

Esophagitis dissecans associated with eosinophilic esophagitis in an adolescent

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Abstract

Esophagitis dissecans superficialis and eosinophilic esophagitis are distinct esophageal pathologies with characteristic clinical and histologic findings. Esophagitis dissecans superficialis is a rare finding on endoscopy consisting of the peeling of large fragments of esophageal mucosa. Histology shows sloughing of the epithelium and parakeratosis. Eosinophilic esophagitis is an allergic disease of the esophagus characterized by eosinophilic inflammation of the epithelium and symptoms of esophageal dysfunction. Both of these esophageal processes have been associated with other diseases, but there is no known association between them. We describe a case of esophagitis dissecans superficialis and eosinophilic esophagitis in an adolescent patient. To our knowledge, this is the first case describing an association between esophageal dissecans superficialis and eosinophilic esophagitis.

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Introduction

Esophagitis dissecans superficialis (EDS) and eosinophilic esophagitis (EoE) are diseases of the esophagus that are defined by distinct clinical and histologic findings. EDS is characterized on endoscopy by sloughing of large fragments of the esophageal mucosa [1]. Histological features include suprabasal intraepithelial splitting, necrotic epithelium with varying degrees of inflammation, and parakeratosis [1]. Patients with EDS may vomit casts of sloughed-off esophageal mucosa [2,3]. Others have been reported to present with dysphagia, epigastric pain, or heartburn, but many are asymptomatic [1,4]. There is generally a good prognosis, with the majority of patients responding to proton pump inhibitor therapy [1,5-6]. Though EDS has most often been associated with bullous skin disease [7-10] and medications [1,4,11], the etiology of this phenomenon

is poorly understood. Only one pediatric case has been published to date [5].

EoE is an allergic disorder of the esophagus in response to food or aeroallergens [12]. Patients with EoE experience symptoms of esophageal dysfunction, such as dysphagia in adults and abdominal and/or chest pain in children [12]. Endoscopic findings are non-specific and include fixed esophageal rings, diffuse narrowing, and exudates [13]. Esophageal biopsies show eosinophil-predominant inflammation in the epithelium [13] at multiple levels throughout the esophagus [14-15]. The disease is responsive to topical steroids [15-16] and/or dietary changes [15,17]. Strictures may form if left untreated [18].

The following is a report of EDS associated with EoE in an adolescent patient.

Case Report

The patient is a 17-year-old female with a history of anxiety who initially presented to the emergency room with severe, acute abdominal pain. Comprehensive metabolic panel was within normal limits. Complete blood count (CBC) showed a white blood cell count (WBC) of $9.7 \times 10^3/\mu\text{L}$ with a left shift (85.4% neutrophils, 10.1% lymphocytes, 4.3% monocytes, 0.1% eosinophils, 0.1% basophils) and normocytic anemia (hemoglobin 8.5 g/dL, mean corpuscular volume 88.4 fL). CT scan revealed free air. She was red-lined to the operating room where the General Surgery team found a 2-centimeter mid-body gastric ulcer that had perforated. They performed a wedge resection of the ulcer. Pathology on the resected tissue showed acute serositis and was negative for *H. pylori* and malignancy. The etiology of the ulcer was thought to be caused by a rarely reported side effect of selective serotonin reuptake inhibitor (SSRI) therapy [19,20] as the patient had been on fluvoxamine for anxiety. She was discharged from the hospital on post-operative day 6. Upon discharge, the patient was instructed to take pantoprazole 40 mg by mouth twice daily and to follow up in Pediatric Gastroenterology clinic.

