Clinical Case Study

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# Eosinophilic Enterocolitis: An Exceedingly Rare Entity

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**Keywords**
Eosinophilic enterocolitis · Ascites · Abdominal pain · Diarrhea

**Abstract**
Eosinophilic enterocolitis is an exceptionally rare condition with few described cases in the literature, representing the least frequent manifestation of the wide spectrum of eosinophilic gastrointestinal disorders. We describe a case of a young male patient presenting with a panmural form of the disease, manifested by abdominal pain, distention, and watery diarrhea with 4 days of evolution, bowel wall thickening, and ascites. Eosinophilic ascites is probably the most unusual presentation form of this entity. It poses a diagnostic challenge because of its nonspecific symptoms, associated with the absence of standardized histological criteria, hence requiring a high level of suspicion. There is also no consensus regarding treatment: it should be individualized according to the patient's age and severity of symptoms.



**Enterocolite Eosinofílica: Uma Entidade Extremamente Rara**

**Palavras Chave**
Enterocolite eosinofílica · Ascite · Dor abdominal · Diarreia

**Resumo**
A enterocolite eosinofílica constitui uma condição extremamente rara, com poucos casos descritos na literatura, representando a manifestação menos frequente do amplo espectro dos distúrbios eosinofílicos gastrointestinais. Descrevemos o caso de um jovem que apresenta uma forma transmural da doença, manifestada por dor e distensão abdominal, diarreia aquosa com quatro dias de evolução, espessamento da parede intestinal e ascite. A ascite eosinofílica é provavelmente a forma de apresentação mais rara desta entidade. Constitui um desafio diagnóstico devido à sintomatologia inespecífica, associada à ausência de critérios histológicos de diagnóstico bem estabelecidos. Não existe igualmente um consenso relativamente à sua abordagem terapêutica, devendo ser individualizada de acordo com a idade do doente e a gravidade dos sintomas.



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## Introduction

Eosinophilic colitis represents the least frequent subset of the wide spectrum of primary eosinophilic gastrointestinal disorders (EGIDs) that can be subdivided into eosinophilic esophagitis, eosinophilic gastritis, eosinophilic enteritis, and eosinophilic colitis [1]. As the small bowel is not frequently biopsied, there are few data related to eosinophilic enteritis [2].

Since 1979, only a few cases of eosinophilic colitis have been reported [2]. Its exact prevalence remains unknown, with a peak of prevalence in neonates and young adults and no gender preference [2].

The etiology and pathogenesis of EGIDs remain not clearly understood, probably resulting from a complex interaction between environmental, genetic, and immunological factors [1]. Even less is known about the etiology of primary eosinophilic colitis. Like other subsets of EGIDs, it is associated with food allergies and atopy in many of the described cases [1] and it may probably be both an IgE- and non-IgE-mediated disease, not fitting completely into either category [3].

The Klein Classification [4] subdivided the disease according to the layer of intestinal wall most extensively infiltrated by eosinophils into mucosa-predominant, muscularis-propria, and serosa-predominant forms. As such, clinical manifestations will depend on the predominantly affected layers, with no distinct clinical presentations differentiating isolated colonic disease from a more diffuse involvement of the gastrointestinal tract [3].

It constitutes a diagnosis of exclusion, usually requiring a combination of nonspecific gastrointestinal symptoms, evidence of eosinophilic infiltration on biopsies, and exclusion of secondary causes of eosinophilic infiltration – parasites, medications, inflammatory bowel disease, malignancy, autoimmune diseases, and hypereosinophilic syndrome [1, 5]. Besides that, there are no standardized histological criteria to make the diagnosis [2].

Treatment of eosinophilic enterocolitis remains a challenge and lacks specific guidelines as there are no randomized controlled trials to date on specific therapy [4].

A high proportion of cases of eosinophilic gastroenteritis are associated with food allergy. Therefore, dietary therapy (6-food elimination diet or an elemental diet) may be successful in symptom improvement [6]. However, management of eosinophilic colitis in adults is more challenging than eosinophilic gastroenteritis, and a trial of oral corticosteroids, usually for 2 weeks plus a 2-week taper, remains the most common approach [5]. Nevertheless, relapse is common, frequently requiring more prolonged therapy or low-dose maintenance therapy [4]. Other therapies targeting immune modulation have been described in case reports and small case series and will probably be useful in the future to treat recurrent or refractory symptoms [5].

