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Mucous membrane pemphigoid: When the mouth can give a clue to the diagnosis of an esophageal stenosis of unknown origin☆

Penfigoide de mucosas: cuando la mucosa oral puede ser la clave para el diagnóstico de una estenosis esofágica de origen desconocido

Dear Editor:

Mucous membrane pemphigoid (MMP) is an uncommon heterogeneous group of autoimmune subepidermal blistering disorders which predominantly involves mucosal membranes. Diagnosis and treatment are challenging and delay may cause severe scarring and complications such as esophageal and urethral stenosis, conjunctival synechia and blindness.

An 88-year-old woman with a 9-year history of dysphagia secondary to an indeterminate esophageal stenosis, requiring several endoscopic dilatations (Fig. 1), was referred to our clinic for evaluation of oral erosions. Examination revealed erosive gingivitis, and extensive oral and genital erosions (Fig. 2). Biopsies of vulvar lesions were non-specific and direct immunofluorescence (IFD) of non-affected genital and labial mucosa were negative. Indirect immunofluorescence on salt-split skin (IIF) revealed IgG antibodies binding to the epidermal side of the blister. IIF showed IgG deposition at the basement membrane. ELISA tests were negative for anti Dg1, Dg3 and BP180 antibodies. Immunoblotting of non-affected epidermal extracts was negative for IgG: BP230, BP180, 210 kDa envoplakin, 190 kDa periplakin, Dg1 and Dg3. Immunoblotting of recombinant protein of C-terminal domain of BP180 (BP180ct) detected IgG reactivity of patient serum. A diagnosis of MMP was established and treatment with prednisone (30 mg/day) in a tapering regimen, dapsone 50 mg/day and tacrolimus in a 2 mg/liter mouth rinse formulation was initiated. Dysphagia, oral and genital erosions remitted, but the patient has developed a scarring fibrosis of the vulva with fusion of labia and urethral meatus.

Erosive esophagitis (EE) is a common finding in esophagogastroduodenoscopy (EGD) of patients with gastroesophageal reflux disease (GERD), drug-induced mucosal damage, infections, malignancies and autoimmune disorders.[1] Among autoimmune disorders, a possible underdiagnosed pathology is MMP. The frequency of esophageal involvement in MMP is between 2% and 30%, and this may be an underestimation as EGD is only performed on symptomatic patients.[2]

In patients with MMP and esophageal lesions, a mean of another 3 mucosal areas are involved, and the oral cavity is affected in 86 % of the cases.[3] Dysphagia can signal esophageal involvement, although clinically it can be difficult to distinguish it from odynophagia. For all the above-mentioned reasons, performing an EGD on every newly diagnosed patient with MMP has been suggested.[2,4] Although, EGD is not free of complications and not always available, we agreed with other authors[2–4] that it should be especially indicated in symptomatic patients or patients with involvement of several mucous membranes.

The mouth is the beginning and the most accessible portion of the digestive tract, and as EGD is performed with a transnasal videogastroscope in these patients, oral exploration may be omitted. In any patient with esophageal erosions, scarring or stenosis, the oral cavity must be clinically explored. The presence of gingivitis or erosions makes examining the anogenital area, nose, throat, eyes and skin necessary in order to rule out MMP, and to evaluate the severity of the disease.

Diagnosis and treatment of MMP can be challenging. In our patient, IIF revealed an epidermal side positivity, which is compatible with bullous pemphigoid, lichen planus pemphigoides and MMP. This finding excludes the diagnosis of acquired bullous epidermolysis, P200 pemphigoid and MMP anti-laminin 332.[5] Finally, immunoblotting was positive for BP180ct, a very specific finding of MMP.[6] On the basis of clini-

