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Case Report Open Access

Oral Pemphigus Vulgaris: A Case which was Misdiagnosed as Stomatitis

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Abstract

Pemphigus vulgaris is a life- threatening chronic autoimmune disease characterized by the formation of intraepithelial blisters on the skin and mucous membranes. Pemphigus vulgaris initially manifests in the form of intraoral lesions which spread to other mucous membranes and the skin. The etiology of Pemphigus vulgaris is still unknown. It results from an autoimmune process in which antibodies are produced against desmoglein 1 and desmoglein 3, normal components of the cell membrane of keratinocytes. Most patients are initially misdiagnosed and improperly treated for many months or even years. General practitioners and other medical professionals must be sufficiently familiar with the clinical manifestations of pemphigus vulgaris to ensure early diagnosis and treatment, as this in turn determines the prognosis and course of the disease. We are reporting a case of oral pemphigus vulgaris, a potentially chronic dermatological condition which was misdiagnosed in its earliest stage as stomatitis.

Keywords: Pemphigus vulgaris; Oral ulceration; Demoglein; Autoimmune

Introduction

Autoimmune blistering conditions are an uncommon cause of oral mucosal ulceration. Pemphigus vulgaris (PV) is a rare disease which affects 1-5 patients per 1,000,000 populations per year with onset in the fifth or sixth decade of life [1-3]. The first manifestations of PV appear in the oral mucosa in the majority of patients, followed at a later date by cutaneous lesions. Nevertheless, it is important to diagnose this disease early and institute treatment as soon as possible, as it can lead to serious involvement of mucosal and cutaneous sites and even death.

PV has been observed more frequently in certain ethnic groups, such as Ashkenazi Jews and those of Mediterranean and Asian origin (especially Indians and Japanese) that show some genetic predisposition [4-6]. There is a fairly strong genetic background to PV with linkage to HLA class II alleles. HLA class II alleles are critical for antigen recognition by T lymphocytes. HLA class I alleles may also play a role in the development of PV [3]. However, PV can appear in individuals with different HLA types and cannot be considered a hereditary disease [7].

Etiopathogenesis

PV is caused by auto antibodies against epithelial intercellular components especially adherins and particularly desmogleins. The role of environmental factors like medicines (especially thiol containing drugs), diet (garlic) and physical and viral agents that may trigger the disease is unclear but there is genetic basis to many cases [1,3,6-9]. PV is an autoimmune blistering disease characterized by circulating pathogenic IgG antibodies produced against normal desmosomal adhesion molecules, desmoglein 3 and desmoglein 1, on the cell membrane of keratinocytes [1]. The binding of antibodies to desmoglein at mucosal or cutaneuos level gives rise to the loss of cell adhesion leading to separation of epithelial layers (acantholysis). Oral lesions are initially vesiculobullous but readily rupture, new bullae developing as older ones rupture and ulcerate. In the majority of the patients, painful mucous membrane erosions are the presenting sign of PV and may be the only sign for an average of 5 months before skin lesions develop [4]. The morbidity and mortality of PV is related to the extent of the disease, the drug dose required to eradicate lesions, the age of the patient, the antibody titre and the presence of other diseases [2,10]. Prognosis is worse in patients with extensive disease and in older patients. Before the introduction of corticosteroids 75% of patients died within the first year. Currently, less than 10% of patients die, usually due to secondary effects of the treatment [3,11,12].

Case Report

A 50-year- old woman came to a dental surgeon (Department of Oral Diagnosis and Radiology) with a 4 months history of painful oral ulceration in the cheeks and lips. The oral ulceration caused the patient considerable discomfort and significantly affected her normal oral function. The patient could not even drink water and she was on a soft diet since four months.

The patient reported that initially, she had started discomfort in the throat during the intake of fluids. She went to a physician for consultation. The physician diagnosed stomatitis and put her on Amoxicillin (625 mg), Levocetrizin and gave Xylocaine for local application. After taking the 7 days course of antibiotic, the patient could not feel any relief. The physician then referred the patient to an otorhinolaryngologist. In the meantime the patient had suffered opportunistic *Candida* infection. Candiadiasis made the condition of the patient even worse and as the patient could not take any kind of food and fluids (not even water) she had to be hospitalized for intravenous rehydration and antibiotic therapy. At this point the patient's hematology test report was normal except for a slightly increased neutrophil count (83). The otorhinolaryngologist treated the patient for oral candidiasis but the remission of mouth ulcers did not occur. Then otorhinolaryngologist asked for sputum culture and antibiotic sensitivity test. Sputum culture was positive for *Candida tropicalis* and *Streptococcus* (scanty growth). The antibiotic sensitivity pattern revealed that *Streptococcus* was resistant to Amoxicillin, Cefixime, Cefuroxime, Cefaclor, Erythromycin and Clarithromycin. *Candida tropicalis* was resistant to Clotrimazole and Fluconazole. The patient was then put on Amphotericin B and Amikacin but despite these treatments the oral ulcers worsened day by day and there was no sign of relief. By this time, the patient and her family became desperate to find a remedy as her condition deteriorated due to lack of proper food and fluids. She was taken for consultations

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to many general practitioners, otorhinolaryngologists and even an oncologist but none could diagnose the actual disease. As the patient was no longer able to maintain her oral hygiene she was then taken to a dentist. The dental surgeon immediately identified the signs and symptoms of the disease and diagnosed the case as Pemphigus vulgaris. The dental surgeon gave oral paste containing topical steroid and referred the patient to a dermatologist. Till then there were not many extra oral or skin lesions. A couple of blisters were present on the skin of the patient which the patient ignored as it was humid summer season.

