Adolescent Oral Pemphigoid: Report of A Case and Review of Literature

C Sumathy, BG Harsha Vardhan, Priya Ramani, A Kannan, D Koteeswaran, K Saraswathi Gopal

1Senior Lecturer, Department of Oral Medicine and Radiology, Meenakshi Ammal Dental College, Chennai, Tamil Nadu, India
2Associate Professor, Department of Oral Medicine and Radiology, Meenakshi Ammal Dental College, Chennai, Tamil Nadu, India
3Professor and Head, Department of Oral Medicine and Radiology, Meenakshi Ammal Dental College, Chennai, Tamil Nadu, India
4Professor, Department of Oral Medicine and Radiology, Meenakshi Ammal Dental College, Chennai, Tamil Nadu, India

Correspondence: BG Harsha Vardhan, Associate Professor, Department of Oral Medicine and Radiology, Meenakshi Ammal Dental College, Alapakkam Main Road, Maduravoyal, Chennai-600095, Tamil Nadu, India, e-mail: bgharshavardhan@yahoo.com

CASE REPORT

ABSTRACT

Pemphigoid is a group of bullous diseases that have a diversified morphologic presentation and affects skin, oral mucosa and other mucosal membranes alone or in combination. In the literature, the condition has been subclassified into bullous pemphigoid and cicatricial pemphigoid (Mucous membrane pemphigoid) on the basis of primary organ of involvement.

Oral pemphigoid, defined as cicatricial pemphigoid limited to the oral cavity, is a clinical subset of cicatricial pemphigoid. Like cicatricial pemphigoid, it occurs mostly in middle-aged women and it is uncommon in children under 20 years of age, with very few cases reported in the medical literature. We present a case of a 14-year-old girl with desquamative gingivitis as the only clinical presentation of this rare disease and lay emphasis on early recognition and clinical awareness.

Keywords: Oral pemphigoid, Autoimmune, Corticosteroids, Immunofluorescence, Bullous.

INTRODUCTION

Immune-mediated subepithelial blistering diseases or autoimmune subepithelial blistering disorders are a large family of skin and mucous membrane conditions which present with fairly common features as a consequence of subepithelial blistering. They include bullous pemphigoid (BP), mucous membrane pemphigoid (MMP), linear IgA disease (LAD), chronic bullous dermatosis of childhood (CBDC) and epidermolysis bullosa acquisita (EBA). Bullous pemphigoid (BP) and cicatricial pemphigoid (CP), referred to in the past as benign mucous membrane pemphigoid (BMMP), are characterized by the presence of subepidermal bullae on routine histologic analysis. Cicatricial pemphigoid MMP is an autoimmune disease characterized by chronic vesiculobullous eruptions, predominantly on mucous membrane of oral cavity, eyes, nasal cavity, pharynx, larynx, esophagus, genitalia and anus, may cause serious complications, such as blindness and stenosis of pharynx, larynx, esophagus, vaginal orifice, urethra, anus due to scar formation. The oral cavity is the most common site for cicatricial pemphigoid accounting for 83 to 100%. The oral cavity may also be frequently the site of onset and the only manifestation of disease (oral pemphigoid). Cicatricial pemphigoid occurs mostly among the elderly, with an average age of 60 and seldom occurs in individuals under 20 years. We present a case of a 14-year-old girl with soresness and edematous gingiva as the only clinical presentation of oral pemphigoid.

CASE REPORT

A 14-year-old girl reported with a history of soreness and burning sensation in the gums for the past 3 months. There were no associated symptoms and her medical history was non-contributory. Oral examination revealed generalized edema and redness in marginal and attached gingiva, predominantly in the upper, lower anteriors and right lower molar region (Fig. 1). Application of lateral pressure on the lesion caused bleeding, sloughing of tissues indicating a positive Nikolsky’s sign. A preliminary differential diagnosis was based solely on the patient’s clinical presentation which included mucous membrane pemphigoid, epidermolysis bullosa and bullous pemphigoid. Following an informed consent, a tissue specimen was taken from her upper anterior region in relation to 12, 13 for histological and immunofluorescence studies. Histological findings include infiltration of lymphocytes, plasma cells and eosinophils with subepithelial bulla and RBCs (Fig. 2). Direct immunofluorescence showed linear deposition of IgG, C3 at the mucosal submucosal junction. No deposition of IgA or IgM, fibrin or fibrinogen was detected. The patient was then referred to an ophthalmologist to rule out ocular involvement. The diagnosis of oral pemphigoid was established based on clinical, histological and immunofluorescence findings.

