



## Pemphigus vulgaris in adolescence: case report

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### Abstract

*Pemphigus vulgaris is an uncommon mucocutaneous disease caused by autoantibodies against desmosomal antigens. It affects mainly middle-aged adults, and juvenile cases are rare. The authors present a case of pemphigus vulgaris in adolescence and review the literature. A 16-year-old girl showed oral and cutaneous lesions suggestive of pemphigus vulgaris. Histopathology and direct immunofluorescence of the oral mucosa confirmed the diagnosis and systemic steroid therapy was efficient in controlling the disease. The recognition of the oral lesions of pemphigus by the clinician, its early diagnosis, and prompt therapy are essential for a favorable prognosis. (Pediatr Dent 22:159-162, 2000)*

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.<sup>1</sup> There are several forms of pemphigus, of which pemphigus vulgaris (PV) is the most common, with acantholysis in the suprabasal layer giving rise to bulla that rapidly rupture, leaving extensive erosions and ulceration. PV antigen is a 130 kD glycoprotein, similar to desmoglein 3, which is associated to plakoglobin, a cytoplasmic plaque protein.<sup>1-3</sup> PV antigen has recently been cloned and shown to be a member of the cadherin family molecules.<sup>1-3</sup>

Oral lesions are the first sign of the disease in up to 50% of the cases, being present in almost 90% of the patients.<sup>2,4,5</sup> Skin and other mucosal surfaces are affected in almost 60% and 15% of the cases, respectively.<sup>2,4,5</sup> Usually, skin and oral mucosa are involved, but in cases confined to the mouth, diagnosis may be delayed because the lesions are unspecific.<sup>5</sup> There are no evidences that PV can be separated in types that preferentially affect the mucosa or the skin. Pemphigus foliaceus, erythematosus, and vegetans almost exclusively affect the skin, and the preference of PV for the mouth must be related to the type of antigen involved and the affinity of the antibodies.<sup>1</sup> PV cannot be cured, and because of its clinical course and the serious side effects of the treatment, diagnosis should be made as early as possible.<sup>2,5,6</sup>

PV affects mainly middle-aged adults in the fifth or sixth decade of life, while endemic pemphigus foliaceus, common in some regions of South America, frequently affects adolescents and young adults.<sup>4-10</sup> The literature data indicates that in adult PV predominates in females, although the male/

female ratio is not well determined. Recently Scully and coworkers<sup>5</sup> reported 55 cases of PV with a mean age of 50 and a male:female ratio of 1:1.5. It seems that there are some geographical differences in the age of involvement, as shown in a comparative study between English and Indian groups with PV in the latter the patients were younger.<sup>10</sup> Nevertheless, there are cases of PV described in children and adolescents.<sup>11</sup> We report a case of mucocutaneous PV in a Brazilian 16-year-old girl, and review the literature of its involvement in children and adolescents.

### Case report

A 16-year-old girl was referred to the Department of Oral Diagnosis, School of Dentistry of Piracicaba, University of Campinas, for evaluation of a five-month history of painful oral ulcers, causing dysphagia. The patient reported that the lesions first appeared in the oral cavity, followed by cutaneous involvement. She also reported a 16 kg weight loss since the beginning of the symptoms and previous treatments without improvement. Personal and family medical histories were uneventful and laboratory tests showed mild leukocytosis, relative and absolute eosinophilia, and increased hemesedimentation rate.

Clinical examination of the skin showed several erythematous, irregularly-shaped, coalescent ulcers on the back (Fig 1). Skin blisters were not observed. There was also bilateral inflam-



Fig 1. Pemphigus vulgaris on the skin of a 16-year-old girl. Erythematous lesions coalesced on the back of the trunk.

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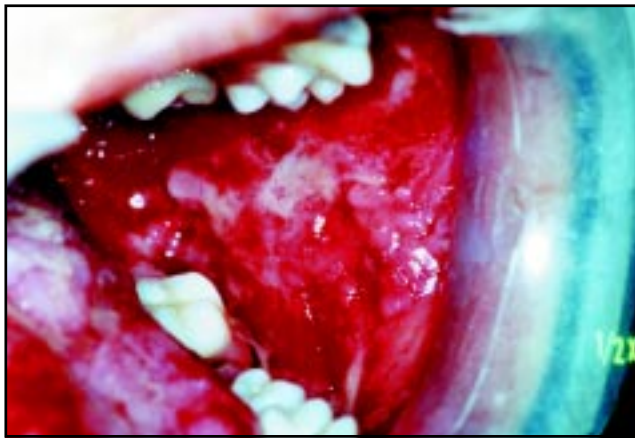


Fig 2. Ulcerated lesions of pemphigus vulgaris in the buccal mucosa.