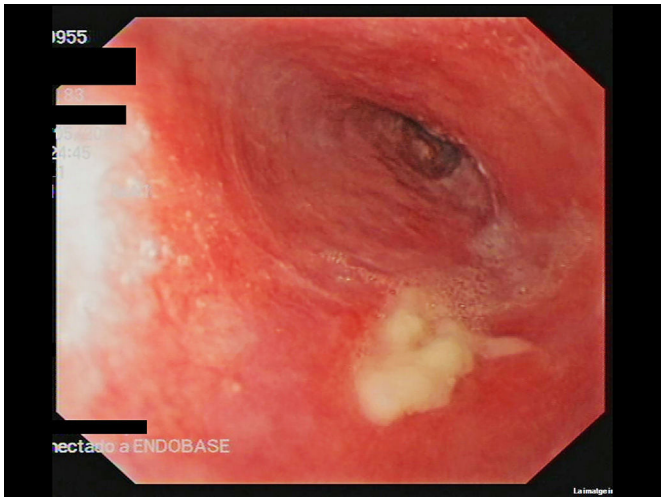

Figure 1 Esophagogastroduodenoscopy. Friable esophageal mucosa with erosions and strictures.

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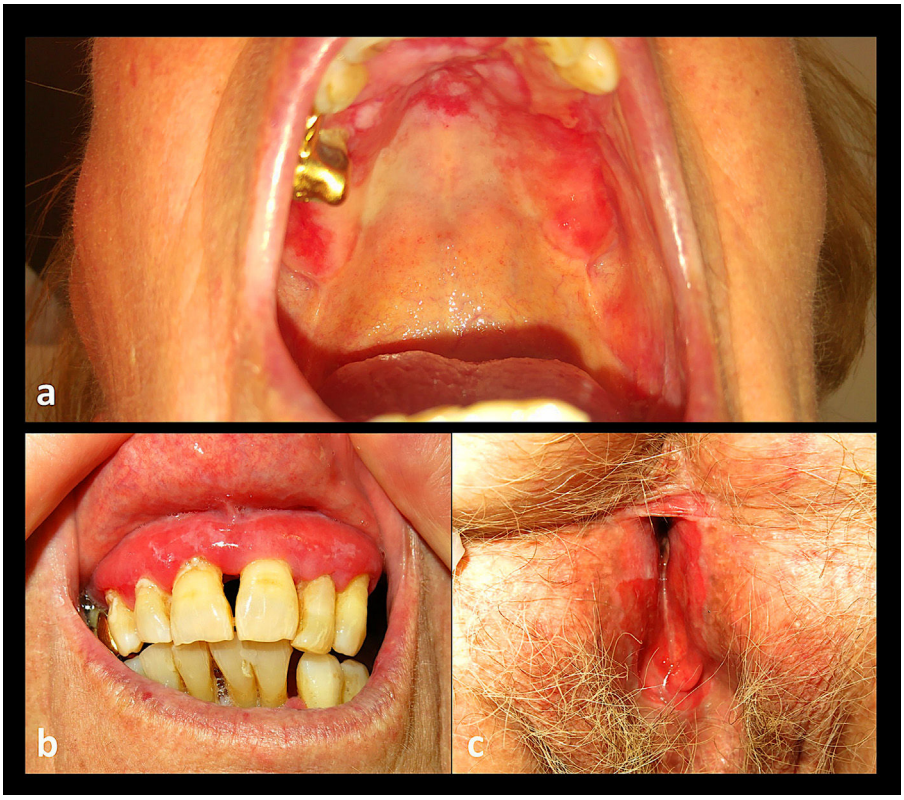

Figure 2 Clinical images. Erosions in hard palate (a) and erosive gingivitis (b) without lichenoid striae. Genital mucous erosions (c) with effacement of *labia minora* and synechiae.

cal, pathological and molecular features, a diagnosis of MMP was made.