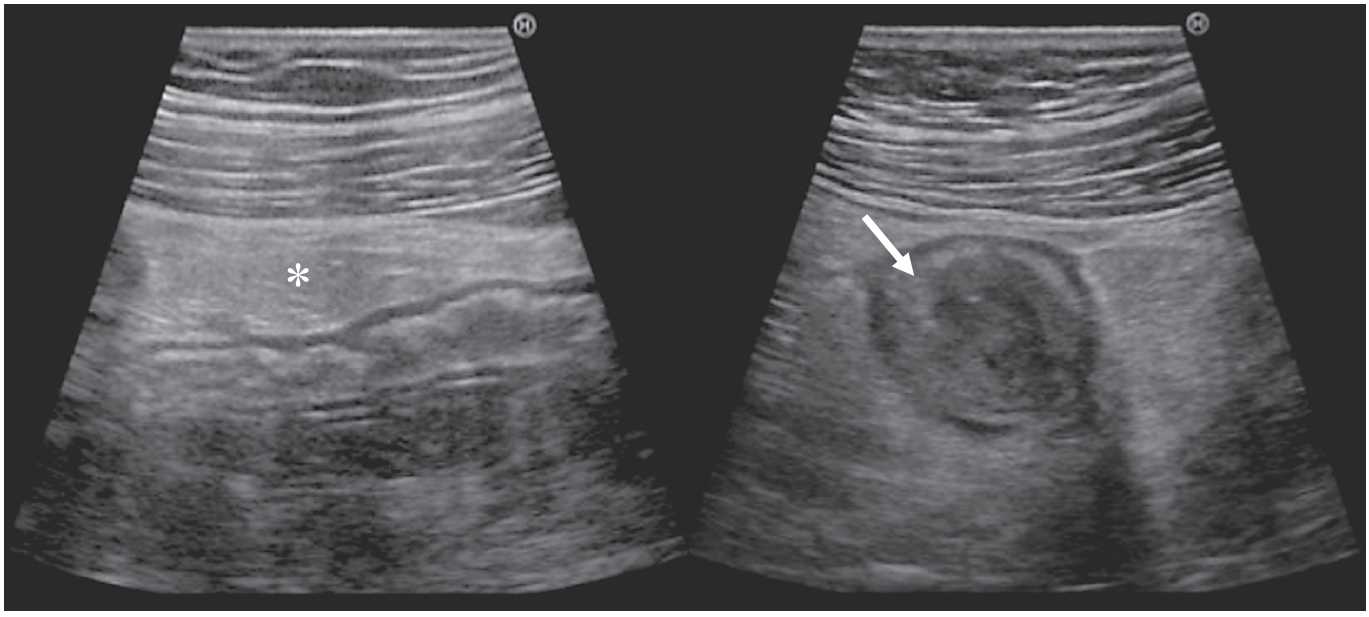

**Fig. 1.** Mesenteric fat edema (asterisk) and terminal ileum wall thickening (arrow).

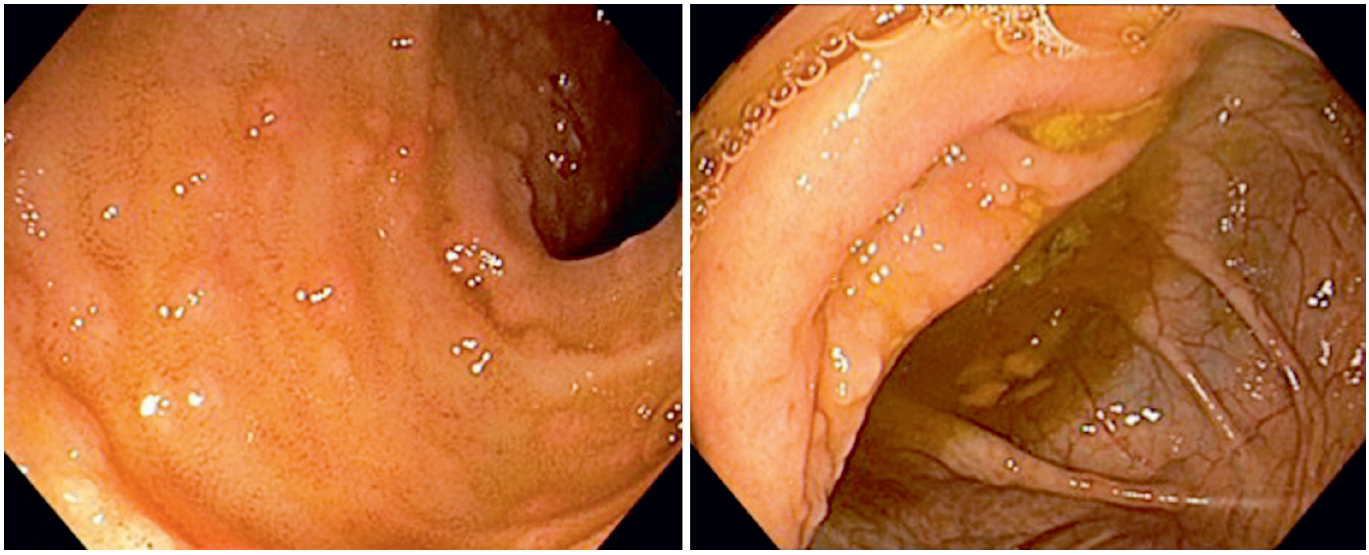

**Fig. 2.** Nodularity of the terminal ileum mucosa and ileocecal valve.

## Clinical Case

We report the case of a 30-year-old white male, with no relevant past medical history, who presented to the emergency department with a 4-day history of diffuse abdominal pain, not related to food ingestion, abdominal distention, and watery diarrhea, without mucus or blood. He had no fever or other associated symptoms. The patient had no history of atopic diseases, no known food or drug allergies, and no recent traveling abroad.

The physical examination revealed mild abdominal tenderness on the epigastric region and right lower quadrant. No signs of peritoneal irritation were present.

Laboratory test results revealed peripheral blood neutrophilia (12,200/μL) and eosinophilia (1,710/μL), elevated serum IgE (905 KU/L), mild elevation of C-reactive protein (46 mg/L), and mild hypoalbuminemia (2.9 g/dL).

Abdominal ultrasonography showed thickening of the terminal ileum wall and edema of the surrounding mesenteric fat, with small volume ascites, compatible with a terminal ileitis (Fig. 1).

