

Eosinophilic Gastrointestinal Disorders

Eosinofilik gastrointestinal hastalıklar

Öz

Eosinofilik gastrointestinal hastalıklar sindirim sisteminin farklı bölümlerinde fazla miktarda eosinofil birikimiyle karakterizedir. Eosinofilik gastrointestinal hastalıklar tutulum bölgesine göre eosinofilik özefajit, eosinofilik gastroenterit ve eosinofilik kolit olarak alt kategorilere ayrılır. Bu hastalıklar hem çocuk hem de erişkin popülasyonunda gittikçe artan bir sıklıkta tanı almaktadırlar. Tipik olarak 3. ve 5. dekatlarda görülmektedir. Eosinofilik gastrointestinal hastalıkların semptomları çeşitlidir ama bulantı, kusma, karın ağrısı, kilo kaybı ya da gelişme geriliği ve yutkunma zorluğu vardır. Ana tedavi seçeneklerini steroidler ve diyet değişiklikleri içerir. Bu yazıda son çalışmalar ışığında eosinofilik gastrointestinal hastalıklar gözden geçirildi.

Anahtar Kelimeler: eosinofil, gastrointestinal, inflamasyon, patogenezi, tedavi.

Abstract

Eosinophilic Gastrointestinal Disorders are caused by excessive levels of eosinophils in various parts of the gastrointestinal tract. There are several subcategories of eosinophilic gastrointestinal disorders including eosinophilic esophagitis, eosinophilic gastroenteritis and eosinophilic colitis. These diseases has become increasingly recognized recently in both pediatric and adult populations. Symptoms of eosinophilic gastrointestinal disorders are nausea, vomiting, diarrhea, abdominal pain, poor growth or weight loss and dysphagia. Main therapeutic options are steroids and dietary modification. In this article we tried to review eosinophilic gastrointestinal diseases under the highlight of the recent studies.

Keywords: Eosinophil, gastrointestinal, inflammation, pathogenesis, therapy

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Introduction

Eosinophilic gastrointestinal disorders (EGIDs) are characterized by gastrointestinal symptoms and increased eosinophils in the intestinal mucosa; the first and earliest comprehensive descriptions were provided by Kaijser and Klein et al. They proposed a novel classification system that separated patients with intestinal eosinophilia into anatomically distinct groupings that was mucosal, muscular, or serosal diseases, depending on where the predominant eosinophilia was located (1,2).

Epidemiology

Scant population-based data is available on incidence, prevalence, and racial diversity of EGIDs. Incidence of these diseases is increasing recently in both pediatric and adult populations. The best-documented EGIDs is eosinophilic esophagitis (3,4).

The incidence of Eosinophilic esophagitis (EoE) may be as high as 1:1000 individuals (5). In a population-based study of adults in Sweden, it is estimated that esophageal eosinophilia is present in about 1% of the population (6). The rapid rise in prevalence of EoE has been documented in several populations and is consistent with changing environmental exposure in vulnerable individuals. It occurs most commonly in the 30s and 50s. There is a male predominance at 3:1 (7).

There is a little data about the epidemiology of Eosinophilic gastroenteritis (EgE). Reported cases of EgE show no predominance of individuals any gender or race. Estimated prevalence of EgE or colitis in United States is 28 per 100,000 (8).

Pathogenesis

The physiopathological mechanism of EGIDs seems to be comprised of mixed disturbances, sharing characteristics of IgE-mediated disorders (oral allergy syndrome and food-triggered anaphylaxis) and exclusively cell-mediated disorders (celiac disease or food protein-induced colitis). A Th2-type immune response seems to be involved in both EoE and EgE. In fact, IL-5 and IL-13, together with granulocyte-macrophage colony-stimulating factor and especially eotaxins may play a central role in the recruitment of eosinophils from circulating blood into tissues. EGIDs has been related to food allergies and also environmental and individual genetic factors effective in the pathogenesis (8).

