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CASE REPORT

Oesophageal pemphigoid: a rare cause of dysphagia

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Abstract
Pemphigus vulgaris (PV) is a rare autoimmune bullous disease which affects the skin and mucous membranes. Oesophageal involvement is rare and has previously been limited to case reports and case series. A recent large case series of 477 PV patients showed that 26/477 (5.4%) had symptomatic oesophageal involvement. We present the case of a 54-year-old Somalian lady with a 10-year history of cutaneous PV, currently in remission, who developed dysphagia and odynophagia and was subsequently found to have oesophageal PV involvement with multiple flaccid bullae which were positive for anti-DSG3 antibodies on in-direct immunofluorescence. She had her treatment switched from azathioprine to mycophenolate and prednisolone, leading to resolution of her symptoms.

Keywords Pemphigus vulgaris · Oesophageal · Dysphagia

Introduction

Pemphigus vulgaris (PV) is a rare autoimmune bullous disease which affects the skin and mucous membranes [1]. It has variable geographical and ethnic distribution, although it is commoner in certain ethnic groups such as Ashkenazi Jews and those of Mediterranean origin [1]. It is characterised by flaccid bullae localised on the cutaneous flexural areas along with the face and scalp. Other commonly affected mucous membranes include the oral mucosa, genitals, and conjunctiva [2]. Oesophageal involvement is rare and has previously been limited to case reports and case series [3–5]. A more recent large case series of 477 PV patients showed that 26/477 (5.4%) had symptomatic oesophageal involvement [6].

We present the case of a 54-year-old Somalian lady with a 10-year history of PV who developed dysphagia and odynophagia and was subsequently found to have oesophageal PV involvement with multiple flaccid bullae which were positive for Anti-DSG3 antibodies on in-direct immunofluorescence.

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Case report

A 54-year old Somalian lady with a 10-year history of cutaneous PV was referred to the gastroenterology department by her Consultant Dermatologist. She had previously been managed with azathioprine and prednisolone. She reported a 2-month history of dysphagia to solids, but not liquids. This was associated with odynophagia, but no reflux or dyspeptic symptoms. She reported 10 kg of weight loss over the preceding year and weighed 90 kg in clinic, with a body mass index (BMI) of 30.2. She had no abdominal pain or change in bowel habit, nor any rectal bleeding. She was on no other regular medication, had no known drug allergies. She did not smoke or consume alcohol. Physical examination revealed multiple superficial erosions on the posterior aspect of her buccal mucosa and on the left side of her tongue. There was no other cutaneous involvement.

Blood investigations including full blood count, urea and electrolytes, liver function tests and bone profile were all unremarkable. She underwent an oesophagogastroduodenoscopy (OGD) which revealed multiple upper and mid-oesophageal flaccid bullae (see Figs. 1a, b, 2). Biopsies were taken in standard formalin for H&E staining, which showed subtle changes not immediately suggestive of PV. However, on review it is clear that the biopsy comprises only detached epithelium in which there are subtle features of acantholysis in the supra-basal layers (see Figs. 3a, b, 4). In-direct immunofluorescence microscopy was performed

