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MANIFESTATION OF PEMPHIGUS VULGARIS IN THE OROFACIAL REGION. CASE REPORT

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A b s t r a c t

Pemphigus vulgaris is a severe disease of the skin and mucous membranes that is characterised by the formation of bullae. It is classified as an autoimmune disorder. The case of a very severe form of this disease in an 81-year-old woman is described. Typical lesions were present on the mucosa of her oral cavity and on the skin of the lower lip and several sites of her face. Clinical, histological and immunohistological findings confirmed the diagnosis of pemphigus vulgaris. The patient responded well to a combined immunosuppressive therapy with Prednison (Léčiva, Czech Republic) and Azamun (Wellcome Foundation, Great Britain). At 7-year follow-up she was free from complains. Her case demonstrated that, as in 70 to 90 % of the patients with this disease, the primary lesions were present on the oral mucosa many years before they manifested themselves as typical dermal signs.

K e y w o r d s

Autoimmune disease, Bullae, Mucous membrane, Pemphigus vulgaris

INTRODUCTION

The group of pemphigus diseases includes dermatological disorders characterised by formation of bullae (*1*). These diseases have been known since they were first described by Hippocrates and Galen as early as in the 4th and 3rd centuries B.C. Pemphigus vulgaris is the most serious of this group. Before steroids were introduced in its treatment, the disease was fatal. Some of the achievements that have facilitated the establishment of diagnosis in this complex disease should be mentioned here. They are, for instance, the description of an acantholytic process (*2*), introduction of cytodiagnostics (*3*) and assays of autoantibodies against intercellular substances in pemphigus or the basal membrane in pemphigoid (*4, 5, 6*). The antibody assays, in particular, have enabled physicians to identify several aetiopathogenetic factors and to better differentiate among various clinical presentations. Further progress in making the diagnosis more accurate was achieved with the advent of immunofluorescence methods.

This paper is concerned with pemphigus vulgaris, a disease known all over the world, which afflicts men and women alike, although some data have indicated that the proportion of female patients is larger (*7*). Some reports have also shown that pemphigus occurs more frequently in the Jewish race, especially in carriers of the HL–A 10 antigenic character (*8, 9*). The onset of disease is usually between 40 and 60 years (*10*) and only occasionally in childhood. Therefore, this diagnosis is rarely taken into account and paediatric patients are usually treated for erythema multiform (*11*). However, a case of pemphigus vulgaris in a 3.5-year-old child has been reported, with the diagnosis based on histopathological and immunofluorescence methods.

Pemphigus vulgaris is an autoimmune disease with an unknown cause. It produces antibodies against the membrane antigens of keratinocytes and intercellular substances; in addition, the acantholytic process results in formation of intra-epidermal bullae. In most cases (70 to 90 %), the first signs of disease appear on the oral mucosa. They can precede the main dermal symptoms by several months or years.

The principal dermal and mucosal changes involve the loss of coherence among layers of keratinocytes (*12*). This is manifested, in the early stages of disease, by the wrinkling of apparently healthy skin under pressure and subsequent exposure of a madescent lesion, which is called a direct Nikolski's sign. The primary lesion is a thin-walled bulla, several centimetres in size, containing clear fluid, developing on both normal and erythematous skin. Under pressure it releases its content through the surrounding epidermis and further increases in size. This is an indirect Nikolski's sign. During the following 2 to 3 days, the content turns opaque and the bulla raptures leaving a raw, painful patch that covers with a crust producing an unpleasant sweetish odour. The surrounding tissue becomes infected and the condition is complicated by development of impetigo. Healing is very slow but no scars will remain.

On the oral mucosa, bullae filled with fluid are also present but no inflammation develops. When the epithelial wall of the bulla raptures and becomes detached, a flat painful lesion arises. Lesions are either uncovered or covered with whitish fibrin pellicles penetrated with leukocytal detritus. The desmosomal coherence of epithelial cells is damaged by an autoimmune reaction and the epithelial function becomes insufficient. Pressure on the mucosa produces a bulla similar to that on the skin, which is also called Nikolski's sign. In some cases, the lesions have an atypical appearance and a chronic course, which may postpone the definite diagnosis of pemphigus. In other cases, oral lesions show clinical and morphological features of aphthae. They may appear at any site of the oral cavity, especially in areas where the mucosa is strongly traumatised and mechanically strained, for instance, when the dentition is defective or a denture does not fit properly. Occasionally, pemphigus vulgaris presents as flat erosions

that persist for a long time and may be taken for denture sores. The other mucosae covered by pavement epithelium, e.g., oropharyngeal, genital or conjunctival mucosae, can also be affected. Increased salivation and problems with chewing and swallowing are the major subjective complaints. The latter may cause that the patient loses weight and gradually becomes cachectic.

