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Case Report

Drug-Induced Versus Eosinophilic Esophagitis: A Challenging Case Report

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Abstract

We describe a challenging case of differential diagnosis between drug-induced esophagitis (DIE) and eosinophilic esophagitis (EoE). DIE is an uncommon cause of esophagitis induced by some categories of drugs that must be taken into consideration when the patient's history does not fully match with EoE. DIE and EoE, although have similar clinical, endoscopic, and even histological features, do not share the same treatment. This case highlights the importance of collecting an accurate medical history and adequate esophageal biopsy sampling during endoscopy to avoid errors with therapeutic implications.

Keywords: Drug-Induced Esophagitis; Dysphagia; Eosinophils; Esophagitis

Introduction

Heartburn, retrosternal chest pain, dysphagia, and odynophagia are symptoms shared by many esophageal diseases. Beyond the most common gastroesophageal reflux disease (GERD), other infrequent diseases must be kept in mind to make a correct diagnosis [1]. These conditions include esophageal motility disorders, eosinophilic esophagitis (EoE), drug-induced esophagitis (DIE), infectious esophagitis such as candidiasis or herpetic esophagitis, and malignancies [1]. Further to the clinical presentation, these esophageal conditions may also share endoscopic and histologic findings, resulting in difficult differential diagnosis [2].

Case Presentation

In July 2022 a 21-year-old male was admitted to the emergency room for acute dysphagia and a foreign body sensation after the ingestion of a tablet of ascorbic acid used as a vitamin supplement after flu syndrome. He was a young healthy man, with a negative medical history and he was not currently taking any other medications.

During the hospitalization, he first underwent routine laboratory tests, all resulted within the normal range values and then an esophagogastroduodenoscopy (EGD). The endoscopy showed two ulcers of 5 mm in diameter (Figure 1a) situated in the middle esophagus at 18 cm below the upper esophageal sphincter (UES), with edema, exudates, and an isolated longitudinal furrow (Figure 1b) in the same esophageal tract. Multiple biopsy sampling for histologic assessment was performed limited in the affected areas, and the endoscopist concluded the report with "endoscopic signs suggestive of eosinophilic esophagitis (EoE)".

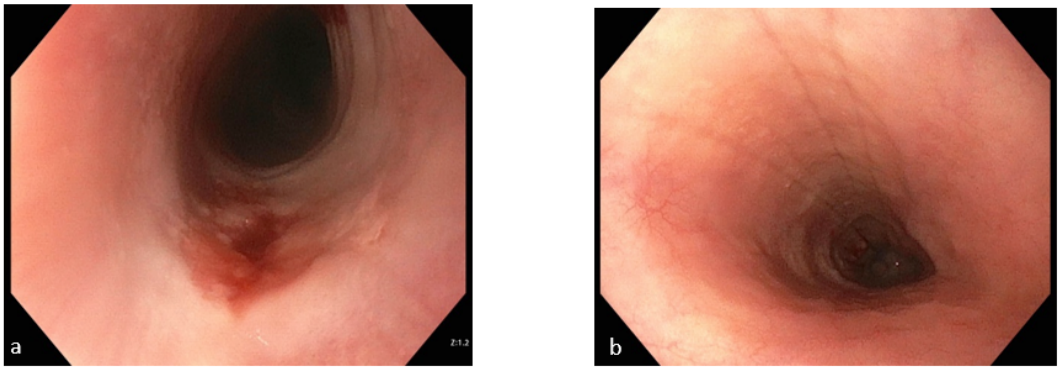

Figure 1: Esophagogastroduodenoscopy (EGD) during hospitalization after the impact episode, showing kissing ulcers (1a) and longitudinal furrows (1b) in the middle esophagus.

The histological report revealed a rich inflammatory infiltrate with 20 eosinophils/high-power field (HPF), neutrophils and lymphocytes, basal cell hyperplasia, and elongated acanthosis epithelium. The gastroenterologist, based on endoscopic and histological data suggestive of EoE, prescribed a first-line therapy with a proton pump inhibitor (PPI, pantoprazole 40 mg/bid for 8 weeks). Furthermore, patients underwent an allergy blood test for food and environmental allergens, resulted in all negative, except for a mild dust allergy.

The patient achieved a rapid clinical remission, and then independently discontinued the PPI therapy due to poor compliance.

In February 2023, during an outpatient evaluation, although the patient reported no symptoms since the impact episode, based on the endoscopic and histological result, the gastroenterologist highlighted the importance of the medical therapy to avoid EoE complications, modified the therapy and prescribed him a topical corticosteroid (Budesonide orodispersible tablets, 1 mg/bid). Also, in this case, the patient has never taken this drug.

In August 2023 the patient came to our gastroenterology outpatient center for a second opinion. We prescribed a second-look endoscopy to perform biopsies from both the distal and proximal esophagus, missing in the first EGD, as well as in the stomach.

Gastroscopy was macroscopically negative and histological reports were normal both in the esophagus and in the stomach. In an outpatient evaluation in October 2023, the patient continued to be asymptomatic, no further impact episode occurred, thus, no specific therapy was prescribed.

Discussion

This case represents a classic example of a challenging diagnosis between EoE and drug-induced esophagitis (DIE).

The young age and male sex of the patient, the mild atopic history (dust allergy), and the eosinophilic infiltrate on the histological report, were all confounding factors that wrongly led the specialist to diagnose EoE.

