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# "THE ONE RING" AND EOSINOPHILIC ESOPHAGITIS AS TRICKY TRIGGERS OF REFLUX SYMPTOMS – A CASE REPORT AND LITERATURE REVIEW

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**ABSTRACT**

**Background:** eosinophilic esophagitis (EoE) and Schatzki ring are distinct conditions, but their clinical presentation may resemble one another. Moreover, they can closely mimic the third common disorder, that is gastroesophageal reflux disease (GERD) making a patient diagnostic approach even more challenging.
**Aim of the study:** presentation of a case with EoE with coexistence of Schatzki ring and related subject literature review.
**Materials and methods:** one case of non-specific GERD symptoms and gradual dysphagia development. Literature review of existing reports and data regarding epidemiology, clinical presentation, and diagnostic approach to patients with EoE suspicion. Presentation of the current guidelines on disease management. Additionally, we discuss the medical challenges that may occur in patients with esophageal dysfunction and highlight that further studies are warranted to better explain EoE's long-term impact on patient outcomes.
**Conclusions:** EoE has become increasingly recognized over the last decade, but may still create a clinical challenge. Its symptoms vary with age, and pathogenesis is still not fully explained. Experts in the field recommend special criteria for diagnosing EoE, which should be followed to establish the proper diagnosis. Further studies are warranted to better explain EoE's pathophysiology and long-term impact on patient outcomes.

**KEYWORDS**

Eosinophilic Esophagitis, Schatzki Ring, Dysphagia

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## Introduction

Eosinophilic esophagitis (EoE) and Schatzki ring are distinct conditions, but their clinical presentation may resemble one another. Moreover, they can closely mimic the third common disorder, that is gastroesophageal reflux disease (GERD) making a patient diagnostic approach even more challenging.

Currently, EoE is an increasingly diagnosed chronic inflammatory disease of the esophagus connected with the infiltration of its mucosa with eosinophils resulting in further organ dysfunction. The most common symptoms presented by adult patients are dysphagia, food impaction, heartburn and chest pain [1].

Similar symptoms may occur in patients with the Schatzki ring, also known as the lower esophageal mucosal ring. It is a circular structure consisting of mucosa and submucosa located at the squamocolumnar junction of the distal esophagus. The development of the Schatzki ring may result in narrowing the esophageal lumen causing problems with food passage [2].

Proper clinical assessment and accurate diagnosis are essential to determine the effective treatment and control of patients' symptoms as well as to prevent esophageal dysfunction and fibrosis. We describe the case of a young adult patient with gradual dysphagia development and introduce the diagnostic steps leading to the final diagnosis.

## Case description

A man aged 29 with recurrent heartburn and noncardiac chest pain without alarm symptoms has been treated for several years with empiric antacids and proton pump inhibitors (PPI) as recommended for young patient groups. Since gradually increasing dysphagia has developed, he decided to seek a doctor's consultation and presented to the Gastroenterology clinic in Luxmed Medical Center in Lublin. He suffered from recurrent heartburn and mild dysphagia that occurred only from time to time and did not seem to be a serious problem for him. Nevertheless, problems with food swallowing gradually increased over the last two or three years.

On his first visit, a detailed medical history was taken, and other than GERD comorbidities were excluded. Allergies were also dismissed. He followed no special diet. As for bad habits, he smoked 2 to 5 cigarettes per day and drank about 3-4 beers during weekends, rarely more alcohol only several times a year.

On routine physical examination, no existing alterations were identified. He seemed to suffer from isolated gastroesophageal reflux disease without extraesophageal symptoms but otherwise he was healthy. As his dysphagia and episodes of food impaction started to respond less adequately to the treatment and recured more frequently increasing concerns about the presence of an organic disorder, the patient started to think about diagnostic testing.

He was referred to perform diagnostic gastroscopy. The procedure revealed characteristic abnormalities of the esophageal mucosa such as rings not modified by esophageal peristalsis and white exudates, together with an additional finding located at the squamocolumnar junction of the distal esophagus. A circumferential membrane-like stricture known as a Schatzki ring was found there. The ring did not impede the scope moving through into the stomach, so the other parts of the upper gastrointestinal (GI) tract were also assessed, and they were normal. The endoscopic presentation of the patient's upper GI tract is shown in **Figure 1.**

Since there was an endoscopic suspicion of EoE, 6 biopsy of mucosa samples were obtained from 2 distinct locations i.e. the proximal and distal regions of the esophagus. Initially, just as in Tolkien's story, our medical attention due to patient dysphagia was focused on a single esophageal lesion, "the One Ring," until the patient returned with the results of the histopathological examination. Histopathology of all mucosa samples taken from both the upper and lower parts of the esophagus revealed changes consistent with EoE described as squamous epithelial hyperplasia with increased intraepithelial eosinophils ≥15 per high-power field (hpf). The final diagnosis of EoE was confirmed. Based on expert recommendations [3,4], the patient met all the criteria for EoE diagnosis including:

1. infiltration of esophageal mucosa with eosinophils (≥ 15 eosinophils/hpf);
2. symptoms of esophageal dysfunction;
3. exclusion of other factors that give rise to esophageal eosinophilia.