The patient was treated with 0.1% triamcinolone acetonide four times daily combined with 0.2% chlorhexidine mouthwash twice a day. With improving clinical signs and symptoms, therapy was gradually reduced and eventually discontinued.
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6 months later. On follow-up visits, there were no recurrences for the next 12-month period.

DISCUSSION

Cicatricial pemphigoid is a disease that primarily affects the middle aged occasionally children and the elderly with a male to female ratio of 2:1. Its name is derived from the latin word cicatrix meaning ‘scar’.

The true incidence of cicatricial pemphigoid is unclear. Data in the medical literature suggests that it is seven times less common than bullous pemphigoid. MMP is predominantly a disease of women with a mean age at onset of 51 to 62 years (Shklar and McCarthy 1959; Hardy et al 1971; Ahmed and Hombal, 1986; Silverman et al 1986). Children are rarely affected, to date less than 20 cases have been reported, presenting primarily as oral mucosal lesions (Moy et al 1986; Wojnarowska et al 1988; Slavounou and Laskaris 1990; Cheng et al 2001; Musa et al 2002; Kuenzli et al 2004).

Oral lesions of pemphigoid most commonly manifest themselves as desquamative gingivitis of the marginal gingiva and the attached gingiva. Patient often presents with complaints of bleeding, pain, dysphagia and peeling of the mucosa. Desquamation is likely to result from frequent exposure of the oral mucosa to inflammation as well as trauma from mastication; it may present clinically as white areas of necrotic slough at the margins of the erythematous zones and may be elicited by palpation with a finger, mouth mirror or periodontal probe.

The pathophysiologic mechanism of MMP is complex and is not yet completely understood. There is clearly a defect in the immune regulation involving the formation of antibodies, usually of the IgG class, directed against normal components (antigens) of the basement membrane zone (BMZ). This interaction triggers a complicated web of immunologic events resulting in the expression of inflammatory mediators that induce migration of lymphocytes, eosinophils, neutrophils and mast cells to the BMZ. The separation of epithelium from the underlying tissue within the BMZ may be the result of direct cytotoxic action or the effect of lysosomal proteolytic enzymes. Fibroblasts are also activated secondary to the production of inflammatory cytokines. The mechanism is further complicated by the inclusion of molecules, such as RANTES, interleukins, tumor necrosis factor alpha (TNF-α), TNF-β, interferon gamma (IFN-γ) and more recently identified molecules, such as etoxin (Verdolini and Cerio 2003). The collagen produced may lead to cicatrization of the eye or mucous membranes. This process is of particular importance in MMP affecting the eyes, where fibrosis or subsequent cicatrization can cause profound tear insufficiency, symblepharon formation, trichiasis, keratinization of the cornea and several other defects.

To have a better understanding of this process several components to the BMZ can be schematically divided into keratinocytes, lamina lucida, lamina densa and sublamina densa. Within this zone, hemidesmosomes anchor keratinocytes to the basement membrane. Components of the hemidesmosomes are proteins, which include the bullous pemphigoid antigen 1 (BPAG 1), a 230-kDa protein, the bullous pemphigoid antigen 2 (BPAG 2), a 180-kDa protein, BP230, the α-6 β-4 integrin, plectin and laminin-5, also called epiligrin. Oral blisters or bullae may occasionally be seen although they tend to rupture rather quickly as a result of mechanical and traumatic forces. Other regions of the oral cavity that may be involved are the tongue, palate, buccal mucosa and floor of the mouth. A significant feature of oral lesions is their ability to heal without scarring.
Commonly, patients with MMP have oral and especially gingival lesions (Fine and Weathers 1980; Laskaris et al 1982; Silverman et al 1986; Gallagher and Shklar 1987). The MMP is one of the main causes of desquamative gingivitis (Laskaris et al 1982; Silverman et al 1986; Scully and Porter 1997; Stooples et al 2003b) and indeed desquamative gingivitis is the main oral feature of MMP (Gallagher and Shklar 1987; Venning et al 1988; Stooples et al 2003b) and may be the presenting feature (Vaillant et al 1990; Stooples et al 2003b). Chronic soreness is common, especially worse when eating acidic foods. The clinical appearance is of gingival erythema and loss of stippling extending apically from the gingival margins to the alveolar mucosa. The desquamation may vary from mild almost insignificant small patches to widespread erythema with a glazed appearance.1