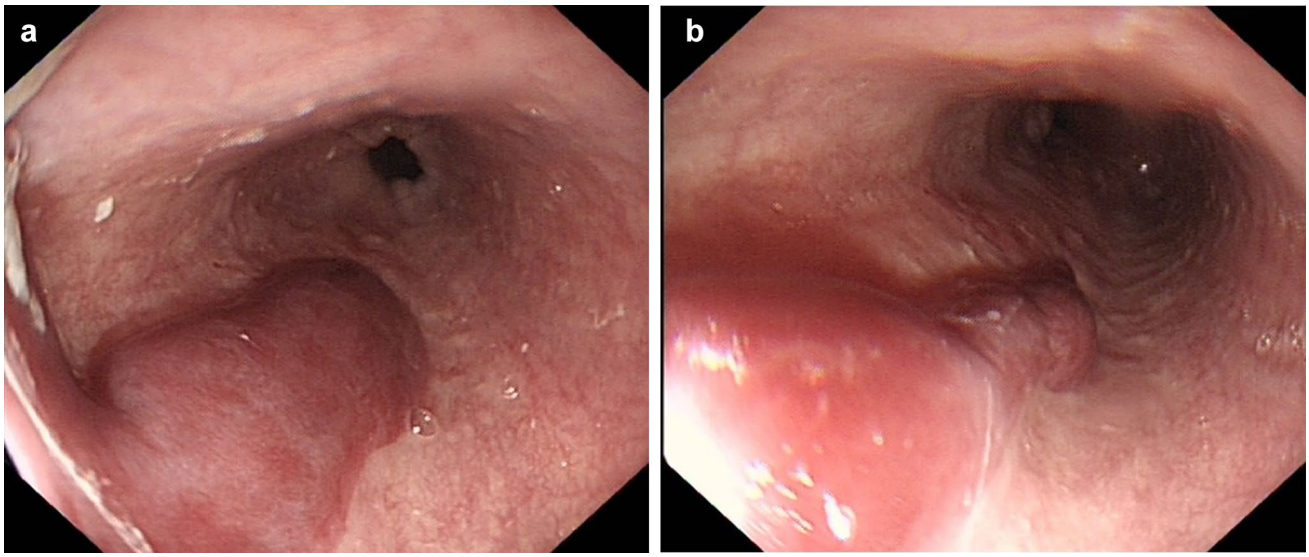

Fig. 1 **a, b** Endoscopic view of the mid-oesophagus showing flaccid bullae

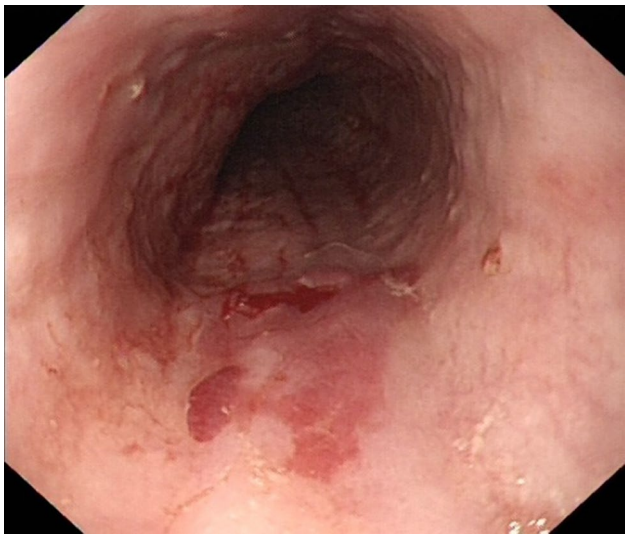

Fig. 2 Endoscopic view of the upper oesophagus, showing a ruptured bullae after it had been biopsied

on further biopsies which showed characteristic intercellular deposition of IgG and C3 within the oesophageal epithelium (see Fig. 5a, b). ELISA for pemphigus antigens showed Anti-DSG1 Antibody negative (13 U/ml) and Anti DSG3 antibody positive (128 U/ml, normal < 30 U/ml), consistent with oesophageal PV.

On discussion with her Dermatologist, her azathioprine was discontinued and she was commenced on mycophenolate, in addition to her ongoing dose of 15 mg per day of prednisolone. She was also started on omeprazole 20 mg per day as she began to develop reflux symptoms. Her symptoms improved markedly on the mycophenolate and her dysphagia resolved. She was discharged from gastroenterology back to her dermatologist.

Discussion

Oesophageal involvement of PV is rare, with only case reports and a rate of 5.4% in a large case series of PV patients [6]. Diagnosis is made on the basis of endoscopic findings in conjunction with immunofluorescent detection of pemphigus autoantibodies, which recognize cell-surface antigens of keratinocytes. These antigens are desmogleins (Dsg's), which are transmembrane desmosomal glycoproteins from the cadherin family of calcium-dependent adhesion molecules. Dsg1 is the autoantigen recognized by pemphigus foliaceus antibodies, whilst Dsg3 is specifically recognized by PV autoantibodies. However, about 50–66% of PV patients also have antibodies against Dsg1. Most patients with early PV and only mucous membrane lesions have only anti-Dsg3 antibodies, whereas most patients with later disease, involving the skin, have both anti-Dsg3 and anti-Dsg1 antibodies [7]. Given the previously known diagnosis of cutaneous pemphigus vulgaris in this patient. the endoscopic findings of multiple flaccid bullae, made the diagnosis of oesophageal pemphigoid almost certain, however, histological confirmation was still required to exclude other causes of oesophageal ecchymoma, particularly given her immunosuppressive medication.

