

Pediatric Patient With Concurrent Eosinophilic Esophagitis, Erosive Reflux Esophagitis, and Barrett's Esophagus

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ABSTRACT

Eosinophilic esophagitis and Barrett's esophagus are believed to be separate disease processes, with erosive esophagitis leading to Barrett's esophagus. We report a rare case of concurrent diagnoses in a pediatric patient and examine the relevant genetic profiles in the esophagus.

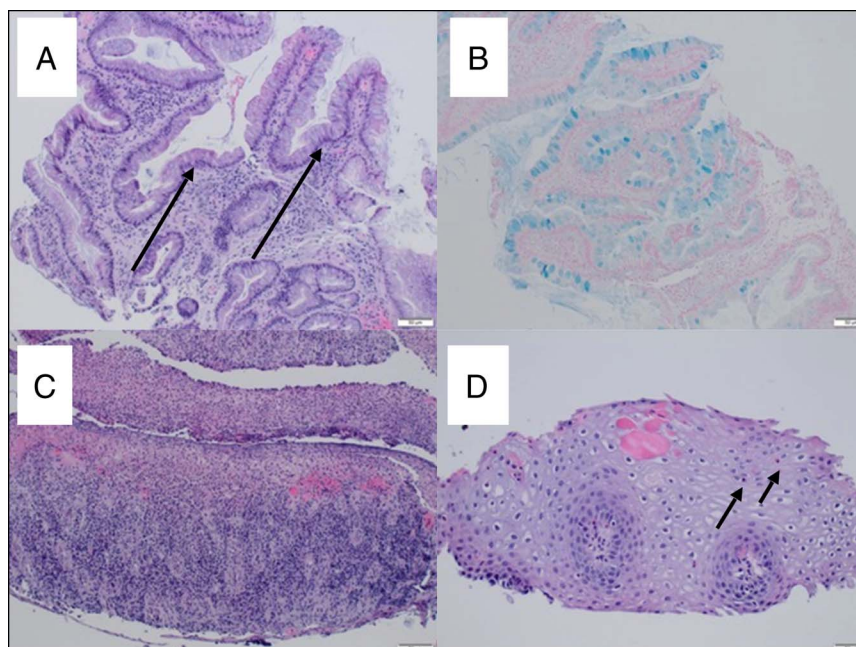


Figure 1. Histologic analysis of esophageal biopsies. (A) Barrett's esophagus (BE) in the distal part of the esophagus (hematoxylin and eosin stain, 100× magnification), (B) BE in the distal part of the esophagus (Alcian blue stain, 100× magnification), (C) erosive esophagitis in the middle part of the esophagus (hematoxylin and eosin stain, 100× magnification), and (D) eosinophilic esophagitis (black arrow) in the proximal part of the esophagus (hematoxylin and eosin stain, 200× magnification).

INTRODUCTION

Esophageal pathologies can occur in the pediatric population, including eosinophilic esophagitis (EoE) and Barrett's esophagus (BE). Erosive esophagitis (EE) due to gastroesophageal reflux disease (GERD) is believed to lead to BE. Although these are known to be distinct diseases with different pathophysiology and gene expression profiles, a patient can have concurrent EoE, EE, and BE.¹⁻³ There are a few reports of patients with concurrent diagnoses. However, the gene expression profile from esophageal biopsies in a patient with concurrent EoE and BE has not been reported. We report a case of concurrent EoE, EE, and BE in a pediatric patient and examine the gene expression.

CASE REPORT

A 15-year-old morbidly obese female patient (body mass index 45) presented with multiyear symptoms of acid reflux uncontrolled by H2 blockers and proton pump inhibitors. In 2016, after a few years of management at another institution for GERD and EoE, including with topical steroids, she developed inflamed cardia-type mucosa with intestinal metaplasia and foveolar hyperplasia in the lower esophagus. In 2017 and 2018, upper endoscopy revealed Barrett's-like mucosa in the lower esophagus with scattered ulcerations and erosions, severe esophagitis with erosions of the middle esophagus, and furrows and white specks in the upper esophagus. Biopsies were obtained from each of these 3 areas. Histologic studies demonstrated concurrent severe EoE with 30 eos/hpf, marked basal layer hyperplasia, with no granulomas and no columnar mucosa in the upper esophagus (22–25 cm); EE in the mid-esophagus (32–35 cm) with 15 eosinophils/high-power field, with no granulomas, negative periodic acid-Schiff with diastase for fungal forms, and negative immunohistochemistry for herpes simplex virus; and columnar mucosa with intestinal metaplasia containing goblet cells (Barrett's metaplasia) and no esophageal epithelium in the lower esophagus (38–40 cm) (Figures 1 and 2). This Barrett's metaplasia was noted to be the Prague classification C2M3.