CASE REPORT AND METHODS

An 81-year-old woman with a severe form of stomatitis was seen at the periodontological ward of the 2nd Department of Stomatology in Brno in May 1995. She presented with numerous erosions on the palate, buccal mucosa and tongue. Her tongue was oedematous and she complained of increased salivation and difficult swallowing. She had extensive haemorrhagic crusts on her lower lip and the skin bellow it (*Fig. 1*). Crusts were also found on the skin of her chin (*Fig. 2*), on her temples and scalp, the genitalia and the big right toe. Her medical history showed that the disease first manifested in March 1994. She was admitted to the Department of Infectious Diseases and the diagnosis of aphthous stomatitis was made. She was treated with Modimunal and, after her condition had improved, was discharged to home care in April 1994 with the diagnosis of recurrent aphthous stomatitis. The disease exacerbated in May 1995 and she was admitted to the Department of Stomatology at St. Anne's Teaching Hospital. The diagnosis of pemphigus vulgaris was suspected and subsequently confirmed by histological and immunohistological examinations (*Figs. 3, 4*). A combined immunosuppressive therapy with Prednison (Léčiva, Czech Republic) and Azamun (Wellcome Fnd. Great Britain) was started. Dermal lesions were treated by applying compresses with the Jarisch solution and 10 % vaseline, later with Triamcinolon in the form of either lotion or cream. The general state of the patient gradually improved, the crusts exfoliated and mucosal lesions healed. She was converted to a low maintenance dose of prednisone. At 7-year follow-up she had no signs of disease recurrence.

DISCUSSION

The aetiology of pemphigus vulgaris is still unknown although the disease has raised much concern (*13, 14*). The pemphigus-group diseases are characterised by the production of autoantibodies against intercellular substances and, therefore, classified as autoimmune diseases (*15*). The presence of a viral infection may also be involved in autoantibody production (*16*). When the disease is initiated by exogenous substances, such as medication, it is called induced pemphigus (*17*). *Tsankov et al*. described the development of intra-oral pemphigus after exposure to the pesticide phosphamide in aerosol (*18*).

Acantholysis, the loss of coherence of epidermal cells and their subsequent detachment, is the main histological finding. Light microscopy observations show that this process starts by the development of oedema among keratinocytes situated above the stratum basale**.** In the next stage, a suprabasal crevice develops that widens to give rise to a bulla. In cellular material scraped from the base and sides of a bulla, typical acantholytic cells can be found by cytological examination (Tzank test). Immunofluorescence methods are used to detect IgG antibodies in the intercellular space of the epidermis or epithelium and circulating antibodies in serum.

