CASE REPORT

Eosinophilic enteritis: the great mimic

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ABSTRACT

Eosinophilic enteritis (EoN), a subtype of eosinophilic gastrointestinal disease, is a rare and complicated inflammatory condition affecting the small intestine. This case report discusses a 42-year-old patient who presented with acute gastrointestinal symptoms including diarrhea, nausea, and vomiting. Initial laboratory investigations revealed leukocytosis, peripheral eosinophilia, and distinctive imaging findings, prompting further evaluation. Endoscopic evaluation revealed extensive mucosal lesions in the small intestine, with subsequent biopsies confirming eosinophilic infiltration, ultimately leading to the diagnosis of chronic enteritis, probably of an eosinophilic nature. The case highlights the complex differential diagnostic process involved in identifying EoN, which requires a comprehensive understanding of all the clinical and histopathological features of the disease. The efficacy of budesonide therapy is also discussed in the management of EoN and it was evidenced by our patient's positive response to treatment. This case report contributes significant insights into the understanding and management of EoN, providing essential information for the medical community to facilitate accurate diagnosis and tailored therapeutic interventions for individuals experiencing this complex disorder.

KEYWORDS: eosinophilic enteritis; chronic inflammatory disorder; eosinophilic infiltration; endoscopic evaluation; budesonide treatment

INTRODUCTION

Eosinophilic enteritis (EoN) is a chronic, inflammatory disorder that is included under the newly revised umbrella term of eosinophilic gastrointestinal disease (EGID) that refers to eosinophilic esophagitis (EoE), eosinophilic gastritis (EoG), eosinophilic enteritis (EE/EoN) (these latter 2 form the eosinophilic gastroenteritis/EGE) and eosinophilic colitis (EoC) [1]. It is characterized by an abnormal eosinophilic inflammation within the bowel wall, with the stomach and small intestine being the most affected areas [2]. Moreover, EoN has been described as a more common pediatric affliction, but it can also affect the adult population in the 3rd to the 5th decade [3]. The evolution of the disease shows that if untreated, EoN rarely remits spontaneously and can lead to severe malabsorption and malnutrition [4,5].

CASE PRESENTATION

A 42-year-old patient, with no personal medical history to date, declares the acute onset of diarrhea, nausea and vomiting 6 days prior to the presentation to our institution in June 2020. On admission, his general condition was relatively good, hemodynamically stable. Biologically, we identified leukocytosis associated with important inflammatory syndrome, peripheral eosinophilia, slight liver cytolysis, high level of lipase enzyme (without criteria for acute pancreatitis) and hypocholesterolemia, hypoalbuminemia, and the absence of antigliadin and antitransglutaminase antibodies. A coprocytogram was performed and revealed no inflammatory reaction, *Clostridioides difficile* toxins A and B negative and tumor markers within normal limits. The parasitological examination of the stool marked the absence of cysts/parasites.

The emergency abdominal ultrasound revealed: hyperperistaltic small intestine loops dilated up to 40 mm in the hypochondrium and the left flank, thin layer of fluid in the hypogastrium, between the loops. Normal abdominal X-ray showed the outline of a hydro-air level in the left hypochondrium. Thoraco-abdomino-pelvic CT evaluation done at the time of the admission revealed: the first jejunal loops downstream of the extended Treitz angle with a caliber of up to 36 mm with a variable thickening of the wall, with discretely stratified contrast uptake, small inflammatory adenomegaly and a thin layer of liquid between the loops in the hypogastrium, measuring a maximum of 12 mm, without lung damage.

The evaluation of the small intestine through the endoscopic videocapsule revealed about an hour from ingestion

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villi with a slight modification in appearance, but the significant changes started after 3 hours from ingestion, when the whole mucosa of the small intestine downstream showed varied aspects such as, edematous, diffuse congestive appearance of the villi, including a pavement appearance, or suggesting infiltration, protruding areas with modified, congestive, fissured mucosa, superficial, linear or irregular ulcers, areas with bleeding, blood coming from ulcerated areas or red blood in the lumen, polypoid areas separated by fibrin-based ulcers, evoking ''paving stone'', stenosed areas due to the presence of the described protrusive/polypoid lesions (Figure 1).

The etiological assessment was completed with an endoscopy, revealing the absence of varicosal esophageal veins, an inflamed gastric mucosa with hypertrophied folds. The instrumentation of the second part of the duodenum (D2) and 60 cm after D2 was also performed and it showed similar mucosal lesions to the ones described by the videocapsule: thickened villi, mosaic-like changes. Biopsies were taken from the stomach and small intestine.

