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Esophageal Stricture Recalcitrant to Repeated Dilation in Complex Rheumatological Disease

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ABSTRACT

We report a case of severe refractory esophageal strictures in the setting of rheumatological disease found to be secondary to isolated esophageal autoimmune bullous disease. She had a history of Sjogren syndrome and esophageal strictures with many previous dilations. After rheumatological workup, she was diagnosed with mixed connective tissue disease. Biopsy showed complement and immunoglobulin G deposition in the basement membrane consistent with bullous lupus or bullous pemphigoid. She had no cutaneous bullae and was diagnosed with isolated esophageal bullous disease. She required multiple dilatations over several months of treatment and was started on mycophenolate mofetil with clinical improvement.

INTRODUCTION

Esophageal strictures are most commonly (70%–75%) caused by acid exposure.[1] Treatment for benign esophageal stricture is endoscopic dilation, successful in more than 80% of cases.[2] Esophageal involvement in autoimmune bullous diseases is rarely seen in the setting of widespread disease and is hardly ever reported as the only affected organ.[3,4] These patients can present with odynophagia, dysphagia, chest pain, hematemesis, or strictures.[5] We present the case of a patient who presented with dysphagia secondary to esophageal strictures refractory to multiple dilations that was found to be secondary to autoimmune bullous disease.

CASE REPORT

A 50-year-old woman from the Middle East with dysphagia for 2 years presented with complete inability to tolerate oral intake for several weeks. Her medical history included Sjogren syndrome, gastroesophageal reflux disease, and esophageal strictures. She developed dysphagia to solids and underwent regular esophageal dilations at 2-week intervals at an outside hospital. At presentation, the patient had undergone 11 esophageal dilations with push-type dilators up to 22 mm in diameter, leading to modest clinical improvement. During the COVID-19 pandemic, she was unable to have dilations as frequently. The dysphagia worsened, and she lost 30 kg of weight (Figures 1 and 2).

Outside laboratory testing was positive for rheumatoid factor, anticyclic citrullinated peptide, and Sjogren syndrome antibodies, and she was diagnosed with Sjogren syndrome. Physical examination findings were relevant for poor skin turgor, dry mucosal membranes, and skin hyperpigmentation over the dorsum of the hands and forearms. The patient was admitted to the hospital for supportive management and diagnostic workup.

Esophagram showed a proximal esophageal stricture at the level of C5-C6 with contrast aspiration. Esophagogastroduodenoscopy showed a proximal stricture which was dilated using a push-style dilator to 14 mm. She declined esophageal manometry. Computed tomography neck and chest showed atrophied parotid, submandibular, and lacrimal glands. She underwent repeated dilation with push-style dilator to 18 mm. She had clinical improvement and was discharged with a close rheumatology follow-up.

Rheumatology clinic evaluation included positive antinuclear antibody at 12.0 IU/mL (normal <1), anti-SSA 8.0 U/mL (normal <1), anti-Smith 3.1 U/mL (normal <1), and anti-RNP 7.8 U (normal <1). Her complement C3 level was 71 mg/dL (normal 65–175), and C4 was 23 mg/dL(normal 14–40). Her anti-Scl70, anticentromere, dsDNA, c-ANCA, p-ANCA, beta 2 GP1, cyclic citrullinated peptide, phospholipid Ab, anti- SSB, Scl 70, anti Jo1, and rheumatoid factor were normal. She had an elevated total

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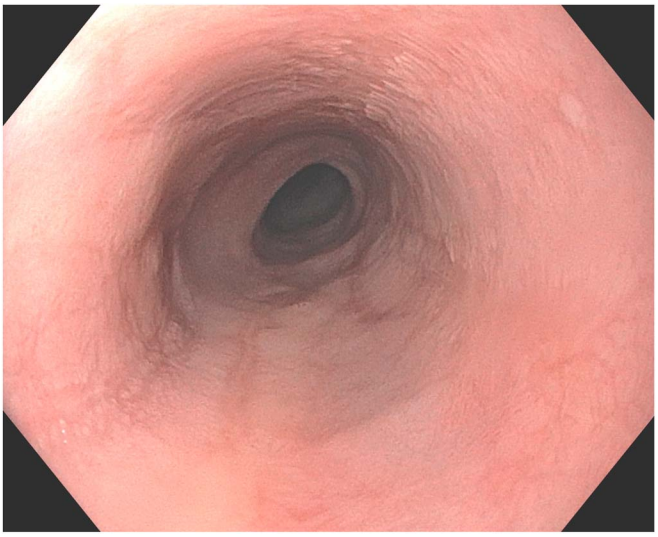

Figure 1. Esophagogastroduodenoscopy of the upper esophagus at initial presentation showing a stricture at C5-C6.