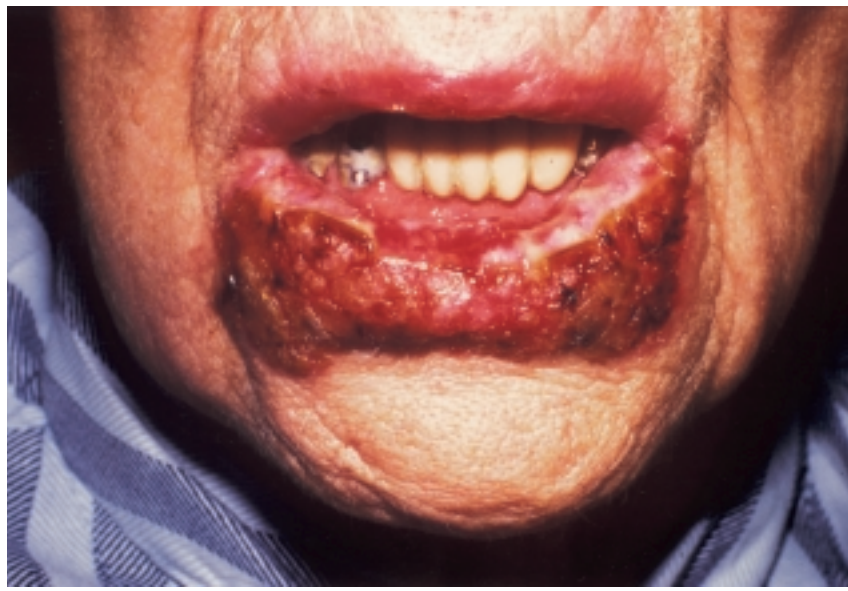

Fig. 1
Swollen lower lip with numerous lesions and haemorrhagic crusts.

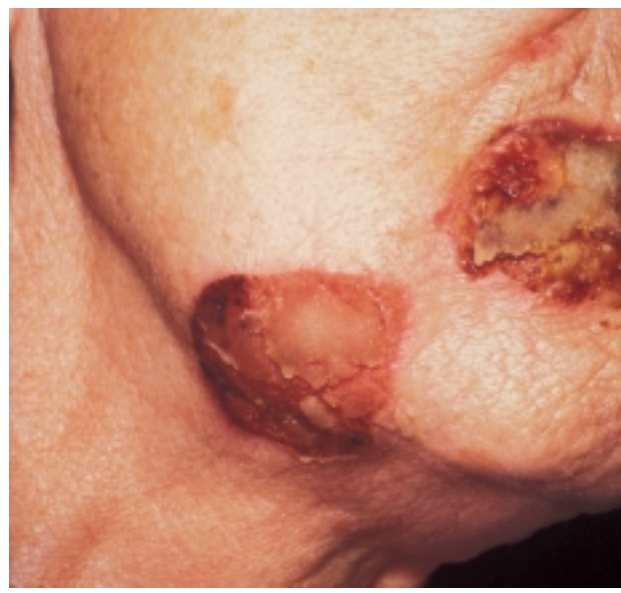

Fig. 2
Sharply demarcated lesion with a haemorrhagic crust on the chin skin.

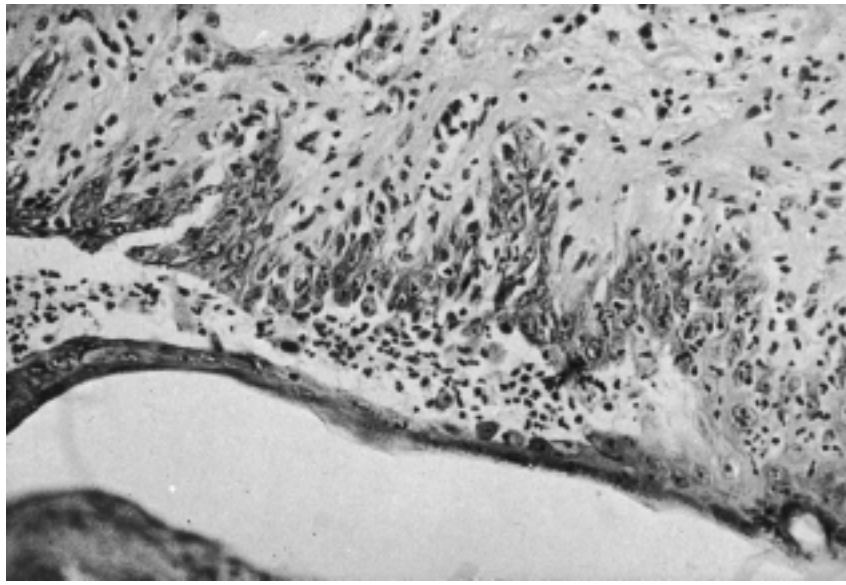

Fig. 3
Histological appearance of a bulla in the lower stratum of epidermis, suprabasally. Haematoxylin-eosin; magnification, x 63.

