

CLINICAL VIGNETTE

Esophageal Eosinophilia – When to Blame the Medications

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Case Summary

A 30-year old male with no significant past medical history presented to Gastroenterology clinic with 2 weeks of odynophagia. He denied prior gastroesophageal reflux disease, dysphagia or odynophagia. The odynophagia was acute in onset and had persisted for 14 days without any change in symptoms. He described severe substernal chest pain immediately upon swallowing liquids or solids that resolved within 5 minutes of no oral intake. He denied dysphagia or regurgitation. The pain was sharp and burning and did not feel like a spasm.

He had a 3-year history of non-traumatic tailbone pain due to a benign coccyx tumor. For chronic lower back pain, he took NSAIDs intermittently, often at night prior to going to sleep and usually with only a few sips of water. He estimated he took ibuprofen 2-3 times a week (600mg) before bed. Last ibuprofen was 5 days prior. He denied any antibiotic use or travel in the last 12 months. His medications included citalopram and Omega-3 fatty acids. Without recent changes. No other past medical history. He denied any personal or family history of heartburn, asthma, eczema, or food allergies. Recent labs including a CBC and CMP were within normal limits. A friend gave him omeprazole 20mg which he had been taking for the last 4 days without a significant improvement in his odynophagia. The assessment was his symptoms were consistent with pill-induced esophagitis related to ibuprofen use; however, alternative etiologies were to be ruled out.

The following day upper endoscopy showed a 3mm clean based ulcer in the mid esophagus endoscopically consistent with a pill-induced ulcer. The GEJ was at 40cm with a regular Z-line. There was no erosive esophagitis. Longitudinal furrows and concentric rings noted (Figures 1 and 2). His stomach and duodenum were normal. Concentric esophageal rings were noted. Four quadrant biopsies were taken at 35cm and 30cm. A 2mm bump at 22cm was also biopsied. Pathology from all the biopsies showed increased intraepithelial eosinophils with a peak count greater than 50 per high-power field. The pathologist commented on some eosinophilic micro abscess formation and possible subepithelial fibrosis supporting the diagnosis of eosinophilic esophagitis.

He was started on daily omeprazole and swallowed budesonide and followed closely by Gastroenterology. The odynophagia resolved within 1 week.

Discussion

Eosinophilic esophagitis (EoE) is an increasingly recognized chronic inflammatory esophageal disorder. The incidence of EoE appears to be increasing, only in part because of increased recognition. There is a male predominance with many patients getting diagnosed in their 20s and 30s. In a retrospective review of 31 Australian patients diagnosed with EoE, the mean age at diagnosis was 34 years with symptoms present on average 4.5 years prior to the diagnosis.¹ The most common clinical presentation of eosinophilic esophagitis is dysphagia (93 %), food impaction (62 %), and heartburn (24 %).² Odynophagia is less common and usually associated with dysphagia. Endoscopic features are evident in 90% of adult patients² and include multiple concentric mucosal rings, longitudinal red furrows, mucosal white exudates and, less common, severe stenosis preventing advancement with a standard upper endoscope. Eosinophilic esophagitis should be diagnosed when there are symptoms of esophageal dysfunction and at least 15 eosinophils per high-power field on esophageal biopsy.³ Assessment of non-EoE disorders that cause or potentially contribute to esophageal eosinophilia is part of the updated EoE diagnostic criteria. The 2018 AGREE consensus guidelines removed proton pump inhibitors (PPI) nonresponse as a diagnostic criterion. PPIs are now classified as a potential treatment option for esophageal eosinophilia.⁴

EoE treatment includes proton pump inhibitors, avoidance diets and oral topical glucocorticoids. The six-food elimination diet (SFGED) (milk, soy, eggs, wheat, peanuts/tree nuts, and seafood) achieves remission in more than 70% of adult patients with EoE but can be challenging to maintain. A prospective multicenter study evaluated a four-food elimination diet (FFGED) (dairy products, egg, wheat and soy) and found it induced remission in 54% of adult patients with EoE.⁵ A 2018 randomized control trial found budesonide oral suspension 2mg BID significantly improved mean dysphagia symptom score and histologic response in adolescents and adults with EoE.⁶