In clinical practice is essential to look beyond the eosinophilic infiltrate and consider the whole clinical history of the patient. In this case, he never showed typical symptoms of EoE such as food bolus impaction or history of esophageal dysphagia, and other causes of esophageal eosinophilia were not adequately investigated [3]. The endoscopic pattern was not completely characteristic because only the middle esophagus was involved [3]. Finally, the histopathological features did not match with EoE criteria, showing a mixed infiltrate with neutrophils and lymphocytes in addition to ≥15 eosinophils/HPF. Moreover, no further pathognomonic hallmarks such as eosinophilic microabscesses, eosinophil degranulation, surface desquamation, or lamina propria fibrosis were found [4].

Furthermore, sampling of the esophagus was limited to the affected area, representing a confounding factor and malpractice in endoscopy. Biopsies need to be taken from both proximal and distal esophagus with a minimum of 6 biopsies. Notably, 6 - 9 mucosal biopsies yield a near 100% diagnostic sensitivity [5] despite a single biopsy sensitivity of 55% [4].

In this scenario, taking an accurate clinical history would have avoided the incorrect diagnosis of EoE, as the impact episode was closely related to the ingestion of a drug known to cause DIE and especially since it was a single and transitory episode.

DIE was first reported in 1970 by Pemberton in a patient with esophageal ulcers after taking potassium chloride tablets [6,7]. From that time, most of the studies available on DIE are case reports and reviews of case reports, which provide a limited understanding of this condition.

DIE is an uncommon cause of esophagitis with an estimated incidence of 3.9/100.000/year [6]. To date, hundreds of drugs have been recognized as possible causes, mostly antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), anti-hypertensive and ascorbic acid (Table 1) [8].

Causative Drugs of Drug-Induced Esophagitis
Antibiotics: Tetracyclines, Especially Doxycycline, Clindamycin, Amoxicillin, Metronidazole, Ciprofloxacin, Rifaximin, etc.
Nsaids
Bisphosphonates: Alendronate, Ibandronate
Ascorbic Acid
Potassium Chloride and Ferrous Sulfate
Acetaminophen
Warfarin
Chemotherapeutic Regimens: Actinomycin, Daunorubicin, Bleomycin, Methotrexate, 5-Fluorouracil, Cytarabine, and Vincristine
Other Medications: Anti-Hypertensives, Quinidine, Glimepiride, Tiropramide, Pinaverium Bromide, etc.

Table 1: Potential causative drugs of drug-induced esophagitis. NSAIDs: Non-steroidal Anti-Inflammatory Drugs [8].

Common symptoms of DIE include retrosternal pain, heartburn, dysphagia, or odynophagia which are often transitory and self-limiting [7]. Major endoscopic findings are more often seen in the middle esophagus and include ulcers (typically "kissing ulcers", ulcer facing each other), bleeding, erosions, coating, impacted pills, and strictures [7]. Histologically, there are no specific features of drug-induced injury, and common findings are intraepithelial eosinophils and eosinophil abscess, intraepithelial neutrophils, dilated intercellular spaces, vacuolization of keratinocytes, basal layer hyperplasia and subepithelial papillary elongation [9]. Notably, many histologic features are shared with other esophageal conditions, i.e. GERD and EoE (Table 2) [7,9].

	DIE	GERD	EOE
Intraepithelial eosinophils	+	+	+++
Intraepithelial eosinophils abscess	+/-	+/-	+++
Surface eosinophils layering	n.a.	n.a.	++
Intraepithelial neutrophils	+++	+++	+/-
Intraepithelial lymphocytes	++	++	+/-
Dilated intercellular spaces	+	+	+
Vacuolization of keratinocytes	+	+	+/-
Dyskeratotic epithelial cells	n.a.	n.a.	+
Basal zone hyperplasia	+	+	++
Subepithelial papillary elongation	+	+	+
Lamina propria fibers	n.a.	n.a.	++

Table 2: Histologic findings of Drug-Induced Esopagitis (DIE), Gastro-Esophageal Reflux Disease (GERD), and Eosinophilic Esophagitis (EoE) [2,9-11].

Among the esophageal conditions, EoE should be ruled out carefully because of its chronic nature which requires long-lasting follow-up and therapies [3]. No specific therapy is required for DIE, however, PPI and cytoprotective agents (i.e. sucralfate) can be prescribed for short-term treatment to favor esophageal healing [12], in addition to discontinuing the causative drug to ensure esophageal mucosa from further damage. Our patient underwent a short therapy with PPI (8 weeks) with no recurrence of symptoms after suspension, supporting the DIE diagnosis. In fact, conversely to EoE which is characterized by a high rate of relapse [13], DIE is mostly transitory and self-limiting [7].

Although DIE is often self-limiting, clinicians must be aware of its existence since its misdiagnosis can lead to serious complications such as ulceration with gastrointestinal bleeding, intramural esophageal hematoma, strictures, and rarely even perforation and mediastinitis [7,10]. Moreover, some clinical conditions such as dysphagia, old age, and anatomical alterations, may favor it, and therefore it must always be excluded in the presence of any of these situations [10].

Unfortunately, many clinicians do not recognize DIE as a possible cause of clinical and endoscopic signs of esophagitis, and this lack of awareness can lead to misdiagnosing this condition and to persistent exposure to the causative drug, resulting in more severe complications over time or wrong therapies.

In conclusion, healthcare professionals must consider DIE as a possible cause of esophageal injury. Since many esophageal disorders share clinical presentation, endoscopic findings, and even histology, a global evaluation of the patient, with particular attention to medical history, must be performed before making the diagnosis and deciding on treatment.

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Informed Consent: Informed consent was obtained from the patient included in the case report.

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