Immunoglobulin G (IgG) 2,490 (normal 767–1,590) and a polyclonal hypergammaglobulinemia (albumin 3.2, alpha1 globulin 0.2, alpha2 globulin 0.8, beta-globulin 0.8, and gamma-globulin 2.2). She was diagnosed with mixed connective tissue disease and was started on mycophenolate mofetil.

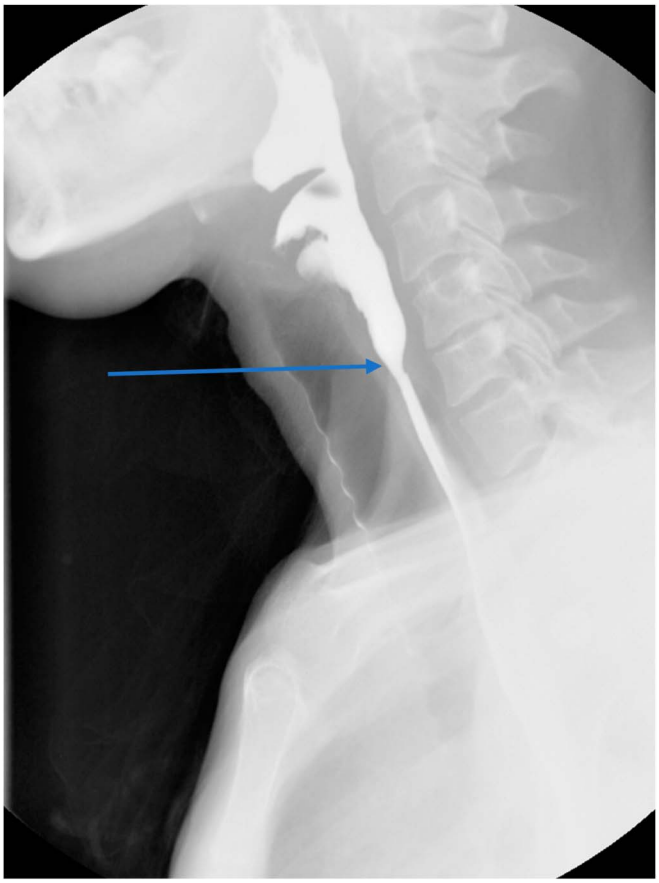

Figure 2. Esophagram on day 14 showing narrowing at C6 (arrow).

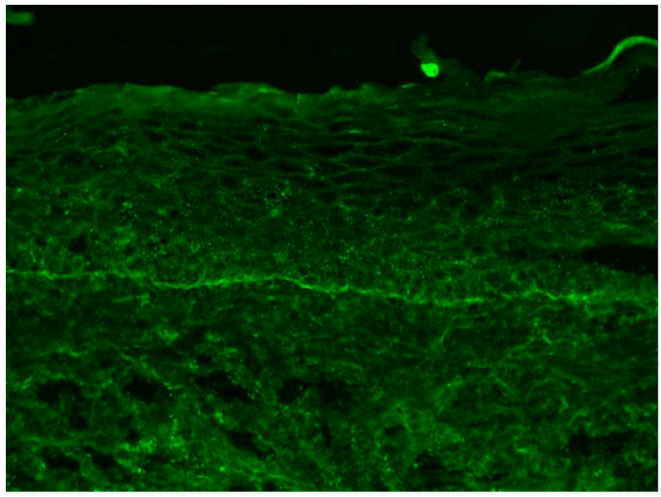

Figure 3. Immunofluorescence showing IgG deposition along the basement membrane.

She had improvement of her symptoms and did not require repeat EGD until recurrence of dysphagia 2 months later. EGD showed an esophageal stricture measuring 7 mm in the upper esophagus and friable oropharyngeal and hypopharyngeal mucosa. Biopsies of the strictured segment were sent for immunofluorescence, which showed continuous strong linear deposition along the basement membrane zone for both IgG and C3. The pattern was consistent with a subepidermal autoimmune mucocutaneous blistering disorder. The biopsies were negative for antidesmoglein 1,3, anti-bullous pemphigoid 180, 230, and cutaneous IgG (Figures 3 and 4). The dermatology bullous disorders clinic was consulted, and her final differential diagnosis included atypical esophageal bullous systemic lupus erythematosus (SLE) and atypical esophageal bullous pemphigoid.