After the identification of the coexistence of EoE and Schatzki ring the multidisciplinary treatment approach was indicated. First of all, an elimination diet with avoidance of cow's milk (the most frequent EoE trigger in all age groups), wheat, and eggs was introduced by a nutritionist. Also, a swallowed topical glucocorticoid (budesonide tablets) was added, and the PPI treatment was continued as the patient presented a PPI-responsive disorder. PPI benefits (eg. mucosal integrity improvement, anti-inflammatory effects, reverse endoscopic features of fibrosis) in adults and children with EoE were suggested by numerous reports [5, 6, 7]. Nevertheless, in the subgroup of EoE patients with good clinical response to PPIs, it did not correlate with histological response [8]. A prediction of PPI effects in patients diagnosed with esophageal eosinophilia requires further investigation.

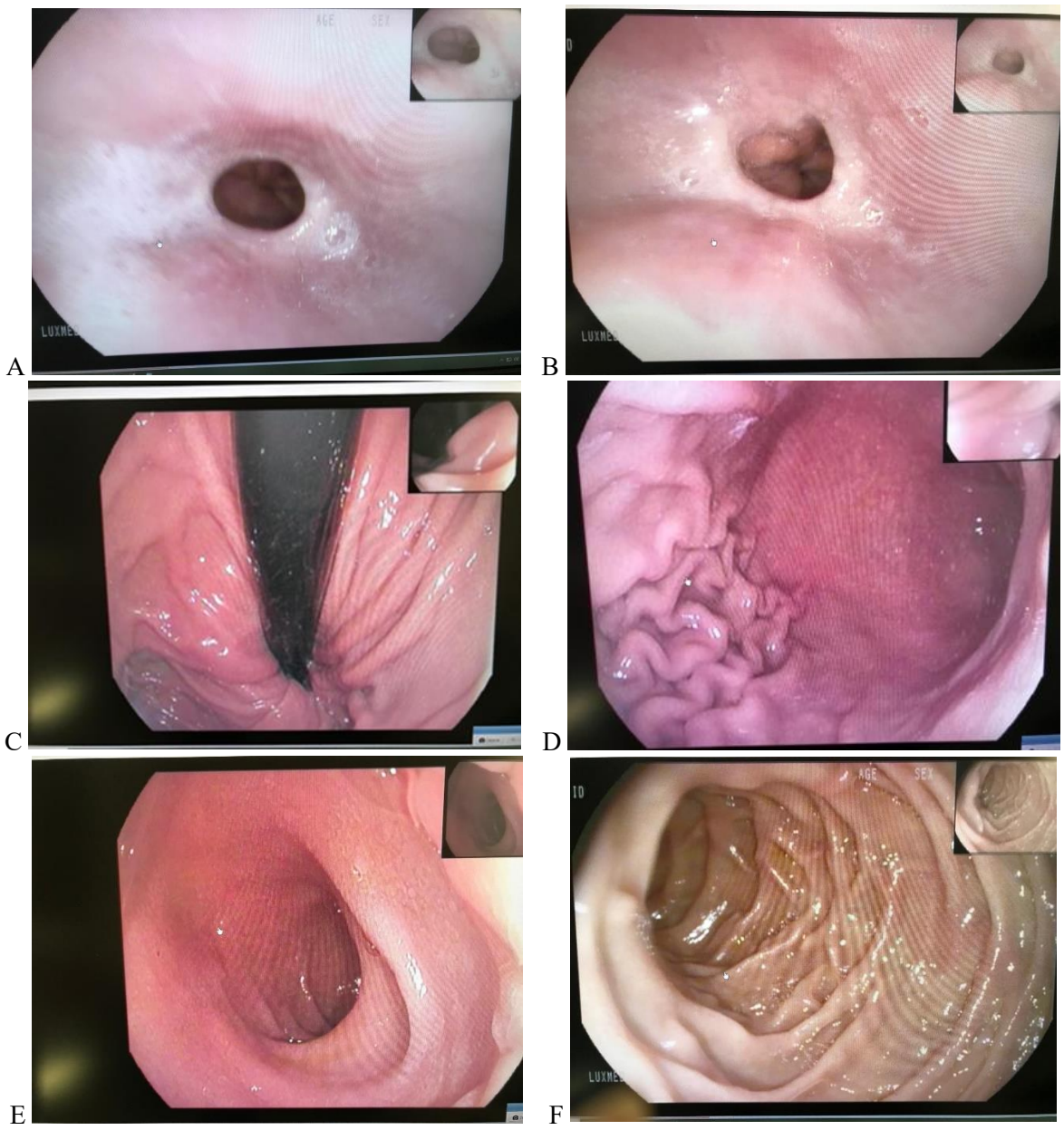


***Fig. 1.*** *Endoscopic presentation of the patient's upper GI tract.*
*A, B- lower esophagus with the Schatzki ring; C- gastric cardia; D- gastric body and pyloric antrum; E- duodenal bulb; F- descending part of the duodenum*