Four biopsy samples were examined. The first one was a superficial fragment of the gastric mucosa in the body area, without pathological changes. Giemsa staining did not identify *H. pylori*. The other samples were fragments of the small intestine mucosa (jejunum) with slightly shortened and thickened villi due to the presence of a marked edema that formed subepithelial vesicles, with a moderate lymphoplasmocytic inflammatory infiltrate with frequent eosinophils (approximately 27 eosinophils/HPF) and congestion in the lamina propria.

The positive diagnosis after the histopathological exam was chronic enteritis, probably eosinophilic. This diagnosis was supported by the clinical presentation with a malabsorption syndrome corresponding to the mucosal form of eosinophilic enteritis, by the histological aspect with the mucosal eosinophilic infiltrate and by the exclusion of all other etiologic possibilities, as it was discussed previously. To further prove this diagnosis, the patient was prescribed a budesonid 9 mg/day for one month, then 3 mg/day for one month.

The patient, with the suspicion of eosinophilic jejunitis, received treatment with budesonide and presented 2 months later for the computer tomography examination to assess the response to the treatment, which showed a significant improvement. Thus, corroborating all the clinical and paraclinical findings, the status of the patient was improved compared to the previous exploration, proving the efficacy of the steroid treatment for this case with the suspicion of eosinophilic jejunitis.

