Eosinophilic colitis: a seldom suspected diagnosis

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Abstract

Eosinophilic gastrointestinal disorders (EGID) are a group of disorders that compromise the gastrointestinal tract. The best known is eosinophilic esophagitis while eosinophilic colitis which was first reported in the literature in 1959 is less well-known. Eosinophilic colitis is characterized by functional digestive disorders, most importantly diarrhea. Although there are no clear diagnostic criteria, blood should be tested for eosinophils and biopsies taken by colonoscopies should be studied for histological findings of eosinophilic infiltration.
Eosinophilic colitis especially affects neonates and young adults and has been linked to genetic and allergic causes. Initial treatment consists of the suspension of allergens. Prednisolone is used to treat the disorder, and medications such as budesonide and immunomodulators can be used in refractory cases to achieve adequate response. We present an update.

Keywords

Colitis, eosinophilic, diarrhea, colonoscopy, biopsies.

INTRODUCTION

The first study of eosinophilic gastrointestinal disease (EGID) was published in Germany by Kaijser in 1937. (1) In 1959, the first publication on this pathology in the English-language literature was a case study of eosinophilic colitis (EC). (2)

EGID etiology is classified into primary and secondary depending on the pathogenesis. It is also categorized into immunoglobulin E (IgE) mediated EGID and that which is not mediated by IgE. Similarly, it can be divided into eosinophilic esophagitis (EE), eosinophilic gastroenteritis (GE) and eosinophilic colitis (EC) based on the segment that is involved. (3)

EGID and EC are rare diseases and about which little is known, and for which no clear histological criteria have been established. Consequently, diagnosis and incidence are difficult to determine. In general, patients present three characteristics: blood counts with 5% to 35% eosinophils (Although, up to 23% of cases have normal blood counts.), eosinophilic infiltration of the gastrointestinal tract, and functional abnormalities. (4-6)

According to a global registry published in 2002, EGID mainly affects the pediatric population although its occurrence has been reported in individuals of up to 68 years of age. (7) Recent research into EE, the most widely studied variety, has revealed that its incidence is increasing. (8, 9) Its prevalence has been found to be 22.7 per 100,000 people in population studies from North America, Europe, and Australia. (9) In the case of the United States, a prevalence of 25.9 per 100,000 inhabitants has been reported. (10)

EC, the least frequent type of EGID, seems to have a bimodal distribution. It affects neonates with a relatively high prevalence but also affects a separate group of young adults among whom its prevalence is lower. (11) A recent review states that EC is exceptionally rare although it is

estimated that this disease may be more common than is assumed. (12, 13)

EPIDEMIOLOGY AND ETIOLOGY

A 5-year review found the prevalence of EC in the United States to be 2.1 per 100,000 people and that this disease is more common among adults than children. (14) Similarly, it established that EC presents a bimodal distribution: occurring in infants and young children and also in adults between 30 and 50 years old.

Although EC's etiology is unclear, important genetic and allergic components have been identified. About 16% of patients have a family history of similar illnesses, while 80% report a history of atopic disease, and up to 62% have intolerance of some type of food. (12, 15)

Histological findings of mast cell accumulations and loss of granular pattern in colonic tissue in children suggest that IgE plays a predominant role. In adults, unusual anaphylaxis related to a particular type of food indicates the existence of a mechanism associated with CD4 + Th2 lymphocytes. (16)

DIAGNOSIS

Symptoms presented by a patient with EC depend on the layer of the colon that is compromised. When the mucosa is infiltrated by eosinophils, patients develop abdominal pain, nausea, vomiting, diarrhea, and malnutrition. Patients with transmural compromises present motility disorders and intestinal obstruction, and those whose serous layer is compromised may present eosinophilic ascites. (17, 18)

Although no global consensus EC diagnostic criteria exist yet, it is considered that diagnosis requires gastrointestinal symptoms, eosinophilia found in a blood test, and a histological finding of eosinophilic infiltration (Figure 1) of one or more segments of the colon. Some authors also say that other causes of EC should be excluded before EC is diagnosed. (15, 18)

Endoscopically, up to 50% of patients have normal colonoscopies. Nonspecific macroscopic changes are seen particularly in the ascending colon and rectum. (19)

Histologically, groups of eosinophils infiltrate the lamina propria with an extension to the submucosa through the muscularis propria (Figures 2A and 2B) with an eosinophilic gradient from proximal to distal. The highest concentration of eosinophils (up to 35 per high power field) is usually found in the cecum. (20) A majority of authors accept 20 or more eosinophils per high power field as diagnostic. (20)

Key differential diagnoses include eosinophilic infiltration of the colon due to parasitic colitis, EG, inflammatory bowel disease (IBD), drug colitis caused by non-steroidal anti-inflammatory drugs (NSAIDs) such as rifampin, carbamazepine, tacrolimus, and other conditions. (15, 18, 19)

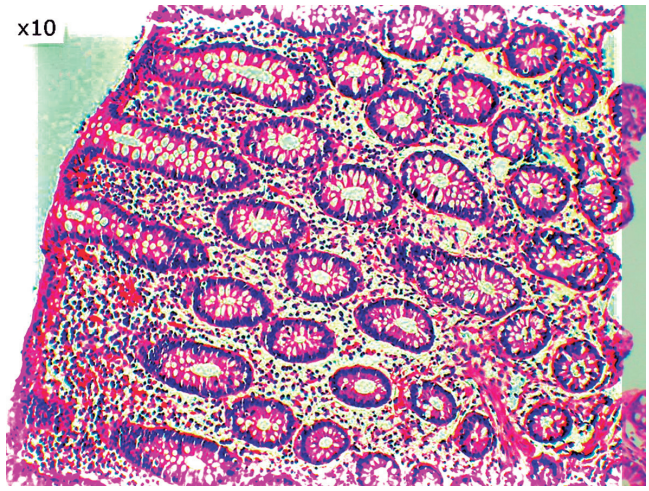

Figure 1. Eosinophilic infiltration of the lamina propria. Image courtesy of Dr. Jorge Monroy, Chief of Pathology at the Central Police Hospital.

