

## Eosinophilic Ulcerative Colitis - Case Report and Literature Review

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**Received:** 17 Mar 2022; **Accepted:** 14 Apr 2022; **Published:** 20 Apr 2022

**Citation:** Isabela Bercovici SP, Danilo QD, Taís Donha YA, et al. Eosinophilic Ulcerative Colitis - Case Report and Literature Review. Recent Adv Clin Trials. 2022; 1(1); 1-4.

### ABSTRACT

*Eosinophilic colitis (EC) is a rare inflammatory disease that is part of the group of gastrointestinal eosinophilic diseases. Its etiology seems to involve allergic mechanisms comprising several interleukins and immune system cells (mainly eosinophils). It presents in distinct ways according to age, but at any stage of life it encompasses gastrointestinal symptoms. In addition, it is a condition with a predominance in males, according to some studies.*

### Keywords

Colite, Diarrhea, Immunotherapy.

### Introduction

Eosinophilic colitis (EC) is characterized by a large infiltration of eosinophils in the wall of the colon without evidence of other causes [1-3].

There is still no consensus on the definition of EC, but taking into consideration recent international literatures, the term "Eosinophilic Colitis" is reserved for symptomatic patients, when asymptomatic patients are given the diagnosis of "Primary Colonic Eosinophilia". This is still a weak definition as pathologists use it to define a "higher than normal" number of eosinophils in the colonic mucosa, as there is in fact no specific value that defines the normal amount of eosinophils in the colonic mucosa [1,2].

Eosinophilic colitis is an uncommon and heterogeneous disease

that appears to have a bimodal age distribution, with a first peak in newborns and a second peak in young adults [3,4].

A slight male predominance is observed in this scenario. However, Reed et al conducted a retrospective cohort study in 2014, in which they found that eosinophilic colitis may be more prevalent in male children and female adults, which is quite different from those reported [3].

A recent review of a population-based database in the US, including over 35 million children and adults, reported an overall prevalence of EC of 2.1 per 100,000 individuals, with a prevalence of 2.3 per 100,000 in adults and 1.6 per 100,000 in children. Furthermore, the prevalence of eosinophilic gastrointestinal disorders appears to be higher in urban and suburban areas than in rural areas [4].

Many studies point to an allergic origin of the disease, especially taking into consideration the involvement of cow's milk and soy

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proteins during early infancy. Data that collaborates with such an assumption is the fact that 80% of patients have a coexisting atopic disease, while 62% have specific food sensitivities [3].

Hypersensitivity to a food allergen can lead to 3 types of reactions: IgE-mediated, non-IgE-mediated or intermediate allergic reactions. The first is manifested by allergic reactions that quickly appear after ingestion of the food responsible, and may affect the lungs, skin or digestive tract. Those not mediated by IgE (which are more frequent), on the other hand, cause semi-delayed or delayed reactions, with a greater probability of affecting the digestive tract [4].

However, in addition to all this, there is undoubtedly an interaction between genetic and environmental factors, considering that 16% of patients with EGID have a relative with a similar disease. Colonic eosinophilic infiltrate can also occur secondary to parasitic and helminth infections (such as *Strongyloides stercoralis*, *Enterobius vermicularis*, and *Trichuris trichiura*) and use of drugs such as clozapine, carbamazepine, rifampicin, gold, and naproxen. Finally, such an event can occur subsidiary to inflammatory bowel diseases (IBD), celiac disease, and autoimmune diseases (such as lupus erythematosus, scleroderma, and Churg-Strauss syndrome) [4].

There is also a more specific classification of the most common type, in which eosinophils predominate in the mucosal layer. This classification divides eosinophilic colitis into primary and secondary and is important when considering differential diagnoses. Primary EC is most often related to allergic reactions, whether IgE-mediated or not. Secondary EC, on the other hand, is usually associated as being a result of an eosinophilic disorder such as hypereosinophilic syndrome, inflammatory bowel diseases, parasitic infections, some medications, and systemic diseases [2,5].

### Case Report

A 43-year-old man who presented with abdominal pain associated with daily watery diarrhea without mucus or blood for 3 months sought treatment. He reported that the symptoms began after treatment for *H. pylori* 3 months ago, treated with antibiotics (amoxicillin and clarithromycin).

The patient reported having no relevant medical history and was not taking any medication. He denied recent hospitalizations and presented a negative COVID-19 test.

She was investigated with laboratory tests, which were normal. A colonoscopy was requested and revealed a normal colon and multiple fibrin-covered enanthematous eruptions in the distal rectum with two shallow ulcers with well-defined borders, besides presenting a fibrin-covered background.

The anatomopathological study evidenced a moderate nonspecific chronic rectitis with marked eosinophilia (more than 35 eosinophils/field of high magnification).

The patient was treated with nutritional counseling and corticotherapy with prednisone 40mg/day with significant improvement of the clinical picture and complete resolution of the symptoms.

### Discussion

The diagnosis of eosinophilic colitis is difficult as there are no symptoms or changes unique to this condition. Establishment of primary EC is often by exclusion of other conditions that may eosinophilic infiltrate the colon wall. To establish disease, one must associate clinical, laboratory, histological, imaging findings and exclusion of differential diagnoses.

It is first important to exclude secondary causes of EC taking into account the conditions that most often generate an eosinophilic infiltrate and manifestations similar to primary EC. The main differential diagnoses to exclude are parasitic infections (*Strongyloides stercoralis*, *Schistosoma* spp, *Trichuris trichiura*, *Angiostrongylus costaricensis*, *Gnathostoma* spp, *Ascaris lumbricoides*, *Ancylostoma caninum*, *Ascaris suum*, *Enterobius vermicularis* and *Dientamoeba fragilis* and others), some drugs (such as NSAIDs, carbamazepine, rifampin, enalapril, radiotherapy among others), vascular, connective tissue diseases, celiac disease, malignant conditions, and inflammatory bowel disease (IBD) [1-4].

