



Letter

Eosinophilic esophagitis as possible complication of aspirin treatment in patient with aspirin-exacerbated respiratory disease

A 44-year-old African American woman with severe, persistent asthma and chronic rhinosinusitis with nasal polyposis due to aspirin-exacerbated respiratory disease (AERD) and allergic rhinoconjunctivitis presented to an outpatient allergy clinic with chief symptoms of epigastric pain and dysphagia while taking aspirin for AERD. The patient was diagnosed with asthma and rhinosinusitis at 31 and 34 years of age, respectively. She initially had symptoms compatible with AERD at 38 years of age when she first reacted to ibuprofen and was diagnosed with sinonasal polyposis. AERD diagnosis was confirmed 3 years later with a positive challenge result to aspirin. She continued aspirin treatment, 650 mg twice daily, for 3 years. She had remarkable clinical improvement in rhinitis and asthma symptoms; her forced expired volume in 1 second improved from 2.6 L (77% predicted value) to 2.8 L; and her Asthma Control Test and Rhinonasal Quality of Life Questionnaire (RQLQ) scores improved from 17 to 20 and 2.53 to 1.46, respectively. Several attempts to decrease the aspirin dose to 325 mg twice daily resulted in asthma exacerbations and anosmia.

After 3 years of aspirin treatment, she presented with 3 weeks of cramping epigastric pain and heartburn. She started taking 20 mg of famotidine twice daily. Aspirin use was discontinued for 10 days. Her initial upper endoscopy revealed esophagus without corrugation or stricture. Biopsies of the gastroesophageal junction revealed mild, patchy inflammation of the gastric cardia with squamous esophageal mucosa absent of eosinophils. Manometry revealed nonspecific esophageal motility disorder with occasional ineffective contractions. A pH study revealed no excessive acid exposure but minimal acid reflux. After the upper endoscopy, she was desensitized to aspirin again and continued to take 325 mg twice daily. The patient continued having severe epigastric pain and chest pressure; 40 mg daily of omeprazole was added to the twice-daily famotidine. Symptoms persisted during the next 10 months and progressed to dysphagia. Ten months after initial endoscopy and a prolonged 10-month trial of daily proton pump inhibitor therapy, the results of another endoscopy were notable for an esophagus with a mildly corrugated appearance. Midesophageal biopsies revealed 25 intraepithelial eosinophils per high-power field (Fig 1), consistent with a diagnosis of eosinophilic esophagitis (EoE). The initial biopsy specimen may have been absent of eosinophils because the biopsy was performed only within the distal esophagus at 2 sites; therefore, the sampling was insufficient to rule out EoE.¹ The patient also developed peripheral eosinophilia of 12%

(1.1k/ μ L) compared with 4% (0.3k/ μ L) the year before. The results of serologic tests for parasites, human immunodeficiency virus, celiac disease, and adrenal insufficiency were negative. The results of tests for antineutrophil cytoplasmic antibodies (PR3-MPO) were also negative. Food allergies include soy that causes shortness of breath.

The patient was asked if she wanted to discontinue aspirin therapy; she declined because of concerns of recurring polyps and suboptimal asthma control. She was started on a 6-food elimination diet, which excluded milk, egg, wheat, soy, peanuts/tree nuts, and fish/shellfish for 6 weeks without improvement. She was then started on a trial of swallowed budesonide (1 mg twice daily) and described a substantial improvement in symptoms, including dysphagia, after 2 weeks. An additional biopsy was not performed given her continued absence of symptoms.

AERD is an adult-onset, acquired syndrome characterized by the presence of asthma, nasal polyps, aspirin sensitivity, and eosinophilia. Aspirin desensitization followed by daily aspirin is a treatment option for AERD that alleviates respiratory symptoms. This patient developed EoE during long-term aspirin treatment.

EoE is a chronic, immune-mediated esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation.² There is a higher rate of EoE in patients with atopic diseases, including asthma and allergic rhinitis. In this condition, eosinophils, mast cells, and T cells infiltrate the esophageal lining and release cytokines, including interleukin (IL)-4, IL-5, IL-13, and granulocyte-macrophage colony-stimulating factor, causing inflammation.² This leads to remodeling and fibrosis followed by bolus impaction, dysphagia, perforation, stricture, and nutritional deficiencies.² The diagnosis of EoE requires a histologic finding of 15 or more eosinophils per high-power field.¹ Current treatment of EoE includes elimination diet, topical corticosteroids, systemic corticosteroids, leukotriene antagonists, and endoscopic dilation.²

Our patient may be the first described patient with EoE that developed during long-term high-dose aspirin therapy for AERD. Although we strongly suspect aspirin as the cause of her EoE, we did not conduct an aspirin elimination trial for 6 weeks because of patient preference. Besides aspirin treatment, other possible causes of EoE in this patient could include sensitivity to food (despite attempted elimination diet). Even if aspirin was not the trigger of the EoE, it could have played an important role in the onset of EoE. Aspirin therapy in AERD has been associated with increased peripheral blood eosinophils³ and gastrointestinal adverse effects.⁴ One study found that 33% of AERD patients undergoing aspirin treatment experienced dyspepsia.⁴ A recent study did not find an association between nonsteroidal anti-inflammatory drug use and

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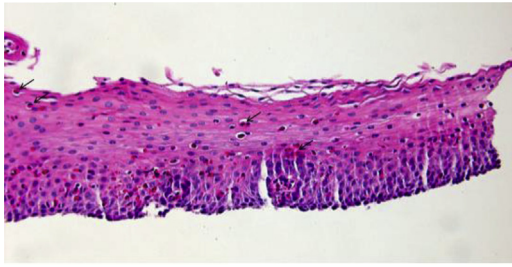


Figure 1. Middle esophageal biopsy specimen showing numerous intraepithelial eosinophils (arrows), up to 25 per high-power field, that involve the superficial layers of mucosa and basal cell hyperplasia.

EoE; however, patients with EoE taking aspirin were more likely to present with a stricture compared with patients who were not taking aspirin.⁵ Therefore, there is a concern that aspirin may aggravate disease progression and may be a risk factor for strictureing EoE. Other medications have been implicated in the development of EoE; 2 cases of EoE were described after administration of carbamazepine, thus indicating that EoE may be triggered by some medications.⁶

A previous case of EoE in a patient with AERD was described, but the patient was not undergoing aspirin therapy.⁷ Cytokines, such as eotaxin-3 and thymic stromal lymphopoietin, have been implicated in the development of both EoE and AERD. Eotaxin-3 has been found in high amounts in AERD-related nasal polyps and esophageal tissue in EoE.^{8,9} Thymic stromal lymphopoietin is indicated in AERD, where its dysregulation drives prostaglandin D₂ production.³ Prostaglandin D₂ was also implicated in trafficking eosinophils into the esophagus in EoE.¹⁰

We present a case of a patient with AERD who developed EoE with associated peripheral eosinophilia while undergoing aspirin treatment. It is not clear whether aspirin was the cause of the EoE; however, it is important for clinicians to be aware of the development of EoE in patients with AERD taking aspirin.

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