Clinical evidences

The major symptom in adults with eosinophilic esophagitis is difficulty on swallowing solid food (dysphagia). Specifically, the food gets stuck in the esophagus after it swallows. Less common symptoms are heartburn and chest pain (9). With regard to pediatric forms of EoE, the first descriptions of gastroesophageal reflux disease-related symptoms in the literature were predominantly reported in children. Other symptoms commonly reported for children are nausea, gagging, regurgitation, chest pain, sialorrhea, decreased appetite or food aversion, delayed growth, sleep difficulties and respiratory complaints (cough, stridor, sinusitis, obstruction and pneumonia) (10).

Eosinophilic gastroenteritis typically presents with a combination of chronic nonspecific gastrointestinal symptoms which include abdominal pain, nausea, vomiting, diarrhea, weight loss and abdominal distension (11). In an infant, EgE may present in a manner similar to hypertrophic pyloric stenosis with progressive vomiting, dehydration, electrolyte abnormalities and thickening of the gastric outlet (12).

Clinical presentation of eosinophilic colitis (EC) is highly variable according to mucosal, transmural, or serosal predominance of inflammation. Mucosa-predominant disease shows evidence of mucosal dysfunction such as protein-losing enteropathy, malabsorption, and diarrhea. Transmural disease is recognized by symptoms of intestinal obstruction and bowel wall thickening on imaging studies. Accordingly, while mucosal EC results with diarrhea, the transmural form is associated with volvulus, intussusception, and even perforation. Involvement of the intestinal serosa may manifest with ascite (13).

Eosinophilic proctocolitis (EpC), also known as allergic proctocolitis has been recognized. This disorder is characterized by the onset of rectal bleeding, generally in children less than six months of age (14).

Diagnosis

Patients with EGIDs present with a variety of clinical problems most commonly failure to thrive, abdominal pain, irritability, gastric dysmotility, vomiting, diarrhea, dysphagia, microcytic anemia and hypoproteinemia. Diagnostic evaluation for EGIDs should be performed on all patients with these refractory problems, especially

in individuals with a strong history of allergic diseases, peripheral blood eosinophilia and/or a family history of EGIDs. There are several symptoms depending on the involved intestinal segment (eg, abdominal pain and dysphagia are most common in EgE and EoE, respectively), but there are no pathognomonic symptoms or blood tests for diagnosis of EGIDs. Notably, blood eosinophil counts are normal in the majority of patients. If an EGID is suspected (on the basis of clinical presentation or evaluation of endoscopic biopsy specimens), then additional tests should be considered to rule out other possible disorders include primary disease process, such as drug hypersensitivity, collagen-vascular disease, malignancy or infection (15).

On endoscopy, it is common to visualize linear creases oriented longitudinally (furling) in patients with EoE. However, in EoE, endoscopic studies have shown strictures, mucosal rings, ulcerations, whitish papules, and polyps. In eosinophilic gastroenteritis, micronodules are noted on endoscopy, and these lesions often contain marked aggregates of lymphocytes and eosinophils. On endoscopic examination of patients with eosinophilic colitis, patchy erythema, loss of vascularity, and lymphonodular hyperplasia are seen typically localized to the rectum but may extend to the entire colon (3).

The definite diagnosis requires the existence of eosinophilia on the samples (16). The number of eosinophils in esophagus are more than 20 to 24 eosinophils/high-power fields is characteristic of EoE (3,17). An infiltration of >30 eosinophils per high-power field at least five high-power fields, exhibiting signs of eosinophilic degranulation and extending to the muscularis mucosa or submucosa are all histological indications of EgE, EC and EpC (8,18).