A definitive diagnosis of Pemphigus vulgaris was made by the dermatologist after evaluating the skin biopsy samples. Histological findings were characterized by suprabasal acantholytic blisters, intercellular edema and disappearance of intercellular bridge in the lower epithelium. The dermatologist prescribed Methylprednisolone (Zempred 8 mg+4 mg=12 mg), Cyclophosphamide (Endoxan 50 mg), Clotrimazole (Clenorush), Rabeprazole (20 mg) and Domperidone (10 mg) (Rabical D), Xylocaine, B-complex vitamins, calcium supplements and topical steroids for one month. The dermatologist recalled the patient every month and checked her blood pressure and blood sugar levels and then repeated the same dose of medicines. The mouth ulcers healed, and in a period of two months the patient returned to her normal oral habits. The oral hygiene was checked and maintained by a dentist. The dermatologist reduced the dose of methyl prednisolone to 8 mg after 4 months of treatment. The dermatologist tried to reduce the dose of prednisolone to 6 mg after 1.5 years of treatment but the oral ulcers returned after one month. The patient was then maintained on a dose of methyl prednisolone (8 mg), calcium supplements, Rabeprazole (20 mg) and Domperidone (10 mg) (Rabical D) for the past 2.5 years.

Discussion

PV is a chronic autoimmune intraepithelial blistering disease. The lesions first appear as small asymptomatic blisters. These blisters are very thin walled and easily rupture, giving rise to painful and hemorrhagic ulcers and the erosions heal with difficulty. PV almost always affects the oral mucosa and it can be the first site of presentation of the disease in most cases (70 to 90%), before the involvement of skin and other mucosal sites like oesophagus, pharynx, larynx and genital. Oral manifestations are the sole symptoms of the disease in PV patients until cutaneous symptoms appear 2-6 months later. Even though the lesions can located anywhere within the oral cavity, they are most often found in areas subjected to frictional trauma, such as the cheek mucosa, tongue, palate and lower lip. Skin lesions occur as flaccid fluid filled blisters on sites exposed to trauma. The blisters break to form large denuded areas of skin which can prove fatal if extensive areas are involved [13,14]. In the present case, the oral lesions mainly in the tongue, palate, cheek mucosa and lower lip were the first manifestation of the disease.

The preliminary diagnosis is generally based on the oral manifestations. The presence of intraepithelial blisters, acantholysis and Tzanck cells in histological findings provide definitive diagnosis of Pemphigus vulgaris [15]. Direct immunofluorescence evaluation of the fresh lesion specimens reveal IgG or IgM and complement fragments in the intercellular space [15]. In our case the diagnosis was based on oral manifestations, skin lesions and histological findings. A biopsy of the skin was obtained. The specimen sections were stained with Hematoxylin-Eosin and the principal histological characteristics were evaluated. Direct immunofluorescence studies were not carried out due to lack of facility.

PV should be suspected in cases of persistent gingivostomatitis, persistent and multiple oral erosions or severe desquamative or erosive gingivitis. The most frequent diagnoses in cases of oral lesions are recurrent aphthous stomatitis, Behcet's disease, erythema multiforme, erosive lichen planus and oral candidiasis. ELISA for the detection of antibodies to Dsg1 and Dsg 3 can be used for diagnosis of PV [14]. Assay of serum antibody titers by indirect immunofluorescence (IIF) may also help to guide procrastination and therapy [14]. Lesions of oral mucosa in patients with low antibody titers may be controlled with mouth washes or topical creams containing corticosteroids [16]. Intralesional injection of triamcinoclone acetonide or paramethasone can be used in refractory oral lesions. The well being of patients may be improved by analgesics, a strict oral hygiene with diluted antiseptic mouth washes, and a soft diet without irritants, correct prosthetic restorations and anti-candida therapy. Traumatisations may trigger or exacerbate PV, therefore some authors recommend the prophylactic use of prednisolone (20mg/day) for 5-7 days before dental procedure involving gums [16].

The age of the patient and initial Dsg 3 antibody levels have a significant impact on the prognosis of Pemphigus vulgaris [17]. The initial aim of treatment should be to induce disease remission. This should be followed by a period of maintenance treatment using the minimum drug doses required to control disease in order to minimize their side effects [18]. Pulse therapy using Dexamethasone and Cyclophosphamide has been used for management of pemphigus in India and abroad for the past 30 years [19].

Conclusion

PV is a rare cause of chronic mouth ulcers. Oral manifestations are the sole symptoms of the disease in PV patients. Dermatological lesions usually occur 2-6 months after the appearance of oral mucosal hemorrhagic lesions. This can lead to misdiagnosis, delayed diagnosis and inappropriate treatment of a potentially fatal disorder. The management of a patient who had previously undergone treatment based on misdiagnosis and whose complaints were not relieved even after a long period of treatment by various specialists is described. The importance of the roles of dentists in early diagnosis and treatment of oral pemphigus vulgaris and the lack of awareness about oral manifestations of PV among general practitioners has been discussed.

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