oral-only corticosteroids (25). In the present case, the patient died as a result of pulmonary embolism in the second year of corticosteroid therapy. This case is the reported fifth patient to have died as a result of complications of corticosteroid therapy.

PV is a chronic autoimmune mucocutanous disease that often primarily involves the oral cavity. Therefore, diagnosis of periodontal lesions is very important in facilitating early treatment of PV. Although there is no consensus regarding the initial steroid dosage needed to induce remission, it is suggested that administration of high dose corticosteroids may cause fatal complications.

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