PEMPHIGUS VULGARIS THAT WAS MISDIAGNOSED AS DIFFUSED GINGIVITIS, A CASE REPORT AND REVIEW

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ABSTRACT
Pemphigus vulgaris is the most common form of autoimmune bullous disorders that produce cutaneous and mucous membranes intraepithelial blisters. Other forms include pemphigus foliaceus, pemphigus vegetans, and pemphigus erythematosus. Pemphigus vulgaris is a life-threatening mucocutaneous disease, with a 10% mortality rate and the incidence of 1 to 5 cases among 1000,000 individuals per year. Although it can occur at any age, but a predilection in women, usually after the fourth decade of life, has been reported.

INTRODUCTION
The etiology of pemphigus vulgaris is not well understood, on the other hand, some medications such as penicillamine and captopril can produce drug-induced pemphigus, which is usually reversible after the withdrawal of the causative drug [1-5]. Blistering in the epidermal and mucous membrane starts when autoantibodies damages the cell-to-cell adhesion structures and binds to the pemphigus vulgaris antigens, which are cell-surface glycoproteins that are present in keratinocytes. These special glycoproteins are members of the desmoglein (DSG) subfamily of the cadherin superfamily of adhesion molecules that are present in desmosomes. Recently it has been reported that high levels of desmoglein 3 (Dsg3) autoantibodies are related with the severity of oral disease and elevated levels of desmoglein 1 (Dsg1) autoantibodies are associated with severity of cutaneous disease in patients with pemphigus vulgaris. [6]. Since oral lesions of pemphigus vulgaris are often the first sign of the disease and usually skin lesions appear after a year or more; it would be a great responsibility for the dentist and the chance of the patient for early diagnosis and treatment in order to reduce the morbidity rate [7-9].

Case report
A 40-year-old male patient was referred to the department of periodontology and implant dentistry of Mashhad University of medical science for periodontal treatment. Since the patient’s chief complaint was gingival bleeding, ulceration and burning sensation on the lower anterior gingiva; the first diagnosis was made as diffused plaque induced gingivitis by a general dentist. On extraoral clinical examination by the periodontist and a postgraduate student of oral and maxillofacial surgery, skin erosive lesions on scalp, cheek, umbilicus and genital area were discovered [Fig1 and 2]. For histopathologic evaluation and reliable diagnosis incisional gingival biopsy was done. Microscopic sections revealed the
presence of para-keratinized stratified squamous epithelium showing intraepithelial separation just above the basal layer and the process of acantholysis. Acantholytic cells within the blister just above the basal layer were seen. Separation of keratinocytes in the lowest part of the epithelial tissue, and projection of keratinocytes that was attached to the basement membrane into the blister cavity had produced a characteristic histologic model which is called tombstones pattern. The intraepithelial cleft showed the presence of acantholytic rounded Tzanck cells. A mild to moderate chronic inflammatory cell infiltrate was seen in the underlying connective tissue (Figure 3). Based on the above findings the diagnosis of pemphigus vulgaris was made and the patient referred to a dermatologist for inclusive treatment.

Figure 1. Photograph showing skin lesion of the cheek and scalp.

Figure 2. Photograph showing anterior mandible gingival involvement, which was misdiagnosed as diffused plaque induced gingivitis.

Figure 3. Histopathologic appearance of pemphigus vulgaris. Intraepithelial clefting with a “tombstone” pattern of the basal cells, which is attached to the basement membrane at the left picture. Acantholysis of epithelial cells and the presence of Tzanck cells are seen in the intraepithelial cleft of the right picture. (Hematoxylin and eosin stain; original magnification×40: right and×100: left)
DISCUSSION AND CONCLUSION