Her mycophenolate mofetil dose was increased. The patient declined systemic steroids. She received weekly dilations of multiple strictures at varying levels to prevent koebnerization

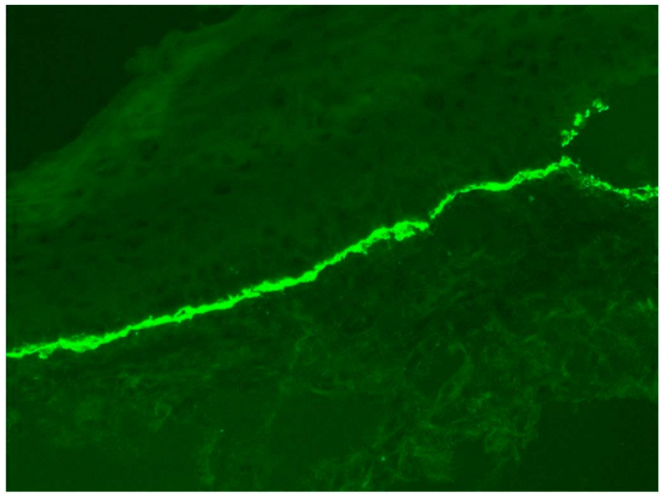

Figure 4. C3 conjugate demonstrating strong and diffuse linear deposition along the mucosal basement membrane zone (200×).

and allow time for medical therapy effect. After 3 months of treatment, she had symptom improvement.

DISCUSSION

This patient presented with Sjogren syndrome and multiple esophageal strictures refractory to repeated dilatation. Her workup included positive antibodies for lupus, Sjogren syndrome, rheumatoid arthritis, and mixed connective tissue disease (MCTD) and the rare finding of isolated esophageal bullous disease.

Rheumatological diseases have known gastrointestinal effects which often affect esophageal motility and the integrity of the musculature of the esophagus. MCTD can have esophageal manifestations, most commonly dysmotility (45%–85%).[6] In studied cases of MCTD, the circular layer of esophageal muscle was primarily affected with severe atrophy and fibrosis. Esophageal findings of other rheumatological diseases including scleroderma, lupus, and Sjogren syndrome can be seen in MCTD. In this patient, her mixed connective tissue disease likely contributed to the development and persistence of her strictures.

Bullous SLE is a very rare presentation and is characterized by subepidermal tense vesiculobullous eruptions on sun-exposed areas.[7,8] Esophageal involvement is uncommon, but cases have been described with esophagitis dissecans superficialis, which is a rare endoscopic finding.[10] On esophagogastroduodenoscopy, esophagitis dissecans can seem as desquamated esophageal mucosa without bleeding, vertical fissures and circumferential cracks with peeling, and red erosion of the esophagus with white sheets of sloughed mucosa.[9] Criteria for the diagnosis of bullous SLE include meeting the criteria for diagnosis of SLE, having an acquired vesiculobullous eruption, having histologic evidence of subepidermal blister and predominantly neutrophilic infiltrate or immunofluorescence demonstrating IgG with or without IgA and IgM deposits at the basement membrane zone, and evidence of antibodies to type VII collagen.[10] This patient had laboratory test results indicating SLE; however, she did not have SLE symptoms.

Blistering diseases can affect mucous membranes including bullous pemphigoid and mucous membrane (cicatricial) pemphigoid.[4] Esophageal involvement in bullous pemphigoid is rare and generally has hemorrhagic bullae with symptoms including dysphagia, hematemesis, or melena.[4] This patient presented with biopsy findings of bullous disease but did not have systemic symptoms or clear esophageal bullae. Mucous membrane pemphigoid most commonly affects the eye and oropharynx but can rarely affect the esophagus, nasopharynx, larynx, and skin.[3] Rupture of bullae can lead to scar and stricture formation.[9,11] Esophagitis dissecans can also be seen in bullous pemphigoid.[9] Diagnosis is made by biopsy in both diseases and can show superficial inflammatory infiltrate containing lymphocytes, histiocytes, and eosinophils and shows linear deposits of IgG and/or C3.[3,4] Treatments include steroids and immunosuppression therapy.[4] Rupture of bullae can lead to scar and stricture formation as was thought to be the case in this patient despite lack of overt endoscopic findings.

This patient's presentation was unusual with severe strictures refractory to repeated dilation in the setting of complex rheumatological disease. Her workup reflects MCTD with features of systemic lupus erythematosus, Sjogren syndrome, RA, and scleroderma, as well as esophageal bullous disease. Esophageal manifestations of bullous disease are rare, especially when seen in isolation.

DISCLOSURES

Author contributions: C.G. Olson reviewed the literature and wrote the article. H. Vora, M. Pang, and P.T. Kröner revised the article for intellectual content. P.T. Kröner provided the images. M. Pang is the article guarantor.

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Informed consent was obtained for this case report.

Previous presentation: Case presented at the Mayo Clinic AZ annual course of esophageal diseases on April 12, 2021 by Dr Paul T. Kroner.

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