Biopsies from the proximal, mid, and distal segments of the esophagus were also analyzed with predesigned polymerase chain reaction (PCR) assays (BioRad EoE H96 and BE H96-well disease state panels) looking at genes known to be associated with EoE and BE and were compared among the 3 segments. This showed differences in each segment (Figure 3). In the BE PCR assay, the genes *AGR2*, *DCKL1*, *TFF1*, *VEGFA*, *CXCR2*, *EGF*, *IL1B*, *IL1RN*, *KRT7*, and *DKK1* were relatively upregulated in the distal esophagus portion consistent with previous genetic studies looking at BE and relatively downregulated in the proximal esophagus portion consistent with previous genetic studies looking at EoE.⁴⁻¹¹ *GSTP1* and *NOTCH1* were relatively downregulated in the distal portion, also consistent with previously described BE genotype.¹²⁻²⁵

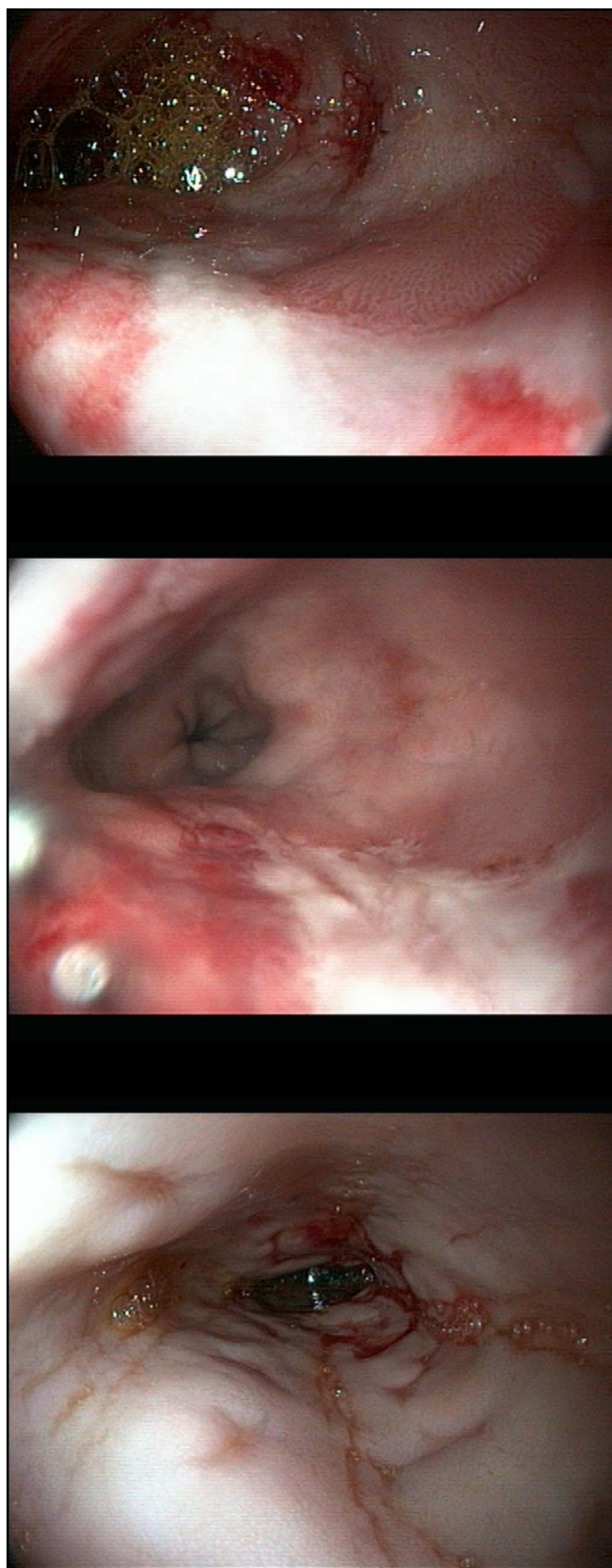


Figure 2. Endoscopic images showing the distal, mid, and proximal esophagus gross findings.