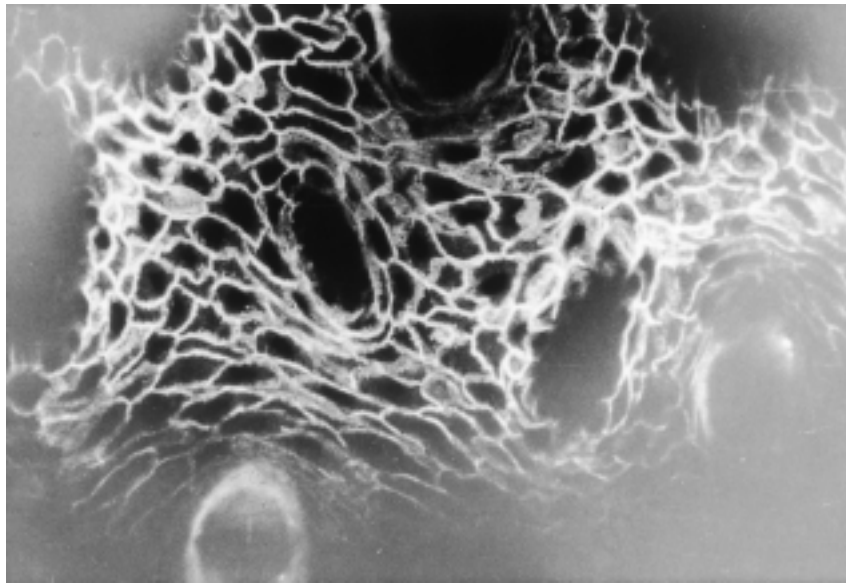

Fig. 4
IgG antibodies on the surfaces of epidermal cells. Direct immunofluorescence staining. Magnification, x 160.

In differential diagnosis of pemphigus vulgaris, other dermatological diseases associated with large bullae on the oral mucosa should be discriminated. One of them is dermatitis herpetiformis, in which lesions are occasional and not too prominent (*19*) and are manifested as erythemas, 1 to 3 cm in size, that infiltrate the palate and buccal mucosa. Aphthae-like lesions occur on the lip mucosa. However, these oral signs develop at a later stage of the disease, usually several months or years after the appearance of dermatological lesions (*20*).

Pemphigoid, a bullous dermatosis of autoimmune origin which does not occur so often, should be differentiated from pemphigus vulgaris. It may accompany, as a facultative paraneoplastic dermatosis, an underlying malignant disease. The oral mucosa is affected in about every fifth patient. Oral lesions do not precede dermatological symptoms. The bullae on the mucosa are smaller, their duration is short and remaining erosions heal relatively fast without scars. Oral signs are nearly always missing in other bullous diseases such as pemphigus erythematosus, pemphigus folliaceus or pemphigus benignus familiaris chronicus Hailey, which is important for differential diagnosis.

The therapy of pemphigus vulgaris is based on systemic corticosteroids. The starting dose is high; a total oral dose of 100–200 mg Prednison is administered daily until subsidence of clinical signs. This dose can gradually be decreased to a maintenance level of 40 to 50 mg daily. Topical application of corticoids is effective if small, isolated areas of the oral mucosa are involved. The acute phase of pemphigus is associated with changes in gastric mucosa and this condition is further aggravated by ingestion of corticosteroids. At present, administration of azathioprin (Azamun or Imuran), which is added to achieve a decrease in antibody production, permits a lower dose of corticosteroids. The combined use of these drugs has recently improved the prognosis of pemphigus; in some patients it may even be possible to discontinue corticosteroid therapy.

It can be concluded that, although great progress has been made in the understanding of bullous diseases of the pemphigus group, still much remains to be elucidated, including the disease aetiology. The fact that the proportion of the general population suffering from various forms of immunodeficiency has recently dramatically increased warrants further thorough research in this field.

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MANIFESTACE PEMPHIGUS VULGARIS V OROFACIÁLNÍ OBLASTI

S o u h r n

Pemphigus vulgaris je kožní onemocnění, které se řadí do skupiny imunodermatóz. Vyznačuje se tvorbou intradermálních puchýřů na kůži nebo intraepiteliálních lézí na sliznicích. V kazuistice je popsán případ těžké formy onemocnění u 81-leté pacientky s výrazným postižením sliznice dutiny ústní, retní červeně a kůže obličeje. Diagnóza byla stanovena na základě klinických příznaků a histologického a imunohistologického vyšetření. Případ potvrdil, že se iniciální projevy onemocnění objeví primárně na sliznici dutiny ústní a mohou o měsíce či léta předcházet výsevu typických kožních morf, jak je tomu u 70–90% případů tohoto onemocnění.

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