Moreover, the patient was referred to the Schatzki ring's endoscopic dilation. Figure 2 presents the summary of our patient's history and management.

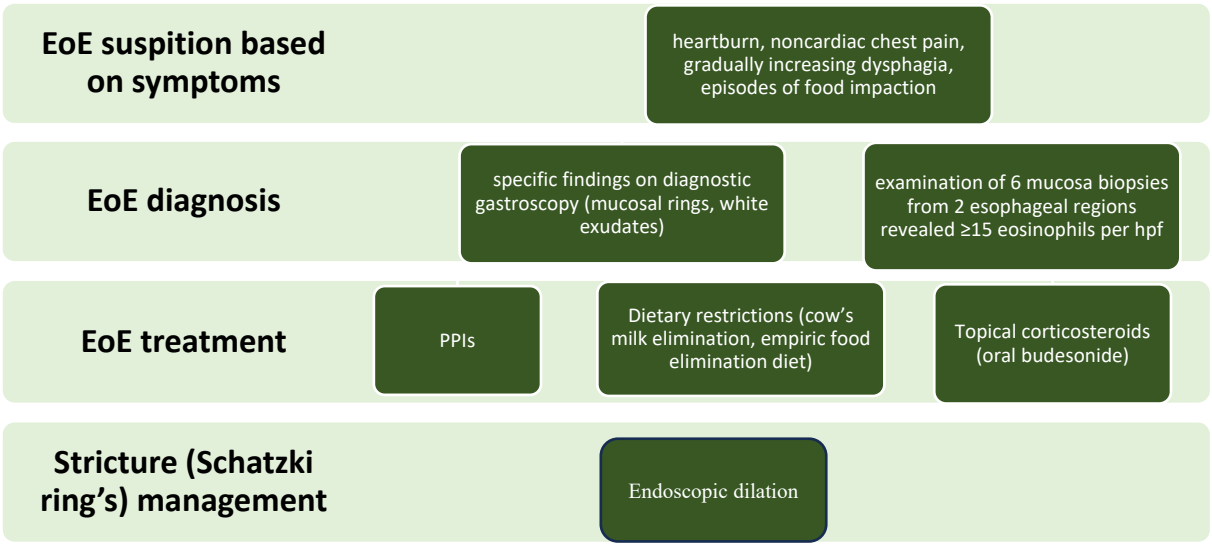


***Fig. 2.*** *The patient's history and management.*

**Literature review**

We performed a literature review of existing reports and data regarding epidemiology, clinical presentation, and diagnostic approaches to patients with EoE suspicion. The current guidelines on disease management are also analyzed. We discuss the medical challenges that may occur in patients with esophageal dysfunction. EoE-associated details are analyzed against the ones of the Schatzki ring to assess and compare similarities and differences. Numerous signs and symptoms might not be specific, so a careful differential diagnosis is required to establish the proper diagnosis, choose the targeted treatment, and prevent complications. In patients with dysphagia, food impaction, heartburn or chest pain, diseases like GERD, EoE, Schatzki ring, other esophageal strictures and/or malignancy should be considered [2]. While some of the aforementioned disorders can be confirmed based on the endoscopic examination, others require more advanced evaluation.