Treatment of PV follows a similar pattern to that seen in inflammatory bowel disease. Corticosteroids at doses of 0.5–1 mg/kg/day are used to induce remission of the disease. These are then used in conjunction with immunosuppressive agents such as azathioprine, mycophenolate mofetil and

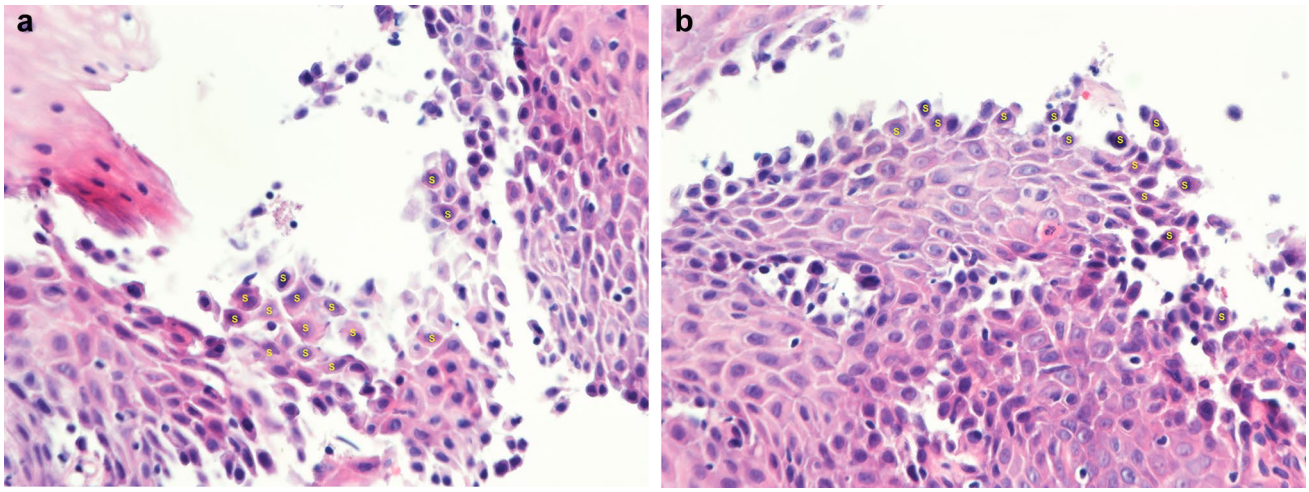

Fig. 3 **a, b** High power view shows acantholytic squamous cells in the basal part of the squamous epithelium. ×20 magnification

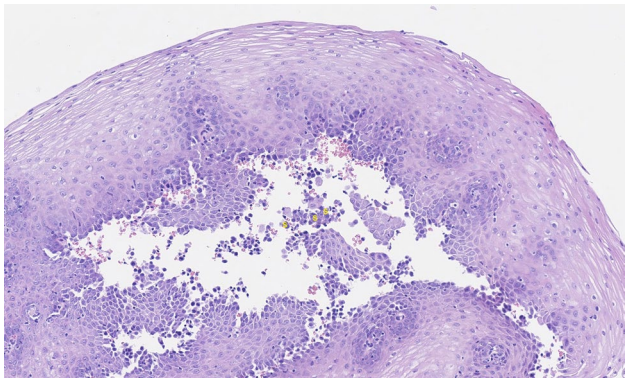

Fig. 4 Low power view shows few detached squamous cells in otherwise unremarkable epithelium

dapsone. Where these agents fail to control the disease, treatment can be escalated to biologic therapy such as rituximab or infliximab [8].

This case highlights a rare organ involvement of a rare dermatological condition, in which diagnostic histopathological features are easily overlooked. The large case series which reported oesophageal involvement in 5.4% of cases ($n=26$), reported that 17 of 26 patients had active oesophageal lesions (intact bullae, erosions and/or erythema), 15 had strictures and 12 had other lesions. Of the 17 patients, only 3 (12%) had bullous oesophageal lesions. This suggests that bullous involvement is itself a rare subset of oesophageal PV involvement.

