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Eosinophilic esophagitis manifesting as intractable hiccups in an elderly patient: a case report

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Abstract

Background Eosinophilic esophagitis is a condition characterized clinically by symptoms related to esophageal dysfunction and histologically by a marked eosinophilic infiltrate in the esophageal mucosa. The most typical symptoms of eosinophilic esophagitis include intermittent dysphagia with episodic food impaction and heartburn with propensity for young individuals. The relationship between hiccups and eosinophilic esophagitis is unclear but has been described.

Case report We report a case of a 93-year-old Middle Eastern male presenting for longstanding treatment-refractory hiccups. Imaging with computed tomography of the chest and abdomen was unremarkable. An upper endoscopy was normal without any endoscopic finding to suggest eosinophilic esophagitis. Given his elevated peripheral eosinophil count, biopsies were taken from mid- and distal esophagus and revealed eosinophilic infiltration in the range of 15 eosinophils per high-power field, favoring a diagnosis of eosinophilic esophagitis. The hiccups resolved following the initiation of eosinophilic esophagitis treatment.

Conclusion This case underscores the need to consider the diagnosis of eosinophilic esophagitis in the setting of chronic refractory hiccups.

Keywords Eosinophilic esophagitis, Refractory hiccups, Vagal nerve, Phrenic nerve

Background

Eosinophilic esophagitis (EoE) is a condition characterized clinically by symptoms related to esophageal dysfunction and histologically by a marked eosinophilic infiltrate in the esophageal mucosa. The etiology and pathogenesis of EoE have not been fully elucidated. Many studies suggest that allergic and genetic factors play the most important role in the pathogenesis of EoE [1]. This condition is commonly recognized among pediatric and adult patients with a preponderance of males between 20 and 50 years of age [1, 2]. The incidence of EoE in individuals above 70 years of age is very low, and the association of EoE with hiccups has been rarely described in medical literature [3]. This article intends to discuss a case of EoE in an elderly male presenting with chronic refractory hiccups. The relationship between hiccups and EoE is not well established. Only two case reports describe an association between chronic hiccups and EoE in young patients [4, 5]. This article underscores the need to recognize this possible association.

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Case report

We present a case of a 93-year-old Middle Eastern male patient with no known food or drug allergies who was known to have hypothyroidism, hypertension, and dyslipidemia. The patient was admitted to the hospital owing to fatigue and refractory hiccups lasting for 2 weeks. He had had hiccups intermittently for more than 2 years and had tried several medications, including proton-pump inhibitors (PPIs), chlorpromazine, and baclofen, with minimal relief of his symptoms. His home medications include levothyroxine, amlodipine, and rosuvastatin. On review of systems, he denies dysphagia, odynophagia, food impaction, heartburn, vomiting, or weight loss. Physical examination was unremarkable. Laboratory studies were only pertinent for an elevated eosinophil count of 18% with a white blood cell count of 9000 per mL. Stool studies were negative for parasitic infection.

Imaging with computed tomography of the chest and abdomen was unremarkable. An upper endoscopy was subsequently performed and was normal, without any endoscopic finding to suggest EoE. Given his elevated peripheral eosinophil count, biopsies were taken from the mid- and distal esophagus and revealed eosinophilic infiltration in the range of 15 eosinophils per high-power field favoring a diagnosis of EoE.

The patient was prescribed a proton-pump inhibitor twice daily in combination with baclofen. Despite partial initial improvement, the symptoms of intractable hiccups recurred, and the decision was made to switch therapy to topical budesonide 2 mg twice daily 30 minutes before meals. The frequency of the hiccups episodes gradually decreased and resolved completely within a week. Repeat blood test showed a decrease in eosinophilic count to 10%. A repeat endoscopy was offered but declined by the patient.

Discussion

EoE is a chronic immune mediated food-antigen driven esophageal disease typically diagnosed through a combination of clinical and pathological features. The diagnosis of EoE can be challenging and is often delayed. EoE affects individuals across all age groups, with a propensity for young adults and children, particularly white males. The condition is often associated with genetic predisposition, environmental exposures, and a personal or family history of allergic conditions [1]. It is found in 2–7% of patients undergoing endoscopy for any reason, but this percentage increases to 12–23% for patients undergoing endoscopy for dysphagia [6].

The pathophysiology of EoE is not fully elucidated. One plausible theory is that antigen exposure stimulates the esophageal mucosa to secrete alarmins, IL-23, and thymic stromal lymphopoietin (TSLP) [7]. These cytokines activate T-helper type 2 (Th2) cells, which in turn release IL-13, IL-4, and IL-5 [7]. The secretion of IL-13 and IL-4 drives basal cell hyperplasia and dilated intra-cellular spaces at the level of the esophageal epithelium. Additionally, chemotaxins, eotaxin-3, and IL-5 mediate granulocyte infiltration of the esophageal epithelium. The interplay of cytokines is conducive to the activation of fibroblasts in the lamina propria, collagen deposition, and tissue stiffness, resulting in the formation of esophageal rings and furrows [7]. However, the esophageal mucosa may exhibit a normal appearance on endoscopy in approximately 10–25% of patients with EoE, as was exemplified in our patient [7].