Pemphigus vulgaris is a rare cause of chronic ulceration of the oral mucosa. The mouth may be the only site of involvement for a year or so and this may lead to delayed diagnosis and inappropriate treatment of a potentially fatal disorder. Oral lesions of pemphigus vulgaris often extend at sites of irritation or trauma and can range from small vesicles to large bullae and ulcerations. Any part of the oral cavity can be involved, but the most prevalent sites in order are 1. Soft palate, 2. Buccal mucosa, 3. Tongue and 4. Lower labial mucosa. Gingival tissues are the least frequent sites for pemphigus vulgaris involvement; thus such lesions can be easily misdiagnosed as plaque induced gingivitis, which is a common form of gingivitis but the lesions do not disappear after scaling, root planning and routine dental plaque control. [10]. Histopathologically, the lesions of pemphigus vulgaris show intraepithelial separation, suprabasal acantholysis, clefting and blister formation. The blister cavity may contain inflammatory cells including eosinophils and rounded acantholytic cells. The bottom of the blister may be lined with intact keratinocytes, which is called “tombstone pattern” Acantholysis, that involves the separation of the epithelial cells of the lower stratum spinosum can be seen, which is characterized by the pattern of round non-polyhedral epithelial cells. The intercellular attachments are lost, and the nuclei are large and hyperchromatic. Large round keratinocyte with a hypertrophic nucleus, unclear or absent nucleoli, and abundant basophilic cytoplasm, which is called Tzanck cell can be present [11-14]. The presence of autoantibodies can be demonstrated in the oral mucosa of pemphigus patients with the use of immunofluorescence techniques. The indirect technique is less sensitive than the direct technique, and it may be negative during the early stages of the disease, particularly in its localized forms. [15].

Treatment

The main therapy for pemphigus vulgaris is systemic corticosteroids with or without the addition of other immunosuppressive agents. If the patient gets better by using corticosteroids, the dosage can be gradually reduced, but a low maintenance dosage is usually necessary to prevent or minimize the recurrence of lesions [17].

It is important for patients with oral pemphigus vulgaris to reduce oral trauma and irritation. Most favorable oral hygiene is essential with pemphigus vulgaris, because there is usually inflammation of the marginal and attached gingivae as well as of other areas of the mouth, which can be exacerbated by plaque associated gingivitis and periodontitis. Periodontal care is an important issue in the overall management of patients with pemphigus vulgaris. In addition, the fit and design of removable prosthetic appliances should receive special attention, because even slight irritation from these prostheses can cause severe inflammation with vesiculation and ulceration [8].

REFERENCES


Table 1. Histopathologic findings in muco-cutaneous lesions that may Present Clinically as pemphigus vulgaris [16, 17].

<table>
<thead>
<tr>
<th>Disease</th>
<th>Histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cicatrical pemphigoid</td>
<td>Subepithelial clefting with epithelial separation from the underlying lamina propria, leaving an intact basal layer</td>
</tr>
<tr>
<td>Bullous pemphigoid</td>
<td>Similar to cicatrical pemphigoid</td>
</tr>
<tr>
<td>Epidermolysis bullosa acquisita</td>
<td>Similar to cicatrical pemphigoid</td>
</tr>
<tr>
<td>Lichen planus</td>
<td>Hyperkeratosis, hydropic degeneration of the basal layer, and sawtooth rete pegs; lamina propria exhibits dense, bandlike infiltrate, primarily of T lymphocytes; colloid bodies are present</td>
</tr>
<tr>
<td>Chronic ulcerative stomatitis</td>
<td>Similar to erosive lichen planus; hyperkeratosis, acanthosis, basal cell layer liquefaction, subepithelial clefting, and lymphohistiocytic chronic infiltrate in a bandlike configuration</td>
</tr>
<tr>
<td>Linear IgA disease</td>
<td>Similar to erosive lichen planus</td>
</tr>
<tr>
<td>Dermatitis herpetiformis</td>
<td>Collection of neutrophils, eosinophils, and fibrin in the connective tissue papillae</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>Hyperkeratosis, basal cell degeneration, epithelial atrophy, and perivascular inflammation</td>
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