Radiological examinations generally do not provide much assistance in the diagnosis of EGIDs because they lack significant sensitivity or specificity. However barium studies may suggest the eosinophilic disorders by revealing oesophageal stenosis, gastric antral stenosis with mucosal irregularity, gastric pseudopolyposis, or thickening in the small bowel due to edema. Ultrasonography may show diffuse, nonspecific bowel wall infiltration and it can be useful in detecting ascites in the serosal form of eosinophilic gastroenteritis. CT findings of EGID depend on the layer of involved tissue, but generally consist of nodular and irregular fold thickening in the stomach, bowel wall thickening, mesenteric lymphadenomegaly and

luminal narrowing without obstruction (19).

The differential diagnosis of EGIDs include parasitic infections, hypereosinophilic syndrome, Crohn disease, milk protein enteropathy, Churg Strauss vasculitis, graft versus host disease, some malignancies and adverse effects of drugs (20).

Treatment

Treatment options include allergy test-guided elimination diet, empiric elimination diet and elemental diets. For dietary therapies, if specific food sensitivities can be identified, patients have responded to targeted elimination diets. In contrast, empiric elimination diets use historical knowledge gathered regarding IgE-mediated food allergy to select which foods to avoid. After disease remission is achieved with dietary therapy, foods are slowly added back into the diet (21,22).

For the treatment of EoE contains corticosteroids, proton pump inhibitor and esophageal dilation (23). The diagnosis of eosinophilic esophagitis should generally include demonstration of persistent esophageal eosinophilia after treatment with a proton pump inhibitor (or with a normal pH study) (24).

Most patients with EoE respond to topical glucocorticoids. The beneficial effects of corticosteroids in eosinophilic disorders are largely mediated by inhibition of eosinophil growth factors: interleukin-3, interleukin-5, and granulocyte-macrophage colony-stimulating factor. Swallowed fluticasone, ciclesonide, budesonide are effective. Recommended dosage for fluticasone is 880–1760 µg per day split into twice or four times daily dosing for 6–8 weeks. Use of systemic steroids has only been published in the paediatric population; a 4 week regimen of 1.5 mg/kg methylprednisolone may be effective (25,26).

Refractory or dependent on glucocorticoid therapy, azathioprine or 6-mercaptopurine are alternatives (15). Dilation of esophageal strictures effective for relieving dysphagia, but has no effect on underlying inflammation. It is often reserved for patients who have failed more conservative therapy, but may be required as initial therapy in patients with high-grade stricture (27).

Food allergy is considered one of the potential underlying causes of EgE. The elimination of pathogenic foods, as identified by any form of allergy testing or by random removal of the most likely antigens should be a first-line consideration. When the use of a restricted or

elemental diet fails, corticosteroids are often employed. Corticosteroids have been the most widely used drugs for treating EgE in both children and adults. Prednisone is used at doses of 0.5–1 mg/kg/daily, has proven highly effective in the initial control of symptoms. After an initial treatment period of 7–10 days, the dose is gradually reduced until the drug is withdrawn after a period of up to 4 months (28,29).

Prognosis

The long-term prognosis for patients with EoE is unknown. Some patients may follow a “waxing and waning” course characterized by symptomatic episodes followed by periods of remission. There have also been reports of apparent, spontaneous disease remission in some patients; however, the risk of recurrence in these patients is unknown. Currently, it is still unclear if dietary or medical therapy modifies the natural history of the disease (30).

The natural history of EgE remains largely unknown. Indeed, only few studies reported follow-up after treatment that was often limited and always described in small cases series (31).

The EpC that develops in infancy carries a good prognosis. It tends to spontaneously resolve, often within days. After a few years these young children can even tolerate the implicated foods. For young adults with EC, its natural history tends to become chronic with periods of activity and periods of apparent remission (32).

As a conclusion : Eosinophilic gastrointestinal disorders are rare. The pathophysiology of eosinophilic gastrointestinal disorders suggests the role of certain food or aeroallergens in a genetically susceptible individual. Although the diseases is more common in adult, children are also affected. Diagnosis requires high index of suspicion and exclusion of various disorders associated with peripheral eosinophilia. Corticosteroids have been used successfully to treat eosinophilic gastrointestinal disorders.

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