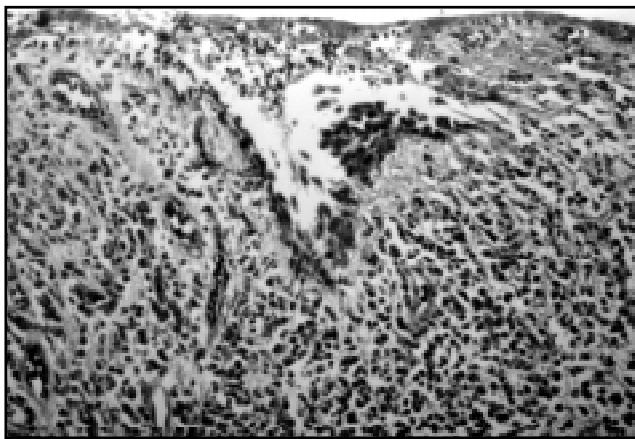


Fig 3. Biopsy of the buccal mucosa. Detachment of the epithelium, with some keratinocytes still adhered to the basal lamina, and intense inflammatory infiltrate in the subjacent connective tissue (HE, 200X).

matory submandibular lymphadenopathy. The mouth presented multiple atrophic, erosive, and desquamative lesions involving the lips, buccal mucosa, soft palate, tongue, and buccal gingiva (Fig 2).

The clinical differential diagnoses were erythema multiforme and pemphigus vulgaris. Biopsies were taken from the buccal mucosa, under local anesthesia, and processed routinely for HE stain and direct immunofluorescence analysis. The microscopical aspects were of pemphigus vulgaris. The specimen showed areas of ulceration with intense chronic inflammatory infiltrate and free rounded-shaped keratinocytes on the surface. Suprabasilar clefts were seen in some regions, with basal cell adhered to the subjacent connective tissue (Fig 3). Direct immunofluorescence analysis showed deposition of IgG and C3 (SIGMA Chemical Co., St. Louis, MO, USA) in an intercellular pattern. Although the histopathological aspects were typical of PV, IgG, and C3 positivity confirmed the diagnosis.

The patient was treated with systemic prednisone 40 mg/day, gradually reduced and tapered to 5 mg/day. The disease showed a favorable course, with only mild lesions on the buccal mucosa one month later. When steroid therapy was stopped, lowered to 3 mg/day or used topically, symptomatic lesions appeared mainly on the buccal mucosa. The patient is under dental and medical control on prednisone 5 mg daily,

without oral and cutaneous lesions. Once she presented with ungueal mycosis that was promptly treated with topical ketoconazol.

## Discussion

Epidemiological reports consider that 1-10% of the cases of PV affect patients in the first two decades of life.<sup>4,7,12,13</sup> Therefore, PV is very rare in juvenile patients, and Fig 4 shows the age distribution of 70 cases described in the last 45 years in the literature. Most of the cases occurred in the second decade of life, with a slight female predominance.<sup>5,7,11,12,14-17</sup>

Others forms of pemphigus as foliaceus, erythematosus, vegetans, paraneoplastic, and drug-induced were also reported in patients under 18 years of age.<sup>18-27</sup> PV-affecting neonates usually have a self-limited course, as it is caused by transplacental passage of maternal IgG, with sporadic episodes of severe course or death.<sup>28</sup> The relation between PV and other autoimmune diseases has been also reported in this age group.<sup>29,30</sup>

It is controversial if PV has a juvenile counterpart. Terminology in this younger group includes childhood PV, juvenile PV, prepubertal PV, pediatric PV, and adolescent PV.<sup>11,12,31</sup> The course of the disease in this age group is similar to the course in adults, usually mild and chronic. We probably are dealing with the same disease, just showing a difference in the age of onset. There are suggestions that PV in adolescents can be more severe, with acute and aggressive evolution eventually culminating to death.<sup>7,11,32</sup>

The majority of cases in youngsters, including the one reported here, exhibit mucocutaneous involvement,<sup>25,30,33</sup> and in several cases the initial lesions were in the mouth.<sup>29,34,35</sup> The condition was eventually restricted to the oral cavity, and other mucosae, including nasal, conjunctival, genital, laryngeal, and esophageal, were involved in some cases.<sup>12,29,30</sup> As in adults, the oral lesions were commonly widespread, affecting mainly the tongue, buccal mucosa, soft palate, lips, and gingiva.<sup>12</sup> The trunk, extremities, face, neck, hands, feet, scalp, abdomen, and nails were the main cutaneous sites of involvement.<sup>11</sup>

Although uncommon, PV must be considered in the differential diagnosis of mucocutaneous blistering diseases in juvenile patients, which allows its early diagnosis and prompt therapy before mucocutaneous spreading, leading to a more favorable prognosis.<sup>2,4,7,11,36,37</sup> In our case, the patient had symptoms initially in the mouth for five months before effective therapy was started, and in the meantime, skin lesions developed. It is common for patients to consider the oral lesions as aphthae or traumatic ulcers, delaying diagnosis and treatment. It seems there is a tendency for symptoms before diagnosis to be longer for men, but the period can range from three weeks up to three to four years.<sup>5</sup> In youngsters, the differential diagnosis include primary herpes, erosive lichen planus, erythema multiforme, Stevens-Johnson syndrome, bullous impetigo, candidosis, and aphthous stomatitis.<sup>18,34</sup> Hailey-Hailey and Darier's disease, although very rare, should be ruled out.