There has been a consistent increase in the prevalence of EoE, with reports indicating its high prevalence in regions such as North and South America, Europe, Asia, and Australia [6]. In a cohort study conducted in the USA, 363 cases of EoE were reported among 74,162 patients across 26 states. The study showed a male predominance, with ages ranging from 1 to 98 years, and a mean age of 37 years, with the highest proportion of cases found in the 30–40-year age range. Only a small percentage of cases (less than 4%) were found in individuals over 70 years old. The most common symptoms prompting endoscopy in adults and the elderly were dysphagia (70.1%) and heartburn (27.1%), while children predominantly reported heartburn (38.1%) and dyspepsia (31.0%) [8]. Hiccups are not reported as typical symptom in large epidemiologic studies.

Prolonged hiccups lasting more than 48 hours are uncommon and may indicate underlying serious conditions such as structural, infectious, or inflammatory disorders affecting the central nervous system, vagus nerve, phrenic nerve, or their branches [9]. EoE presenting with hiccups has been only reported in two cases, the first in a 24-year-old woman with 3-year history of hiccups and dyspepsia and the second in a 7-year-old boy presenting with longstanding symptoms of throat clearing, excessive night time cough, and hiccups [4, 5]. The pathogenesis linking esophageal disease to hiccups is unclear, but one proposed mechanism suggests that esophageal receptors send impulses via the vagal nerve to respiratory motor neurons, resulting in hiccups [5]. Despite the typical endoscopic findings of esophageal trachealization characterized by the presence of multiple rings, linear furrows, and white exudates in EoE, it is important to recognize that the esophagus may appear normal on endoscopy and the diagnosis is only made histologically when random biopsies are taken from the esophagus. A retrospective study looking at 381 patients diagnosed with EoE revealed esophageal anomalies in 68% of cases, while 32% exhibited a visually normal esophagus despite pronounced histologic eosinophilia [10].

The gold standard for diagnosing EoE is the finding of more than 15 eosinophils per high-power field on histological examination from biopsied esophageal samples [1]. Elevated serum IgE levels with peripheral eosinophilia are seen in approximately 50% of cases [11]. EoE is known to manifest in a patchy manner throughout the esophagus, and studies have demonstrated that obtaining five biopsies from the esophagus can increase the sensitivity of diagnosis to 100% [12].

Treatment options for EoE include elimination diet, PPIs, and topical steroids [1]. Comparative studies examining the effectiveness of PPIs, steroids, and dietary modifications are limited, with only small case series available for analysis [13]. Most studies recommend initiating standard full-dose PPI once daily, with the option to escalate to twice daily if symptoms persist after 4 weeks of therapy [14]. In cases of persistent symptoms, alternative therapies such as topical glucocorticoids may be considered [13]. Among topical glucocorticoids, fluticasone and budesonide have been the most extensively studied agents for the treatment of EoE. In a randomized trial comparing budesonide with fluticasone in 129 adult patients with a new diagnosis of EoE, both drugs showed similar improvements in symptoms of dysphagia, endoscopic features, and reduction in esophageal eosinophil count [15]. Benralizumab is currently under investigation for treating EoE. Benralizumab is an eosinophil-depleting monoclonal antibody directed against IL-5 receptor alpha. In a trial comparing benralizumab with placebo in 211 older children and adults with symptomatic EoE, benralizumab resulted in higher rates of histological remission after 24 weeks. However, dysphagia symptom scores and endoscopic severity scores were not significantly different between the groups. These findings highlight the discordance between histologic and symptom response in EoE and the need for additional biomarkers for evaluating response to investigational therapies [16].

In our case, one could argue that the increased eosinophils are due to gastroesophageal reflux disease rather than EoE since, unlike the other two reported cases in the literature, the number of eosinophils were at the lower limit needed for the diagnosis of EoE and the typical endoscopic features for EoE were absent. However, the persistence of symptoms while on PPI therapy and their improvement when topical steroids were used argue in favor of the diagnosis of EoE. A decrease in the esophageal eosinophilia on repeat endoscopy would have been helpful but could not be done in this case due to patient's preference.

Conclusion

EoE should be considered in the differential diagnosis in patients presenting with chronic refractory hiccups even when the typical symptoms of EoE are lacking, and prompt treatment with topical steroids should be considered.

Abbreviations

EoE Eosinophilic esophagitis
PPI Proton-pump inhibitors

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Author contributions

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Availability of data and materials

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Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors have no relevant financial interests and no potential conflicts of interest to disclose.

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