Odynophagia as a sole symptom is a rare presentation of eosinophilic esophagitis. In contrast, pill-induced esophagitis is characterized by odynophagia, dysphagia and chest pain. Unlike eosinophilic esophagitis, there is a female predominance with pill-induced esophagitis. Medications that can cause mucosal injury to the esophagus include nonsteroidal anti-inflammatory drugs, certain antibiotics (including doxycycline often used in acne treatment), bisphosphonates, and potassium

chloride. Often a clinical diagnosis of medication-induced esophagitis can be made in a patient with acute esophageal symptoms after taking a medication history. The esophageal ulcer is located in the middle third of the esophagus in over 75% of patients⁷ and varies in size from a few millimeters to a few centimeters. The majority of patients report symptom improvement within a few days after discontinuing the culprit medication. Treatment includes a course of proton pump inhibitors and/or sucralfate. If the offending medication is continued, patients are advised to take them with a full glass of water and remain upright for 30 minutes after ingestion.

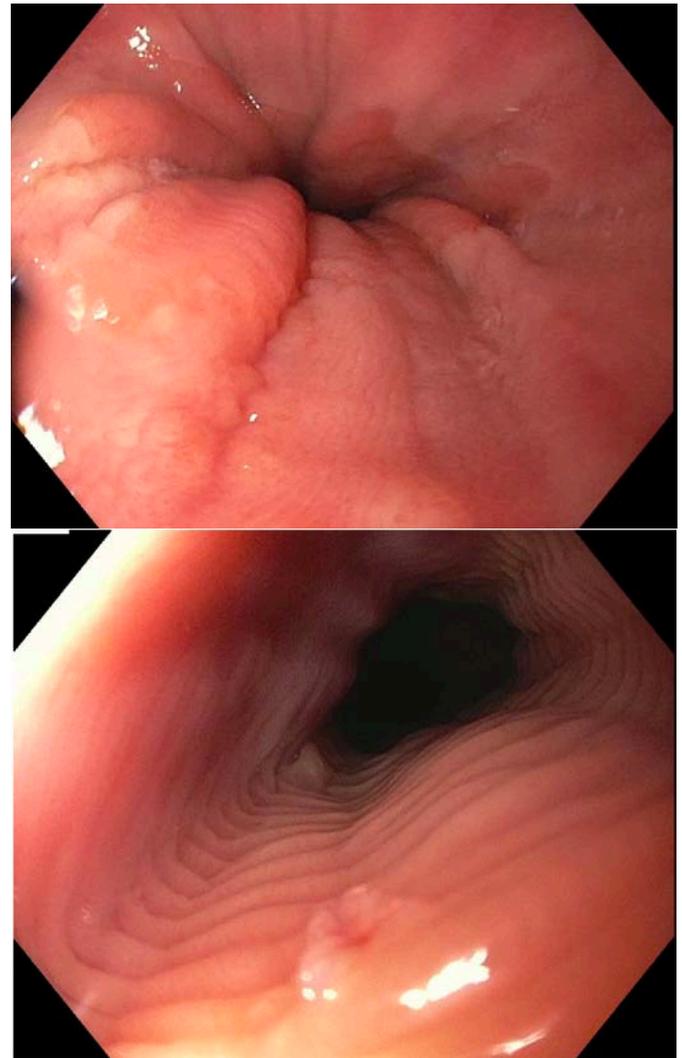
Esophageal eosinophilic infiltration can be found in both eosinophilic esophagitis and medication-induced esophagitis⁴ making the differential diagnosis between EoE and pill induced esophagitis sometimes unclear. (Table 1.) The differentiation between the two needs to be a clinicopathological diagnosis. Esophageal dysmotility from eosinophil infiltration in EoE may increase the risk for developing pill-induced esophagitis by delaying passage of medications. This case report illustrates a unique scenario where a patient presented with both eosinophilic esophagitis and pill-induced esophagitis. Diagnosis was made based on the history and endoscopic findings and highlights the importance of evaluating for underlying esophageal disorders in patients with pill-induced esophagitis.