**Eosinophilic esophagitis**

According to recent reports, the global pooled incidence and prevalence of EoE have increased particularly in high-income countries and in men and showed 5.31 cases per 100,000 inhabitant-years and 40.04 cases per 100,000 inhabitant-years, respectively [9]. The clinical signs and symptoms of EoE are non-specific and may change with age. They differ significantly in children in comparison to adults. In infants and young children feeding difficulties, vomiting, abdominal pain, and poor weight and height gain predominate [10]. The adolescent and adult spectrum may vary from heartburn, acid regurgitation, and mild dysphagia to severe episodes of food impaction. Therefore, misdiagnosis or diagnostic delay frequently may occur. Current guidelines and criteria of the EoE Endoscopic Reference Score (EREFS) with the simultaneous detection of at least fifteen eosinophils per high power field at esophageal mucosa microscopic examination enables appropriate diagnosis [11]. The features of eosinophilic esophagitis (linear furrows, mucosal rings, small caliber esophagus, white plaques and/or exudates, strictures) are not always visible on endoscopy. Therefore, the gold standard is a microscopic examination of biopsy samples taken from the proximal and distal esophagus. The eosinophilic infiltration might vary in different parts of it. Therefore, it is recommended to obtain at least 5-6 samples. The final diagnostic criteria for the EoE include: infiltration of esophageal mucosa with eosinophils (≥15 eosinophils/hpf), symptoms of esophageal dysfunction, and exclusion of other factors that give rise to esophageal eosinophilia. The treatment of EoE includes an empiric elimination diet (avoidance of the most common food allergens: dairy/milk, eggs, soy, wheat, peanuts, and seafood) [1]. According to the recent study a simple 1-food elimination diet (FED) (dairy products) seems to be as effective as a 6-FED [12]. Moreover, PPIs at high doses (e.g. omeprazole 40 mg twice a day) induce remission in 30-50% of patients. Swallowed topical corticosteroids (budesonide, fluticasone) are strongly recommended with the best response

among older patients and those suffering from food allergies. Systemic immunosuppression (prednisone) can lead to a greater degree of histologic response than swallowed fluticasone, but the clinical response to both mentioned medications does not vary significantly. If untreated, EoE results in fibrostenosis and esophageal remodeling, causing narrowing of its lumen and increasing the risk of food impaction [13]. For patients who are refractory to the above-mentioned therapy, the monoclonal anti-IL4/13 antibody Dupilumab is an alternative therapeutic option. Currently, it is the only biologic therapy approved by the European Medicine Agency and US Food and Drug Administration for the treatment of EoE [14]. The patient's response to treatment should be assessed after 6 to 12 weeks based on endoscopy and repeated mucosa sampling. However, either EoE treatment response or treatment endpoints have not been clearly defined so far [15].

Since discrepancy between clinical presentation and histological EoE activity is frequent, patients should be monitored by repeated esophagogastroscopy with mucosa biopsies every 1–2 years, even if they are asymptomatic [3].

Beveridge et al. observed a high prevalence of persistent EoE symptoms despite histologic remission in adults with mental disorders (i.e. anxiety, depression), esophageal fibrostenosis, or only partial resolution of histological disease activity [16].

Of note, a recent report indicates that the risk of Barrett's esophagus (BE) and esophageal cancer (EC) in patients with EoE is similar to that of the average population, so they should follow standard BE screening recommendations [17].

**The Schatzki ring**

The Schatzki ring presents as a benign, circular tissue fold located at the gastroesophageal junction. Although in most of the patients it causes no symptoms, some of them may have intermittent solid food dysphagia which may be confused with EoE-related strictures, therefore, microscopic evaluation is crucial [18]. Various types of esophageal rings and webs might be revealed during gastroscopy and should be distinguished from each other. Circumferential mucosa rings throughout the esophagus are the hallmark of EoE. On the other hand, the single esophageal ring located at the esophagogastric junction is referred to as a Schatzki ring and is covered by squamous epithelium on the esophageal side and by columnar epithelium on the gastric side of the membrane [19].

The prevalence of esophageal webs in the general population is not well established so far due to a shortage of clinical studies [19]. The predominant symptoms of the Schatzki ring include dysphagia to solid foods or pills and food impaction, but it may be asymptomatic too. It has been called the "steakhouse" or "backyard barbeque" syndrome. Perforation is a rare complication of the ring. As previously stated, a similar presentation may occur in EoE, so differential diagnosis is mandatory. There is some evidence linking the development of Schatzki rings and GERD [19, 20].

The diagnostic procedure of choice conducted when Schatzki ring is suspected is a barium esophagram which in the subgroup of patients may be more accurate in comparison to esophagogastroscopy. On radiographic images, it can reveal a circumferential structure in the distal esophagus. Endoscopic examination is also advised in order to rule out malignancy or other causes of stricture. If an irregular Z-line is found, Barrett esophagus should be excluded. The treatment of the Shatzki ring includes endoscopic dilation using bougies or pneumonic balloons. The procedure usually requires repetition as in up to 64% of patients the stricture re-occurs in the first 2 years. If the Schatzki ring does not cause any symptoms, it does not require treatment [2].

**Conclusions**

EoE, a chronic immune-related disorder of the esophagus, has become increasingly recognized over the last decade, but may still create a clinical challenge. Its symptoms vary with age, and pathogenesis is still not fully explained. Experts in the field recommend special criteria for diagnosing EoE, which should be followed to establish the proper diagnosis. With a better understanding of the pathogenesis of this complex disease, the diagnostic approach to patients with EoE suspicion, their treatment, and monitoring have significantly improved and may change patient prognosis. Further studies are warranted to better explain EoE's pathogenesis and long-term impact on patient outcomes.

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