At this point, the most suitable differential diagnoses were infectious ileitis, inflammatory bowel disease, and EGID.

A diagnostic ultrasound-guided paracentesis was performed, revealing a marked increase of eosinophils in the abdominal fluid: 5,182 cells/mm$^3$ with 83% eosinophils (4,301 cells/mm$^3$). Bacterial and mycological cultures were all negative.

Parasitological examination and bacterial culture of stool, as well as HIV serology, were all negative. Flow cytometries for lymphocyte subsets were all normal.

Upper endoscopy was performed and esophageal, gastric, and duodenal biopsies were obtained, with no abnormal macroscopic and histological findings.

Ileocolonoscopy revealed diffuse nodularity of the terminal ileum and ileocecal valve, without inflammatory mucosal signs (Fig. 2). Cecum mucosa showed focal areas of erythema.

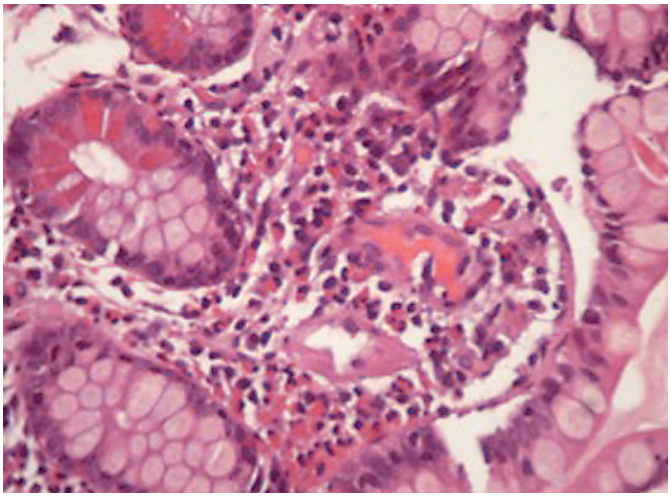

**Fig. 3.** Lamina propria of the colonic mucosa with multiple eosinophils. ×200. Hematoxylin-eosin staining.

Biopsies from the terminal ileum and all segments of the colonic mucosa revealed infiltration of eosinophils into the lamina propria, with more than 20 eosinophils per high-power field (HPF), with well-preserved mucosal architecture, consistent with eosinophilic enterocolitis (Fig. 3). Rectal mucosa was normal.