TABLE 1

Conditions Associated with Esophageal Eosinophilia *
<ul style="list-style-type: none"> • Eosinophilic esophagitis • Eosinophilic gastritis, gastroenteritis, or colitis with esophageal involvement • GERD • Achalasia and other disorders of esophageal dysmotility • Hypereosinophilic syndrome • Crohn's disease with esophageal involvement • Infections (fungal, viral) • Connective tissue disorders • Hypermobility syndromes • Autoimmune disorders and vasculitides • Dermatologic conditions with esophageal involvement (i.e., pemphigus) • Drug hypersensitivity reactions • Pill esophagitis • Graft vs host disease • Mendelian disorders (Marfan syndrome type II, hyper-IgE syndrome, PTEN hamartoma tumor syndrome, Netherton syndrome, severe atopy metabolic wasting syndrome)

* Adapted from the proceedings of the AGREE conference

Figures 1 and 2. Upper endoscopy. Longitudinal furrows and concentric rings noted in distal and mid esophagus respectively.



REFERENCES

1. **Croese J, Fairley SK, Masson JW, Chong AK, Whitaker DA, Kanowski PA, Walker NI.** Clinical and endoscopic features of eosinophilic esophagitis in adults. *Gastrointest Endosc.* 2003 Oct;58(4):516-22. PubMed PMID: 14520283.
2. **Sgouros SN, Bergele C, Mantides A.** Eosinophilic esophagitis in adults: what is the clinical significance? *Endoscopy.* 2006 May;38(5):515-20. Review. PubMed PMID: 16767590.
3. **Kim HP, Dellon ES.** An Evolving Approach to the Diagnosis of Eosinophilic Esophagitis. *Gastroenterol Hepatol (N Y).* 2018 Jun;14(6):358-366. PubMed PMID: 30166949; PubMed Central PMCID: PMC6111507.
4. **Dellon ES, Liacouras CA, Molina-Infante J, Furuta GT, Spergel JM, Zevit N, Spechler SJ, Attwood SE, Straumann A, Aceves SS, Alexander JA, Atkins D, Arva NC, Blanchard C, Bonis PA, Book WM, Capocelli**

KE, Chehade M, Cheng E, Collins MH, Davis CM, Dias JA, Di Lorenzo C, Dohil R, Dupont C, Falk GW, Ferreira CT, Fox A, Gonsalves NP, Gupta SK, Katzka DA, Kinoshita Y, Menard-Katcher C, Kodroff E, Metz DC, Miehke S, Muir AB, Mukkada VA, Murch S, Nurko S, Ohtsuka Y, Orel R, Papadopoulou A, Peterson KA, Philpott H, Putnam PE, Richter JE, Rosen R, Rothenberg ME, Schoepfer A, Scott MM, Shah N, Sheikh J, Souza RF, Strobel MJ, Talley NJ, Vaezi MF, Vandenplas Y, Vieira MC, Walker MM, Wechsler JB, Wershil BK, Wen T, Yang GY, Hirano I, Bredenoord AJ. Updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis: Proceedings of the AGREE Conference. *Gastroenterology*. 2018 Oct;155(4):1022-1033.e10. doi:10.1053/j.gastro.2018.07.009. Epub 2018 Sep 6. Review. PubMed PMID: 30009819; PubMed Central PMCID: PMC6174113.

5. **Molina-Infante J, Arias A, Barrio J, Rodríguez-Sánchez J, Sanchez-Cazalilla M, Lucendo AJ.** Four-food group elimination diet for adult eosinophilic esophagitis: A prospective multicenter study. *J Allergy Clin Immunol*. 2014 Nov;134(5):1093-9.e1. doi: 10.1016/j.jaci.2014.07.023. Epub 2014 Aug 28. PubMed PMID: 25174868.
6. **Dellon ES, Katzka DA, Collins MH, Hamdani M, Gupta SK, Hirano I; MP-101-06 Investigators.** Budesonide Oral Suspension Improves Symptomatic, Endoscopic, and Histologic Parameters Compared With Placebo in Patients With Eosinophilic Esophagitis. *Gastroenterology*. 2017 Mar;152(4):776-786.e5. doi: 10.1053/j.gastro.2016.11.021. Epub 2016 Nov 23. PubMed PMID: 27889574.
7. **Kim SH, Jeong JB, Kim JW, Koh SJ, Kim BG, Lee KL, Chang MS, Im JP, Kang HW, Shin CM.** Clinical and endoscopic characteristics of drug-induced esophagitis. *World J Gastroenterol*. 2014 Aug 21;20(31):10994-9. doi: 10.3748/wjg.v20.i31.10994. PubMed PMID: 25152603; PubMed Central PMCID: PMC4138480.