First-line therapies for MMP include systemic corticosteroids, usually in combination with other immunosuppressive treatments.[7] Dapsone or methotrexate can be considered in mild-to-moderate stages.[8] In more severe cases, particularly in ocular involvement, cyclophosphamide has been used in monthly intravenous low-dose pulsed 500 mg with good outcomes and with better tolerance than continuous regimen.[9] Off-label use of anti-TNF and especially, anti-CD20 with or without intravenous immunoglobulins, have also been described in recalcitrant cases with satisfactory results, but frequent relapses.[7]

In conclusion, multidisciplinary management is indispensable to achieve a rapid diagnosis and a better assessment of the disease extension and severity, identifying early involvement of high-risk areas such as the larynx, eye and esophagus, which require more aggressive therapies.[10]

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Persistent Pruritic Papules AND Plaques and Flagellate Erythema as Presenting Manifestations of an Adult onset Still's Disease☆

Pápulas y placas pruriginosas persistentes y eritema flagelado como manifestaciones de una enfermedad de Still del adulto

Dear Editor:

A 21-year-old lady presented to our hospital with an 8-month history of persistent polyarthralgias, sore throat, intermittent fevers, and intense pruritic skin lesions over her face, upper back and chest, buttocks and extremities. Her past and family history was unremarkable and there was no history of any drug intake prior to onset of these symptoms. Cutaneous examination revealed erythematous and hyperpigmented, slightly scaly excoriated papules over forehead, upper back and chest and similar lesions in a linear manner over her buttocks and upper and lower extremities (Fig. 1). Laboratory investigations revealed leukocytosis (16,800/uL, 90% neutrophils) and elevated erythrocyte sedimentation rate [ESR] (40 mm/hr), ferritin (12,000 ng/mL) and C-reactive protein (8 mg/dL). Antistreptolysin titers, antinuclear antibody, rheumatoid factor, antineutrophil cytoplasmic antibodies, serum creatine phosphokinase, and aldolase were negative or within normal limits. Blood and urine cultures and other investigations for hepatitis B, C and A viruses, and chikungunya were all negative. Chest radiograph, echocardiogram, ultrasonography of abdomen and pelvis, and electromyogram did not reveal any abnormality.

Histological examination revealed microabscesses in the stratum corneum with necrotic keratinocytes and perivascular and periadnexal inflammatory infiltrate (Fig. 2). Considering her clinical and histological findings, diagnosis of adult onset Still's disease (AOSD) was made and she was treated with oral steroid (1 mg/kg/day). There was significant resolution of her cutaneous lesions and other symptoms also ameliorated at the 4 weeks of follow-up.

Discussion

Still's disease is an idiopathic systemic inflammatory disorder with seronegative arthritis. Patients with 16 years of age or older having Sill's disease are labeled as AOSD, whereas younger than 16 years are termed as Juvenile Still's disease.[1] Yamaguchi et al.[2] have led the major diagnostic criteria to diagnose AOSD, which include high spiking fevers $\geq$39 °C for at least 1 week, leukocytosis with neutrophilia, arthralgia for more than 2 weeks, and typical skin

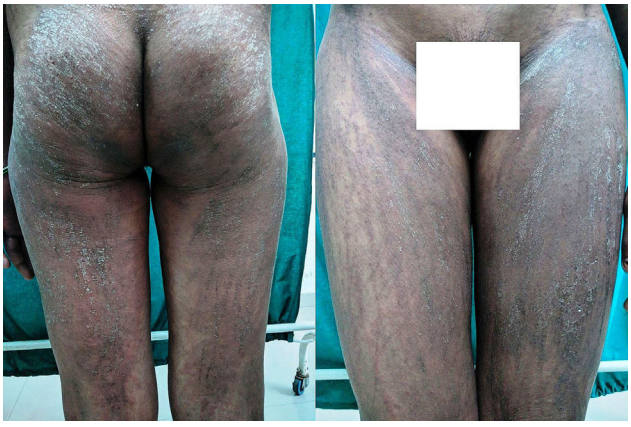

Figure 1 Flagellate erythema and linear papules with scales showing Koebner's phenomenon over buttocks (left panel) and thighs (right panel).

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