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CLINICAL AND HISTOLOGICAL CHARACTERIZATION OF ORAL PEMPHIGUS LESIONS IN PATIENTS

J.A. Rizaev [1], O.S. Imamov [2], G.Sh. Toxtayev [2]

1 Samarkand State Medical University, Samarkand, Uzbekistan
2 Tashkent Medical Academy, Tashkent, Uzbekistan

ABSTRACT

Pemphigus is a rare group of life threatening mucocutaneous autoimmune blistering diseases. Frequently, oral lesions precede the cutaneous ones. This study aimed to describe clinical and histological features of oral pemphigus lesions in patients attending. In addition, the study aimed to assess the diagnostic significance of routine histolopathology along biopsy specimens in patients with oral pemphigus.

Key words: ulcer, pemphigus, mucous membrane of the mouth, topographic zones, bladder.

INTRODUCTION

Pemphigus is a group of chronic inflammatory autoimmune bullous diseases. Although rare, they are potentially life-threatening diseases that are associated with high morbidity and mortality, if not properly treated [1, 2]. The disease is associated with immunoglobulin (Ig) G and complement factor (C) 3 antibodies against intercellular adhesion structural components in the epithelium [3]. The immune reaction eventually breaks down the adhesion components and leads to epithelial cell detachment, which is clinically seen as intraepithelial blisters, erosions or ulcers in the skin and mucous membranes [4]. The underlying cause and activating mechanism that initiates the immune response is unidentified. However, both genetic and environmental factors have been postulated to play a role in the pathogenesis of pemphigus [5]. In this context, social habits like use of traditional cosmetics and smoking have been implicated [6–8].

Pemphigus has several subtypes, of which three have been associated with oral mucosal involvement; pemphigus vulgaris (PV), pemphigus foliaceus (PF),

and paraneoplastic pemphigus [9]. The first two subtypes are differing with respect to the localization of intraepithelial blisters. In pemphigus vulgaris, the blisters are located suprabasally, while in PF they are more superficially located. Paraneoplastic pemphigus, although uncommon, is associated with internal malignant neoplasia [10].

Oral lesions present as vesicles or bullae that quickly break, leaving painful erosions or ulcers with irregular borders; they most often affect buccal mucosa and gingivae and heal slowly, without scarring. In pemphigus vulgaris, the oral lesions are reported as the initial sign of the disease in 50% of patients, yet these oral lesions have the greatest resistance to efficient treatment.

Pemphigus vulgaris is the most predominant type of pemphigus, affects middle-aged adults without gender predilection [9, 11–16] and has an incidence varying from 0.76 to 32 per million inhabitants per year [17–19]. While pemphigus vulgaris is a prevailing diagnosis in the Mediterranean region, South Asia and in the Jewish population [20, 21], it is a rare disease in Northern Europe, USA, South Africa and northern region of Africa [6, 18, 19, 22–24]. Reports from Mali and South Africa have shown that pemphigus vulgaris is rare in the black ethnicity [22, 24]. The disease is associated with immunoglobulin (Ig) G and complement factor (C) 3 antibodies against intercellular adhesion structural components in the epithelium [3]. The immune reaction eventually breaks down the adhesion components and leads to epithelial cell detachment, which is clinically seen as intraepithelial blisters, erosions or ulcers in the skin and mucous membranes [4]. The underlying cause and activating mechanism that initiates the immune response is unidentified. However, both genetic and environmental factors have been postulated to play a role in the pathogenesis of pemphigus [5]. In this context, social habits like use of traditional cosmetics and smoking have been implicated [6-8]. Pemphigus has several subtypes, of which three have been associated with oral mucosal involvement; pemphigus vulgaris (PV), pemphigus foliaceus (PF), and paraneoplastic pemphigus [9]. The first two subtypes are differing with respect to the localization of intraepithelial blisters. In PV, the blisters are located suprabasally, while in PF they are more superficially located. Paraneoplastic pemphigus, although uncommon, is associated with internal malignant neoplasia [10]. Oral lesions present as vesicles or bullae that quickly break, leaving painful erosions or ulcers with irregular borders; they most often affect buccal mucosa and gingivae and heal slowly, without scarring. In PV, the oral lesions are reported as the initial sign of the disease in 50% of patients, yet these oral lesions have the greatest resistance to efficient treatment. PV is the most predominant type of pemphigus, affects middle-aged adults without gender predilection [9,11-16] and