Conventional histopathology with suprabasilar cleft, acantholysis and intra-epithelial bulla, and direct immunofluorescence, with intercellular deposition of IgG and C3, are routine procedures to diagnose PV also in this age group.<sup>18</sup> IgG and C3 intercellular positivity are present in 90% and 40% of the cases of PV, respectively.<sup>4</sup> The damage to the keratinocyte-keratinocyte adhesion could be mediated

by antibody and complement deposition. Cytological examination and indirect immunofluorescence were also reported as diagnostic tools. It is controversial to consider if indirect immunofluorescence should be used as a parameter to monitor disease activity.<sup>18</sup> Based on clinical, histopathological, and immunofluorescence data, the diagnosis in our case was PV, because the patient had no family history, indication of drug use, or presence of concomitant neoplasia.

Treatment of PV in this age group, as in adults, is still empirical and based in systemic corticosteroids.<sup>29,38</sup> Some cases are more resistant to treatment and death can occur as a consequence of the disease or from side effects of the drugs used. The main side effect and cause of death is infection, particularly during the first months of treatment, when high doses of corticosteroids are required. Other common side effects are adrenal suppression, candidosis, hypertension, and tiredness.<sup>14</sup> Diabetes that developed before diagnosis or during the treatment of pemphigus can increase morbidity and probably mortality.<sup>39</sup> The case reported here had a mild course, although the patient is still maintained with prednisone 5 mg/day after four years of diagnosis. The only side effect up to now was an ungueal candidosis, promptly treated. When the dose was tapered below 5 mg/day, painful ulcers in the buccal mucosa were the initial symptom of recurrence. Adjuvant therapy was not used, although azathioprine, dapson, methotrexate, tetracycline, gold salts, cyclophosphamide, and cyclosporine can be useful in many cases.<sup>5,26,36,40,41</sup> Nevertheless, they can also induce side effects, and the benefits must be better evaluated.<sup>41</sup> Immunoabsorption was also used as treatment of PV in this age group.<sup>42</sup> It is considered that pemphigus cannot be cured, and most of the cases respond well to current treatment, although flare-ups are common. Some cases show complete remission for long periods, as reported by Mourellou and coworkers<sup>39</sup> in 10% of patients with PV.

The clinician should include PV in the differential diagnosis of oral mucosal ulceration even in juvenile patients. Biopsy specimens from intraoral bulla or lesional and perilesional mucosa are essential for diagnosis using HE stain, which can be confirmed by direct immunofluorescence. Patients with oral PV should be referred for medical evaluation and management. The dentist has an important role helping to monitor the response of the oral lesions and possible side effects of the immunosuppressive treatment as candidosis.

In summary, there are about 70 cases of PV described in children and adolescents, with variable forms of treatment and evolution. The dentist should be aware that oral involvement in PV is common and frequently the first sign or complaint of the disease. Also, PV should be considered as a possible diagnosis in the younger groups, as well. There is no standard treatment protocol for PV in teenagers or adults. There is no large series of PV described in youngsters, and more patients must be followed to better determine its clinical and biological characteristics.

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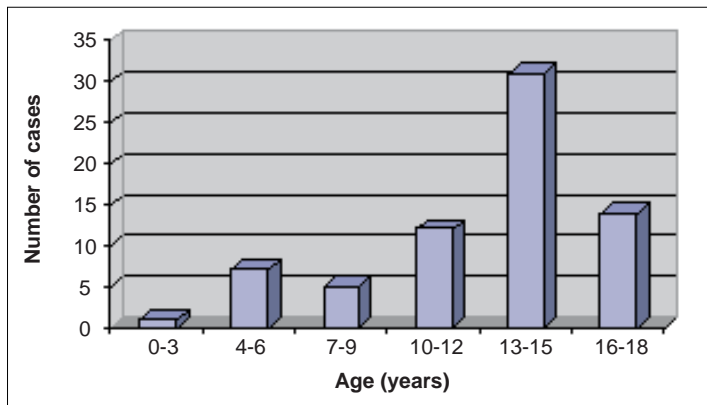


Fig 4. Age distribution of 70 cases of juvenile PV described in the literature.

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