Given the histopathological findings, ascites with a marked eosinophil predominance, moderate serum eosinophilia, and lack of involvement of other organs, in the absence of secondary causes of intestinal eosinophilia, the diagnosis of eosinophilic enterocolitis with panmural involvement was established.

The patient began a 6-food elimination diet, which he accomplished for 4 weeks, together with 40 mg/day of prednisolone for 2 weeks, followed by a 2-week taper. There was significant clinical and laboratory improvement after 2 weeks of treatment: no symptoms and normalization of peripheral eosinophilia.

The patient was referred to an immunoallergology consultation: skin prick tests and radioallergosorbent tests were positive for several fungi, house dust mite, dog, and cat. As no food allergy was found, no dietary restrictions were advised.

The patient remains asymptomatic after 1 year of follow-up.

## Discussion

Eosinophilic colitis constitutes the rarest form of the spectrum of EGIDs, whether or not it is associated with disease in other segments of the gastrointestinal tract [7].

EGIDs have 3 hallmarks: peripheral eosinophilia, segmental eosinophilic infiltration of the gastrointestinal tract, and functional abnormalities; all 3 were present in this patient at admission.

According to the classification made by Klein [4], there is a good correlation between the clinical manifestations and the pathological findings. This patient in particular had manifestations of mucosal involvement (abdominal pain and mild protein-losing enteropathy), muscular layer disease (bowel wall thickening), and serosal involvement (eosinophilic ascites), representing a panmural form of the disease [1].

Another drawback of this entity is related to its diagnosis. Colonoscopy findings in eosinophilic enterocolitis are variable and nonspecific, including mucosal erythema, nodular appearance, edema, and loss of normal vascular pattern [5], requiring multiple biopsies even with a normal endoscopic examination [8]. Normal values for colonic tissue eosinophils vary widely between different segments [2]. Furthermore, there is no specific cutoff for the number of eosinophils per HPF on histological examination to make the diagnosis: most authors use a diagnostic value of >20 eosinophils/HPF [5]. In this particular case, the pathologist used a threshold of 20 eosinophils/HPF, considering that the presence of more than 20 cells into the lamina propria and preservation of the architecture were sufficient to make the diagnosis. Indeed, the pathologist's experience remains extremely important [5]: the absence of defined histological criteria makes the diagnosis challenging.

Treatment should aim to resolve symptoms and not target tissue eosinophilia, as there is no correlation between reduction in tissue eosinophilia and symptom improvement [2]. An initial attempt to begin an empiric 6-food elimination diet (soy, wheat, egg, milk, peanut/treenuts, and fish/shellfish) was made. However, as there is evidence that eosinophilic colitis in adults usually requires medical management, because IgE triggers are rarely identified [1] and corticosteroid therapy seems the most effective instrument for symptom control [9], it was decided to simultaneously start a corticosteroid cycle of 4 weeks.

Once the diagnosis of EGID is established, an evaluation by an allergologist is often performed, including environmental allergen detection, food allergy testing, food-specific IgE by immuno-CAP, and atopy patch test. However, the clinical utility of allergy testing remains controversial [10], as the development of the disease likely involves a combined IgE- and non-IgE-mediated hypersensitive response, involving CD4(+) Th2 lymphocytes [11].

Not much is known about the natural course of the disease. Eosinophilic colitis that develops in childhood is usually associated with a good prognosis [1], as symptoms tend to resolve after discontinuation of the causative allergen [5]. On the other hand, young adults with eosinophilic enterocolitis tend to have a more chronic presentation [3], often with a relapsing-remitting course of the disease [2]. In this particular case, the patient remains asymptomatic and has not required repeated or long courses of steroid therapy.

Our clinical case report highlights a rare entity, with a nonspecific and variable presentation, requiring a high level of suspicion in order to make the diagnosis. In this specific case, the presence of eosinophilic ascites constituted an important clue, directing our subsequent diagnostic workup having this entity in mind. Colonic eosinophilia has a vast range of differential diagnoses, requiring a thorough investigation and careful elimination of secondary causes, aiming to reach a definite diagnosis.

More studies are needed in order to better define the pathophysiology and the etiologic factors of this entity. Randomized controlled trials are also needed to establish the best specific therapeutic approach.

## Statement of Ethics

This study did not require informed consent or review/approval by the appropriate ethics committee.

## Disclosure Statement

The authors have no conflicts of interest to declare.

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