has an incidence varying from 0.76 to 32 per million inhabitants per year [17-19]. While PV is a prevailing diagnosis in the Mediterranean region, South Asia and in the Jewish population [20,21], it is a rare disease in Northern Europe, USA, South Africa and northern region of Africa [6,18,19,22-24]. Reports from Mali and South Africa have shown that PV is rare in the black ethnicity [22,24]. Diagnosis of pemphigus is based on careful correlation of disease history and clinical findings with histopathologic characteristics. Direct immunofluorescence (DIF) on sections from a fresh frozen biopsy or indirect immunofluorescence (IIF) performed on patient's serum are important for verifying the diagnosis [25]. However, in situations where IF is difficult to perform, immunohistochemistry (IHC) on formalin-fixed tissue samples may be an alternative test to confirm the diagnosis [26].

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According to that study, oral mucosa was the second most common site of the lesion to occur after the trunk. The highest frequency of pemphigus vulgaris was found in the third decade of life [27]. Another study conducted in the same clinic in 2008, revealed a prevalence of oral pemphigus vulgaris of 2.8% among skin diseased outpatient attendees [28]. This study also showed that the frequency of oral pemphigus vulgaris among patients with skin disease with any oral mucosal lesions was 4.8%. In both studies, clinical information and conventional histological examination of biopsies using haematoxylin and eosin (H&E) staining were the only methods for diagnosing skin lesions. The pemphigus group of disorders is characterised by loss of epidermal cell cohesion (acantholysis), resulting in fragile blisters, and erosions of the skin and mucous membranes. The clinical subtypes are listed in Table 2. PV is the commonest form, account- ing for 80% of all cases. It often presents with oral ulceration, which may be extensive. In all variants, cutaneous blisters rupture easily, forming large crusted erosions, and intact blisters may not be evident. The target antigens of PV and pemphigus foliaceus (PF) antibodies include desmogleins, desmo- somal glycoproteins which are com- plexed with the desmosomal plaque protein, plakoglobin, and play an important role in cell adhesion. Heterogeneity in the composition of desmosomes at different levels in the epidermis may explain why blistering occurs at a

suprabasal level in PV, and higher in PF. Para- neoplastic pemphigus antibodies recognise multiple antigens including those derived from non-stratified epithelia, and this may represent a cross-reaction with tumour antigens. The geographical clustering of endemic Brazilian PF suggests trigger- ing by an infective agent, possibly borne by the Simulium Black Fly.

On the basis of these considerations and due to the scarce information available regarding pemphigus in populations, the present study, presenting a further analysis of the data conducted [28], aimed to describe clinical presentation of patients with oral pemphigus attending the dermatologic clinic. Given the fact that conventional histology was the only diagnostic tool in public hospitals in Sudan, the study also evaluated the diagnostic significance of combining this technique with IHC analysis of the formalin-fixed, paraffin-embedded oral biopsy specimens.

Purpose of our research Patients with confirmed disease diagnosis completed an oral examination and a personal interview. Clinical evaluations supported with histopathology were the methods of diagnosis. Location, size, and pain of oral lesions were used to measure the oral disease activity.

Research methodology. An analysis of outpatient records of patients with pemphigus who applied to the Tashkent Dermatovenerological Dispensary for three years was carried out. The following research methods were used: clinical interview, clinical examination, determination of dental status, cytological examination smear impressions on acantholytic cells from the bottom of fresh erosions, a general blood test, a biochemical blood test, a clinical urine test, and the affected areas in patients with vulgar, erythematous, foliaceous and other forms of pemphigus were studied.

Analysis and results. 19 patients were diagnosed with pemphigus vulgaris, 17 of them presented with oral manifestations. Pemphigus foliaceus was diagnosed in one patient. In pemphigus vulgaris, female: male ratio was 1.1:1.0. Buccal mucosa was the most commonly affected site. Exclusive oral lesions were detected in 18.7%. In patients who experienced both skin and oral lesion during their life time, 65% had oral mucosa as the initial site of involvement, 82.9% had skin as the primary site, and simultaneous involvement of both skin and oral mucosa was reported by 15.2%. three patients did not provide information regarding the initial site of involvement. Oral lesion activity score was higher in those who reported to live outside were outdoor workers, had lower education and belonged to Histologically, all tissues except one had suprabasal cleft and acantholytic cells.

Conclusion. Pemphigus vulgaris was the predominating subtype of pemphigus in this study. The majority of patients with pemphigus vulgaris

presented with oral lesions. Clinical and histological pictures of oral pemphigus vulgaris are in good agreement with the literature. IHC confirmed all diagnoses of pemphigus vulgaris.

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