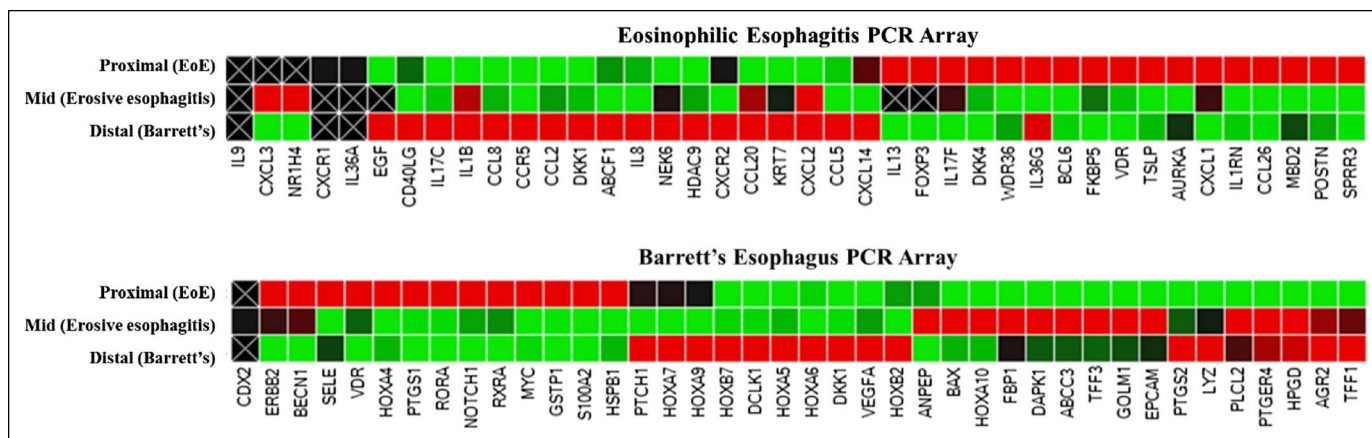


Figure 3. PCR array analysis of different regions of the esophagus showing gene expression heat map for EoE and Barrett's esophagus performed on the esophageal biopsies obtained from the proximal, mid, and distal esophagus and compared among the 3 segments (red—relatively upregulated, green—relatively downregulated, and black—relatively similar activity). EoE, eosinophilic esophagitis; PCR, polymerase chain reaction.

In the EoE PCR assay, the genes CCL26, FDX3, CXCL1, IL13, POSTN, TSLP, and WDR36 were relatively upregulated in the proximal portion, which is consistent with previous studies gene expression of EoE and relatively downregulated in the distal portion, which is consistent with that of BE.^{12–25} The genes ANPEP, EPCAM, ERBB2, MYC, S100A2, TFF3, AURKA, BCL6, CCL2, CCL20, CXCL2, CXCL3, DKK1, and SPRR3 showed activity inconsistent with the previous literature studies of genetic expression in EoE and Barrett's.^{4–25} The patient was started on a strict dairy-free diet and high-dose proton pump inhibitor therapy with significant improvement in GERD symptoms, endoscopic improvement in EoE, and EE characteristics and is receiving nutritional counseling for weight loss with surgical consultation for possible bariatric surgery.

DISCUSSION

EoE and BE are believed to be 2 distinct diseases, with different pathophysiology, management, and outcomes. Concurrent diagnosis of EoE and BE in a single patient has been previously reported.^{1,2} However, the gene expression profile from esophageal biopsies in these patients has not been reported. Our patient is obese with chronic reflux, which increased her risk of developing EE and BE. Although this patient does not have the typical phenotype for EoE (white male with asthma and atopic disease), her features are consistent with EoE based on endoscopic and histologic findings.²⁶

Several studies have looked at the gene expression associated with these diseases separately; however, to date, there is no known genetic study in a patient with concurrent EoE, EE, and BE. PCR studies evaluating genes known to be involved in EoE and in BE show a similar pattern in our patient corresponding to the segment of esophagus biopsied. In the upper esophagus, the patient had a gene expression most similar to that described for EoE. In the lower segment, the patient had a gene expression most similar to BE. However, of the 81 genes analyzed, 16 showed activity

different than what has been described in the previous literature for either EoE and BE. This could be attributed to a combined pathophysiology in patients with concurrent diagnoses, which perhaps differentiates it from patients with exclusively one disease process. Based on these genetic profiles, the proximal esophagus pathophysiology and genetic expression is different from that of the distal esophagus, lending further evidence to the theory that EoE and BE are distinct clinical and pathologic entities.

DISCLOSURES

Author contributions: All authors contributed equally to this manuscript. I. Sharma is the article guarantor.

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Informed consent was obtained for this case report.

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