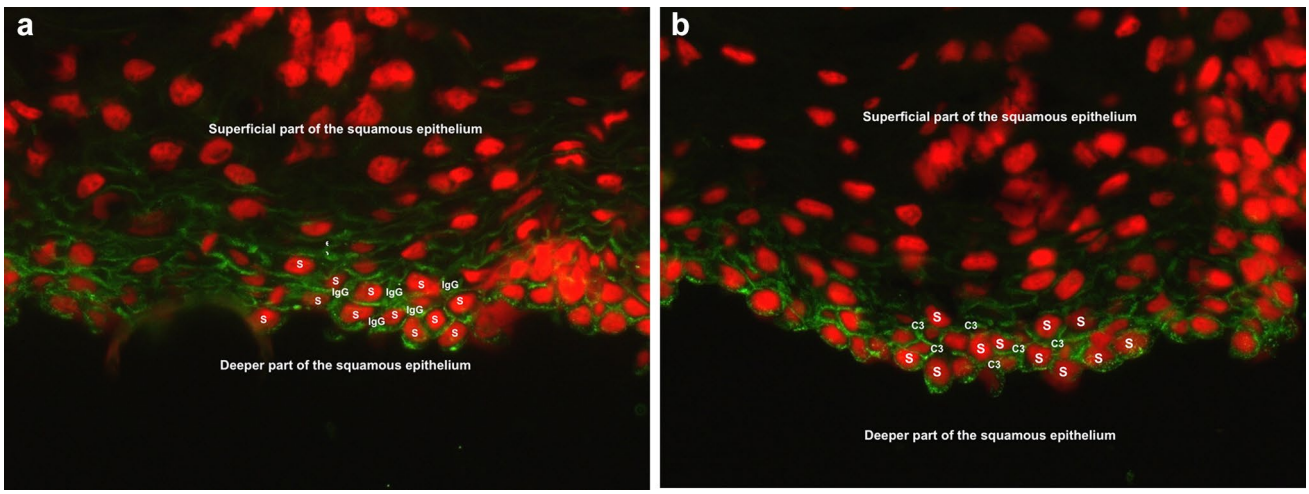

Fig. 5 **a, b** Immunofluorescence reveals intercellular deposition of IgG and C3 in a characteristic 'chicken-wire or fish-net' pattern. *S* squamous cell. ×40 magnification

Given the rarity of oesophageal involvement in PV, it has been suggested that endoscopy is indicated only for patient who are symptomatic and it should be performed by forewarned and experienced endoscopist [6].

Compliance with ethical standards

Conflict of interest M.McFarlane, A. Azam, D. Snead and B. Disney declare that they have no conflicts of interest.

Human rights All procedures followed have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed consent Informed consent was obtained from all patients for being included in the study.

References

1. Kridin K. Pemphigus group: overview, epidemiology, mortality, and comorbidities. Immunol Res. 2018;66:255–70.
2. Joly P, Litrowski N. Pemphigus group (vulgaris, vegetans, foliaceus, herpetiformis, brasiliensis). Clin Dermatol. 2011;29:432–6.
3. Kaplan RP, Touloukian J, Ahmed AR, et al. Esophagitis dissecans superficialis associated with pemphigus vulgaris. J Am Acad Dermatol. 1981;4:682–7.
4. Schissel DJ, David-Bajar K. Esophagitis dissecans superficialis associated with pemphigus vulgaris. Cutis. 1999;63:157–60.
5. Chang S, Park SJ, Kim SW, et al. Esophageal involvement of pemphigus vulgaris associated with upper gastrointestinal bleeding. Clin Endosc. 2014;47:452–4.
6. Zehou O, Raynaud JJ, Le Roux-Villet C, et al. Oesophageal involvement in 26 consecutive patients with mucous membrane pemphigoid. Br J Dermatol. 2017;177:1074–85.
7. Mahoney MG, Wang Z, Rothenberger K, et al. Explanations for the clinical and microscopic localization of lesions in pemphigus foliaceus and vulgaris. J Clin Invest. 1999;103:461–8.
8. Gregoriou S, Efthymiou O, Stefanaki C, et al. Management of pemphigus vulgaris: challenges and solutions. Clin Cosmet Investig Dermatol. 2015;8:521–527.