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SOME ASPECTS OF DIAGNOSIS AND TREATMENT OFEOSINOPHILIC ESOPHAGITIS

Yevstihnieiev Ihor Volodymyrovych
c. m. s., assistant
State Institution «Dnipropetrovsk
Medical Academy»
Dnipro, Ukraine
Poleshko Viktoriia Yuriivna
Road clinical hospital of station Dnipro of
State Enterprise «Prydniprovska Railway»
Dnipro, Ukraine

Abstract. In recent years, the number of publications on the pathogenesis, diagnosis and treatment of eosinophilic esophagitis (EoE) has increased. However, the lack of awareness of primary care physicians is the cause of late diagnosis and effective treatment of this disease. It is necessary to exclude EoE in all patients with dysphagia or dyspepsia, when the etiology is not specified and there is no effect of treatment.
Key words: eosinophilic esophagitis, pathogenesis, clinical, diagnostics, treatment

EoE is a chronic antigen-mediated disease with severe infiltration of the esophageal mucosa by eosinophils and clinical manifestations of esophageal dysfunction. The disease is one of the manifestations of atopic pathology, often combined with food allergies, atopic dermatitis, bronchial asthma and other diseases [1, p. 58].

In the pathogenesis of the disease, food and air allergens, a genetic predisposition and activation of type 2 helpers (Th2) are important. The role of food allergens in the development of EoE is confirmed by the effectiveness of the elimination diet in this disease. Exacerbations of EoE can be seasonal and related to the pollen production of

certain plants. Air and food allergens are triggers; in the presence of a hereditary predisposition, mechanisms of immunopathological reactions are activated [2, j4482]. After presentation of allergens and processing, Th2 is activated. These cells, together with mast cells, synthesize IL-4, IL-5, IL-13, activate fibroblasts, and stimulate the production of eotaxin-3. As a result, chemoattraction of eosinophils in the mucous membrane of the esophagus occurs [3, p. 506].

Eosinophil mediators lead to the development of fibrosis of the own plate of the mucous membrane, an increase in the height of the papillae of the basal layer of the epithelium and its hypertrophy. The progression of fibrosis leads to esophageal cramping, progression of dysphagia and further to the development of esophageal strictures [4, p. 5]. The latter recur with EOE more often than in patients with peptic ulcers with gastroesophageal reflux disease (GERD).

Diagnosis of EoE involves the establishment of a clinical and morphological diagnosis. *Big signs* of EoE include:

1) more than 15 eosinophils in the field of view of a high-resolution microscope (× 400) in the study of biopsy samples of the mucous membrane of the esophagus;

2) eosinophilic microabscesses (accumulation of 4 or more eosinophils in the epithelial layer);

3) superficially located eosinophilic infiltrates;

4) degranulation of eosinophils.

Small signs of EoE include:

1) hyperplasia of the basal layer (more than 20% of the thickness of the epithelium);

2) intercellular edema;

3) an increase in the number and lengthening of the papillae of the own plate of the mucous membrane (more than 75% of the thickness of the epithelium), its sclerosis;

4) an increase in the number of intraepithelial lymphocytes and mast cells.

In the EoE diagnostic algorithm, the following should be considered:

1. *Clinical features*: the presence of episodes of dysphagia and wedging food in the esophagus. The absence of a positive result of treatment for 2 months with high doses of proton pump inhibitors (PPI) eliminates GERD;

2. *Endoscopic features*: vertical grooves, circular rings, strictures, eosinophilic microabscesses, exudate.

A further strategy involves a multiple biopsy from the proximal and distal sections of the esophagus. Biopsy specimens of the mucous membrane of the stomach and duodenum are taken to exclude eosinophilic gastroenteritis. With EoE, the mucous membrane is not involved in these sections.

3. *Histological features*: in the presence of eosinophil infiltration, their degranulation, and the formation of microabscesses, the number of eosinophils in several biopsies with the highest density of eosinophil infiltration is counted.

After obtaining a result of ≥ 15 eosinophils in the fields of view with an increase in the microscope × 400 and the exclusion of other causes of eosinophilic infiltration, a trial treatment of PPI at a dose of 20-40 mg per day is performed depending on the drug for 8 weeks. After the end of the course of treatment, esophagogastroduodenoscopy (EGDS) is performed with a biopsy. If less than 15 eosinophils are detected in the fields of view with an increase in the microscope × 400 and positive dynamics of clinical symptoms are observed, a diagnosis of PPI-sensitive esophageal eosinophilia is established. Patients are observed with this disease and PPI is further treated.

If, after 8 weeks of treatment with PPI, after taking biopsies in the field of view with an increase in the microscope × 400, ≥ 15 eosinophils are determined, the clinical symptoms remain, the diagnosis of EoE is established, diet therapy and local corticosteroids are prescribed.

There are 3 main options for diet therapy. *Elemental mixtures* are expensive and not very palatable. The *elimination diet* involves the exclusion from the diet of the six most significant foods in the occurrence of atopic reactions: eggs, milk, wheat, nuts, soy, seafood [5, p. 614]. The diet is easier to tolerate and in ¾ patients, following the dietary recommendations, both the clinical symptoms and the histological picture improve [6, e155].

In a significant proportion of patients with dysphagia, PPI therapy leads to a significant improvement in clinical symptoms and histological manifestations. In

these patients, the diagnosis of EoE is more often excluded and further treatment of PPI-sensitive esophageal eosinophilia or GERD is carried out. This tactic allows you to not prescribe an unreasonable diet and topical corticosteroids [7, p. 1415].

With EOE, the use of PPI is also included in the treatment regimen, since EOE and GERD are often combined. In these patients, doses of PPI are 20-40 mg per day (depending on the drug), the course of treatment is 8-12 weeks. The high efficacy of topical corticosteroids in EOE is determined by a decrease in the synthesis of eosinophil growth factors (IL-5, GM-CSF) and eotaxin-3 chemoattractant.

Of the topical corticosteroids, fluticasone propionate and budesonide are more studied. These drugs are prescribed for the induction of remission and maintenance therapy. The oral bioavailability of fluticasone propionate is 1%, budesonide - 6-11%. When prescribing a course of treatment of less than 3 months, the drugs do not significantly affect adrenal function [8, p. 241].

To induce remission of fluticasone, propionate is prescribed at a dose of 440-880 mg 2 times a day. A metered-dose inhaler is used in the press-sip mode, food and water are not consumed for 30 minutes. Viscous budesonide for oral administration is sucralose with the addition of nebulbudesonide (0.5 mg / 2 ml). This thick suspension is used at a dose of 2 mg per day. After induction of remission, long-term maintenance therapy is necessary.

Endoscopic dilatation as a treatment method effectively reduces the severity of dysphagia. Patients have no complaints on average 2 years. In the absence of severe stricture, patients can still swallow. They are prescribed an elimination diet and are treated with a topical corticosteroid.

In patients with severe stricture of the 3rd degree, endoscopic dilation is carried out without a preliminary course of therapy. This intervention does not affect the activity of the inflammatory process in the mucous membrane of the esophagus, only the clinical symptoms of dysphagia are facilitated. After dilatation, pain behind the sternum may periodically disturb.

The pathogenesis of EoE is still not well understood, the diagnosis and treatment of the disease are being improved. Late diagnosis of the disease contributes to the lack

of alertness of doctors, especially primary care in relation to EoE. The disease should be excluded in patients with dysphagia of unknown etiology and in the absence of a clinical effect of PPI in the presence of an atopic constitution.

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