A differential diagnosis of MMP may include pemphigus vulgaris, and bullous SLE (Scott and Ahmed 1998) as well as pemphigoid subtypes and other immune-mediated subepithelial blistering disease (IMSEBD).1 Routine histopathology of a properly obtained specimen will demonstrate sub-basilar cleavage. The most appropriate area to biopsy is not erosion, which will show loss of epithelium, but a vesicle or perilesional tissue. Some suggest inducing a vesicle by rubbing the mucosa first before taking a biopsy (Siegel and Balciunas 1994). It is better to avoid gingival biopsy since the chronic inflammation of gingivitis may obscure the histological details. Also obtaining a diagnostic gingival biopsy can be technically challenging and result in a periodontal defect (Siegel and Anhalt 1993).1

The MMP is histologically characterized by junctional separation at the level of the basement membrane giving rise to a subbasilar split as in other forms of pemphigoid. Classical histopathological features include a subepithelial split with a chronic inflammatory infiltrate containing eosinophils, lymphocytes and neutrophils as well in the lamina propria. However, routine biopsy of a patient suspected of having MMP is often not enough to fully differentiate the disease from other mucocutaneous disorders.1

To further substantiate the diagnosis, direct immunofluorescence (DIF) is often helpful in making the broad diagnosis of pemphigoid, if immunostaining shows deposition of IgG and C3 in a homogenous linear manner in the BMZ along the dermoepidermal junction as demonstrated in our case.1

Essentially, all patients with MMP and CP have, on DIF in vivo bound IgG, IgA or C3, presenting as a homogenous line in the BMZ of lesional and perilesional mucosa. Deposition of C3 in the BMZ is detected in almost all patients, sometimes is the sole immunologic reactant, and is considered diagnostically significant. The DIF analysis of biopsy specimens of MMP where the epithelium is separated from the underlying connective tissue may show IgG deposits on the basal pole of the epithelial cells in an interrupted linear pattern (Siegel and Anhalt, 1993). DIF is thus useful in several ways; first a positive result confirms the diagnosis of IMSEBD. Second, DIF differentiates IgG-mediated diseases [BP, MMP, HG and acquired epidermolysis bullosa (EBA)] from IgA-mediated diseases (dermatitis herpetiformis and linear IgA disease) (Mutasim 1997).1

Similar to MMP in adults, childhood MMP are also treated with topical and systemic corticosteroid therapy, depending on severity. Immunosuppressant drugs, such as dapsone, sulphasalazine and azathioprine combined with systemic steroids have also been reported to control severe childhood cases. There is no absolutely effective agent for MMP and the prognosis among childhood varies.5,15,16

In addition to our case, literature has reported five childhood oral pemphigoid patients and it was striking to find out that all of them showed desquamative gingivitis as the only clinical manifestation. All six cases including ours have been treated successfully with corticosteroid therapy. The prognosis for childhood oral pemphigoid is good, although long-term follow-up is needed.

Hence, oral physicians could be the first healthcare professionals to recognize this rare disease. Patients with oral MMP can be a challenge to treat, especially because the condition is chronic and is associated with frequent exacerbations and remissions. In addition, with the advent of new diagnostic studies, clinicians should consider using the pathologic techniques described in this article to characterize more accurately patients diagnosed with MMP. A delay in diagnosis not only prolongs the morbidity of the patient but also delays appropriate therapy which compromises the prognosis.

Ultimately, uniformity in reporting the clinical, histopathologic and immunopathologic findings associated with all SEBDs in general will allow a better clinical definition of various subgroups of pemphigoid based on the molecular findings.

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