After excluding secondary causes of EC it is important to associate the clinical and epidemiology of the patient such as higher prevalence in females, family history of allergy and age, as the diagnosis is usually made in the adult aged between 33 and 50 years [2].

Laboratory analysis is limited as it has low specificity and sensitivity, but possible to find peripheral eosinophilia which is often transient. A stool sample is important when excluding parasitic infections. Blood IgE values may be increased, because of the relationship with atopy it is recommended to perform allergy skin test (AST) and radioallergo sorbent test (RAST), even so, AST has a high rate of false-positive results. Non-IgE dependent Th2 allergy tests can also be performed, but have the same limitations as AST and RAST [1-6].

Imaging studies are nonspecific regardless of age group, but it is important to have them on hand. In general, ultrasound, CT, radiography or barium fluoroscopic studies may show intestinal wall thickening, ascites, edema, intestinal wall nodularity, the spiral spring sign (because of intestinal wall stratification) and/or the "araneide-limb-like" sign mainly in the ascending and transverse colon, this last sign occurs because of the prominence of contrast on CT at these site [1,3,5]. Colonoscopy hardly shows changes, when present, they are nonspecific and consist of erythematous irregular mucosa, ulcer, polyps. The right and left colon are more affected.

The gold standard for diagnosis is considered histology, the

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problem is that the reference values for eosinophilia are not well established, however the most adopted values are > 50/ HPF in the right colon, > 35/HPF in the transverse colon and > 25 per HPF in the left colon. In addition to the increased number of eosinophils, degranulation and cryptitis can be found in the lamina propria, muscularis, submucosa, or all of them [1,2,5]. Fibrosis and edema can also be found [5].

Because of the irregular distribution and the nonspecific findings, multiple biopsies in different locations are necessary for a more accurate result [1-6].

### **Treatment**

Eosinophilic colitis is a rare disease, there is not much information on available treatments and most evidence is from few reported cases and some that progressed more severely [1-3].

### **DIET**

Diet restriction is the first-line treatment for cases of eosinophilic colitis, however it only shows efficacy in children (75%), while there is no evidence of improvement in adults. In its allergic form, antigenic exclusion is often effective, but of transient efficacy. The most commonly identified allergens are milk, nuts, hazelnuts, shellfish, fish, eggs, wheat, and milk. Low dietary compliance by older children and adults limits the therapeutic potential of the diet [1,2].

### **Corticosteroids**

Corticosteroids are the first-line pharmacological treatment if dietary restriction is not effective or possible, shows improvement in 90% of cases. Its beneficial factors are related to the inhibition of eosinophilic growth factors (IL-3 and IL-5). The use of prednisone (20-40mg per day for 2 weeks) showed efficacy in most patients, but in some cases, they required higher doses of the drug (0.5-1mg per kg). The negative effects of corticosteroids are in the high recurrence rate [2] and their long-term side effects should be considered. Budesonide (3-9mg per day) is a therapeutic alternative as it has longer remission periods and fewer side effects [1,2].

### **Steroids Sparing Agents**

Steroid sparing agents are a good alternative for people who do not respond to corticosteroids or need a new therapeutic option. Mesalazine has been used in some cases and showed good results. Some immunomodulatory agents such as azathioprine/6-mercaptopurine or anti-TNF agents have been tested in severe, steroid refractory or steroid dependent cases, all with good results [1,3]. Leukotriene receptor antagonists are also a therapeutic option, but their effects have not been evaluated yet, but they have great potential. Antihistamines and mast cell stabilizers, such as ketotifen, are agonists of the histamine H1 receptor and prevent the infection from migrating to its target tissues, several studies show its efficacy and safety and have indicated it as an alternative to corticosteroids. A new antibody that binds to CCR3 has been shown to decrease eosinophilic inflammation in tests performed in mice, as it binds to the eotaxin receptor that is released by

eosinophils, hindering their recruitment to sites of inflammation [1].

### **Fecal Microbiota Transplantation**

Fecal microbiota transplantation has proven effective in the treatment of inflammatory bowel diseases. This treatment associated with oral corticosteroid use, showed a long period of remission of a patient with severe refractory eosinophilic colitis. It is unclear whether fecal microbiota transplantation alone could maintain the positive effects without the use of corticosteroids [1,3].

### **Surgery**

Surgery is only indicated for patient with complications (intestinal inflammation, stenosis, intractable obstruction or perforation) of eosinophilic colitis and consists of a colon resection. However even in an acute setting, symptoms can ease with conservative treatment using immunosuppressants [1].

### **Prognosis**

The evolution of eosinophilic colitis is still poorly understood due to lack of studies. The prognosis in older children and adults is good, but it often turns into a chronic condition with alternating periods of symptoms and intervals of varying duration [2,3].

The clinical features and prognosis are related to the layers of the intestine affected by the eosinophilic infiltrates. Cases of the mucosal type, are more associated with chronic, persistent symptoms without remission, the muscular type presents recurrence and relapse of symptoms and the serous type has a single outbreak and no relapses, thus being the one with the best prognosis.

Some more severe cases have reported diarrhea with the presence of blood or severe rectal bleeding. In cases that had transmural lesion of the colon wall, some other complications were reported such as perforation, occlusion, stenosis, intussusception and volvulus [2].

### **Conclusion**

Eosinophilic Colitis is a rare entity that still remains with the understanding of the pathophysiology unknown, as well as an accurate diagnostic criterion. Currently there are few studies available, which generates the need for a greater number of cases to define a more precise diagnostic criterion and establish an appropriate treatment.

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