When seen in the Pediatric Gastroenterology clinic 5 weeks later, she reported that she had been clinically asymptomatic since her discharge. The physical exam was notable for the absence of bullous skin lesions. Repeat CBC showed a WBC of $3.9 \times 10^3/\mu\text{L}$ without eosinophilia (40% neutrophils, 47% lymphocytes, 9.4% monocytes, 3.1% eosinophils, and 0.5% basophils) and microcytic anemia (hemoglobin 9.3 g/dL, mean corpuscular volume 76.9 fL) with a low total iron of 17 mcg/dL. Given the persistent anemia combined with the acuity and severity of her initial presentation, we elected to perform an esophagogastroduodenoscopy to survey for other ulcerations or mucosal inflammation. The endoscopy was remarkable for gross abnormality in the mid-esophagus, which showed areas of ulcerations, furrowing, streaks of white layering of mucosa with sloughing, and friability from approximately 25 cm to 30 cm (Fig. 1a-c). Given the significant amount of sloughing, no esophageal rings or narrowing were appreciated. The more proximal and distal esophagus as well as the stomach and duodenal bulb appeared normal. Histology from multiple mid-esophageal

biopsies showed severe esophagitis with marked infiltration of squamous epithelium by neutrophils and eosinophils, as well as mucosal separation resulting in the formation of bullous spaces and ulceration. No viral inclusions or fungal organisms were present. Focally in one of the mid-esophageal biopsies, the number of intraepithelial eosinophils reached up to 35 per high power field with much less pronounced neutrophilic inflammation and no mucosal separation (Fig. 2a-c). The most distal esophageal biopsy showed no neutrophilic or eosinophilic inflammation and was histologically normal. Gastric biopsies showed mild chronic gastritis, without evidence of *H. pylori* infection or malignancy. Duodenal biopsies did not show any histopathologic abnormality. The pathology appeared consistent with both EDS and EoE. Notably, the patient did not report any history of esophageal symptoms and had no personal or known family history of allergies or atopy. Given that these findings were present despite ongoing proton pump inhibitor therapy, she was instructed to take fluticasone 220 mcg, two puffs swallowed twice daily.

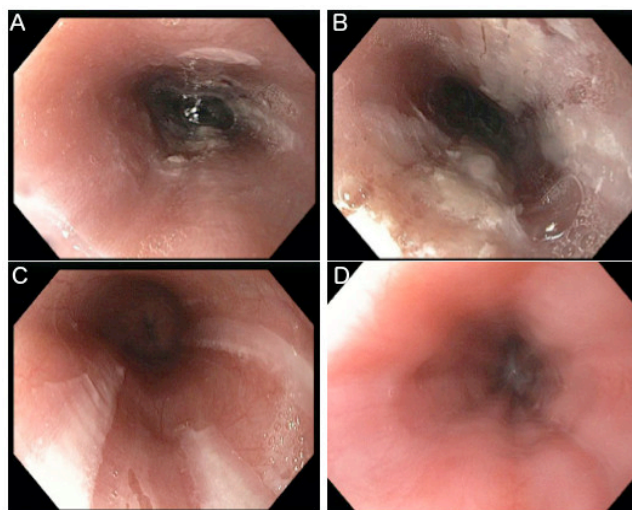


Figure 1. (a) Proximal, (b) mid-, and (c) distal esophagus on initial endoscopy. Starting at 25 cm the esophagus was characterized by sloughing of white layers of mucosa with associated furrowing and ulcerations, consistent with EDS. The distal esophagus showed termination of the peeling white streaks with normal-appearing mucosa closer to the gastroesophageal junction. (d) Repeat endoscopy following treatment for EDS showed resolution of the abnormal mucosal findings in the mid-esophagus.

The patient was seen for follow up 12 weeks later. At this time, she remained asymptomatic. Labs were unremarkable, including a CBC with WBC of $4.2 \times 10^3/\mu\text{L}$ without eosinophilia (40.4% neutrophils, 52.7% lymphocytes, 4.8% monocytes, 1.9% eosinophils, and 0.2% basophils) and normal hemoglobin of 13.6 g/dL. A repeat upper endoscopy to document histologic improvement performed 2 weeks after this visit showed normal architecture and vascular pattern throughout the esophagus (Figure 1d). Biopsies showed complete resolution of the severe inflammation seen in the mid-esophagus (Fig. 2d). A pH/impedance probe placed at the time of the endoscopy showed no gastroesophageal reflux disease and normal esophageal clearance. Importantly, she had stopped taking the proton pump inhibitor several months prior to this study. She was instructed to continue taking fluticasone at a decreased dose of one puff twice daily and has remained asymptomatic.