Unusual causes of EC include leukemia, lymphoma, vasculitis such as Churg-Strauss syndrome, and polyarteritis nodosa. (12, 21) There have also been reports cases of EC progressing to ulcerative colitis after several months, (21) and cases related to scleroderma and its appearance after liver transplantation in children. (22)

TREATMENT

Childhood EC generally has a benign course and symptoms resolve within a few days after allergens are discontinued. One allergen is cow's milk. In this scenario, breastfeeding should continue, but consumption of cow's milk by the mother should be suspended. (11) Before adults start steroid treatment with steroids, parasitic infections should be ruled out with blood and stool tests. (12, 19)

The use of 1-2 mg/kg/d of prednisolone for 8 weeks followed by administration of decreasing doses has been effective in 80% to 100% of both pediatric and adult patients according to non-randomized studies. (12, 18)

Immunomodulators (azathioprine and 6-mercaptopurine) and budesonide have been shown to be useful in refractory, severe, or steroid-dependent cases. (17, 23) Sodium cromoglycate, a leukotriene antagonist, has been relatively effective for treating EG, but its role in EC has not yet been evaluated.

Some authors have reported the use of ketotifen, omalizumab (monoclonal antibody against IgE), mepolizumab (monoclonal antibody against interleukin-5), infliximab,

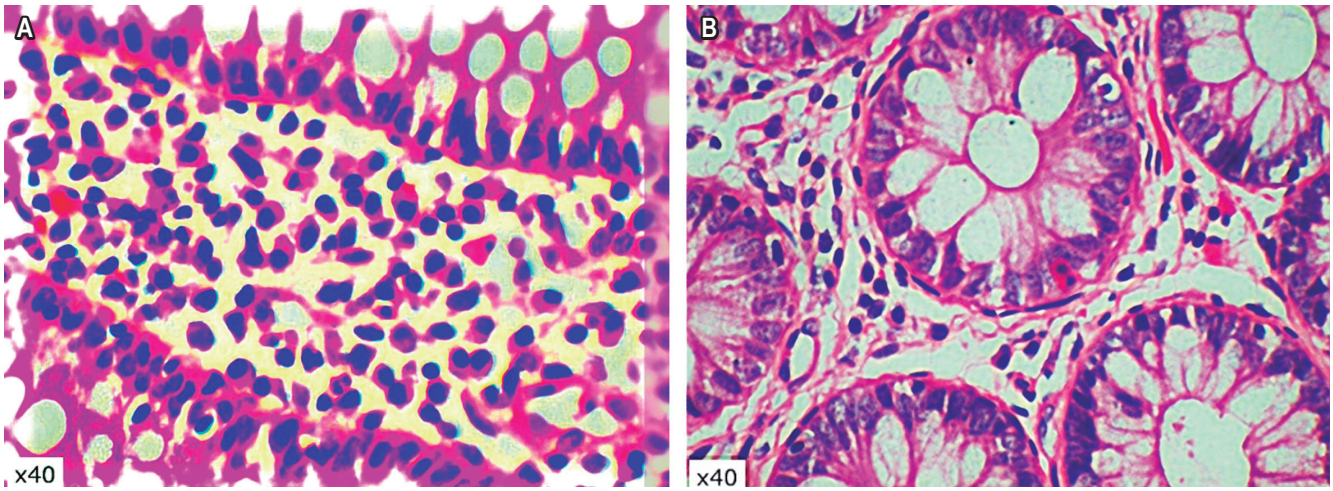

Figure 2. A. Dense mononuclear inflammatory infiltrate with abundant eosinophils in the lamina propria. **B**. Eosinophil-permeated epithelium. Images courtesy of Dr. Jorge Monroy, Chief of Pathology at the Central Police Hospital.

and proton pump inhibitors (PPIs), but there is less evidence for the effectiveness of these drugs. (19, 20, 24)

EC in adults is considered a chronic disorder with periods of activity and remission. Long-term follow-ups have shown that up to 30% of patients have spontaneous remissions, 60% respond to steroids or diet, and up to 10% have refractory disease. (12, 18)

CONCLUSIONS

The diagnosis of EC should be considered part of the study of patients with chronic diarrhea. For this purpose, colonoscopy with staged biopsies is necessary. Although there is no consensus regarding diagnostic criteria, the existence of EC should be suspected in people with gastrointestinal symptoms whose blood tests show eosinophilia and whose histological findings corroborate the diagnosis.

Although EC's prevalence is considered to be low, insufficient records and little-suspected records may mask its real prevalence. Consequently, it is of great importance to carry out studies needed for proper diagnosis and treatment of these patients.

Conflicts of interest

The authors have no conflicts of interest related to this article.

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