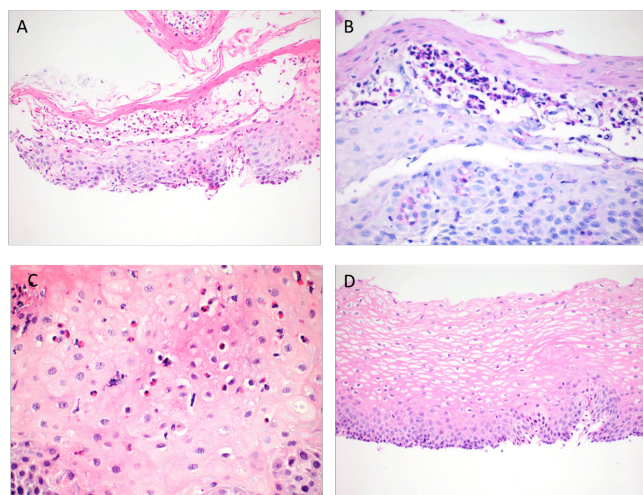


Figure 2. (a, b) Histologic sections of biopsies of the mid-esophagus showed severe esophagitis with sloughing of the superficial squamous epithelium, parakeratosis, and intraepithelial bullous formation with neutrophils and eosinophils. (100x, 400x) (c) Focal areas showed prominent intraepithelial eosinophils, but without significant neutrophilic inflammation or mucosal separation. (400x) (d) Repeat biopsies taken almost 4 months later showed complete resolution of the esophagitis and histologically unremarkable squamous mucosa. (100x)

Discussion

This case identifies an adolescent whose endoscopic findings were suggestive of EDS and whose histologic findings were consistent with both EDS and EoE. She met histologic criteria for EoE based on the presence of significant eosinophils in the squamous epithelium of the esophagus, with up to 35 eosinophils per high power field, as well as reactive changes such as basal layer hyperplasia and spongiosis. She had been on proton pump inhibitor therapy for 7 weeks prior to the endoscopy, ruling out protein pump inhibitor-responsive esophageal eosinophilia. A normal pH/impedance probe while off acid suppression therapy also ruled out gastroesophageal reflux disease. Although she initially presented with severe, acute abdominal pain due to perforated gastric ulcer, she denied any history of esophageal symptoms and was asymptomatic at the time of the first endoscopy when she was diagnosed with EDS and EoE. To our knowledge, this case represents the first association between EDS and EoE.

The etiology of EDS remains poorly understood. Previously it has been associated with bullous dermatoses [7-10] and medications including bisphosphonates [11,21] and non-steroidal anti-inflammatory drugs [1]. Notably, our patient was taking an SSRI at the time of diagnosis, which has also been associated with EDS [4]. EoE is an allergic process that occurs most commonly in response to food or aeroallergens. It has been associated with connective tissue disorders [22] and cystic fibrosis [23]. Interestingly, both EDS and EoE have been linked to celiac disease [24-27]. This suggests there may be a common pathophysiology driven by a topical allergic or immune-mediated response.

Given that most reports of EDS are in adults, it is unclear if EDS is less common in children or simply not recognized and/or underreported. The first published case report of EDS in a pediatric patient described a 14-year-old female who presented with non-bilious vomiting, with an atopic history and elevated IgE [5]. Although this presentation may be suggestive of EoE, no eosinophils were noted on histology.

To our knowledge, there are no previous reports of EDS associated with EoE. Endoscopic findings in EoE are generally non-specific, such as fixed

esophageal rings and diffuse narrowing [13]. This report suggests that EDS may be another non-specific finding of EoE and should be considered on the differential by the clinician who encounters EDS on endoscopy.

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