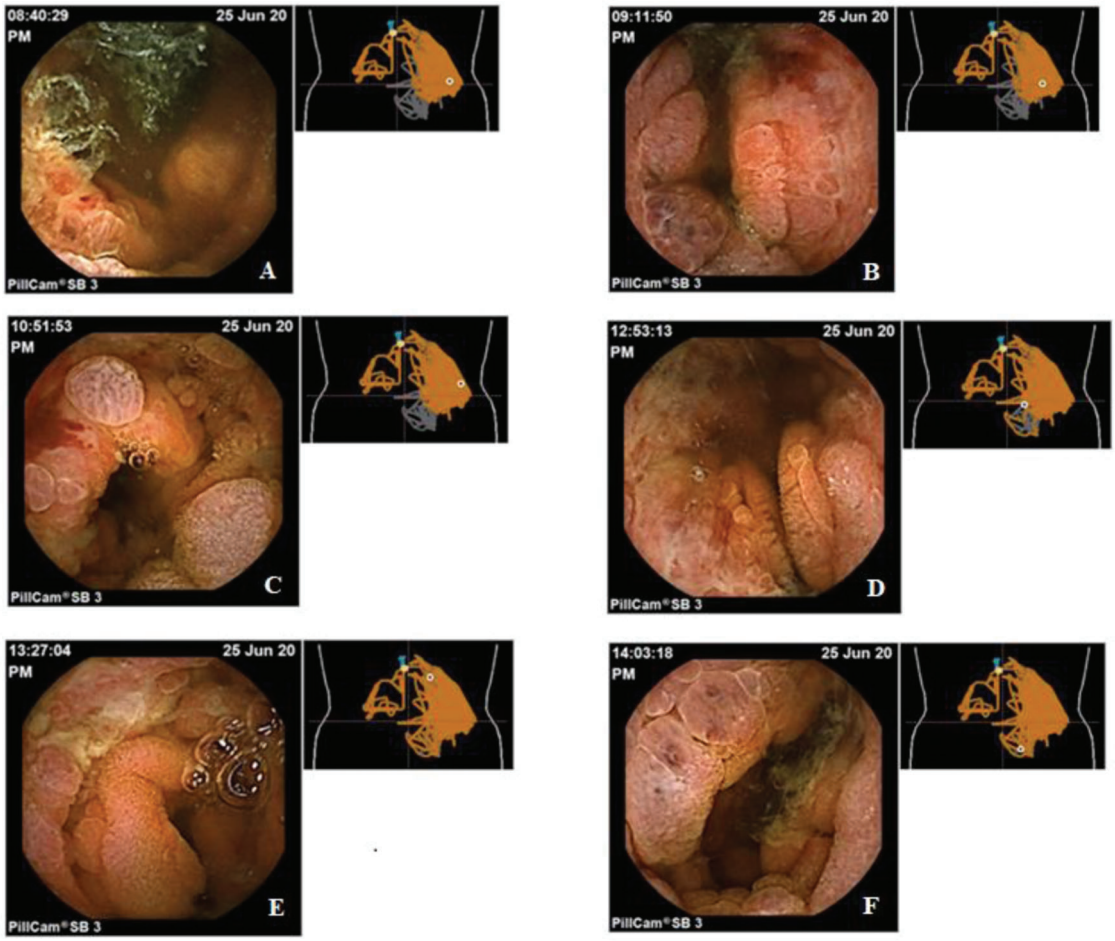

Fig. 1. Aspect from the endoscopic videocapsule: A: edematous mucosa; B: diffuse congestive appearance of the villi, including a pavement appearance, or suggesting infiltration; C: areas with bleeding, blood coming from ulcerated areas or red blood in the lumen; D: protruding areas with modified, congestive, fissured mucosa, superficial, linear or irregular ulcers; E: polypoid areas separated by fibrin-based ulcers, evoking ''paving stone''; F: stenosed areas due to the presence of the described protrusive/polypoid lesions.

DISCUSSIONS

Until recently, the term ''eosinophilic gastroenteritis'' was the term used for all non-EoE EGIDs. Now, individual locations within EGIDs can be further defined as: EoG (involvement of the stomach), EoN (involvement of just the small intestine), and EoC (involvement of the colon). The eosinophilic enteritis which references the immune inflammation of the small bowel can have several specific locations and they can be further defined as eosinophilic duodenitis (EoD), eosinophilic jejunitis (EoJ) and eosinophilic ileitis (EoI) [1].

In regards to risk factors, there has been a genetic factor identified, which was suggested by the reports of familial cases [6]. In addition, obesity, higher socioeconomic status, and the Caucasian race have been presumed to lead to EoN [7]. However, most importantly, 45 to 63% of EoN cases reported some sort of allergic conditions such as eczema, rhinitis and food or drug intolerances [7,8] and 64% illustrated family history of atopic diseases, but a triggering agent is not always identified. Nonetheless, 50% of the EoN cases have been discovered while testing for a suspicion of food allergy [7,9].

According to Klein et al., EoN can be categorized according to the location of the eosinophilic inflammation in mucosal, muscular, and serosal. Each of these forms has their own histological and clinical presentation [5]. Mucosal EoN shows eosinophilic infiltration in the mucosal part of the small bowel and can manifest with abdominal pain, diarrhea and signs of protein losing enteropathy or malabsorption, which was also the case for the 42-year-old patient presented earlier. Muscular EoN manifested itself with nausea, vomiting, abdominal pain due to formation of intestinal strictures which can evolve in the form of intestinal occlusion. Finally, the serosal EoN was characterized by abdominal pain and bloating due to ascites rich in eosinophiles. As of now, there is no clearly defined cut off for eosinophils per high power field (HPF) and for the diagnosis of the eosinophilic infiltration it is highly recommended that a physician with experience may determine if the number of eosinophils in a certain small bowel area is bigger than expected. Even so, some suggestions have been made and they state that for the diagnosis of EE in the duodenum more than 52 eosinophils per HPF can be considered or more than 56 eosinophils per HPF in the ileum [10]. According to this criterion, our patient may not qualify for an EoN diagnosis, seeing that his eosinophilic infiltrate consisted only of 27 eosinophils per HPF in the jejunum. However, as stated before, the cut off for the diagnosis is not clearly defined and an experimented physician may weigh in. Furthermore, many other conditions may present gastrointestinal symptoms and intestinal eosinophilia [11]. Some of the more frequent ones are medications and intestinal parasites, but others may be *H. pylori* gastritis, gastroesophageal reflux disease, celiac disease, gastrointestinal vasculitis and inflammatory bowel disease [12]. In our case, most of the differential causes associated with intestinal eosinophilia have been excluded, as discussed in the case report. Due to its versatile clinical manifestation, the diagnosis of EoN must include symptoms from the gastrointestinal realm combined with abnormal eosinophilic infiltration of the small bowel and must exclude secondary causes of intestinal eosinophilia [13, 14] (Table 1).

Table 1. Secondary causes of intestinal eosinophilia [14].

1.	Allergic disorders (the most common cause of gastrointestinal eosinophilia in developed countries)
2.	Gastrointestinal reflux disease
3.	Inflammatory bowel diseases
4.	Malignancy
5.	Churg-Stauss syndrome
6.	Celiac disease
7.	Systemic lupus erythematosus
8.	Drug reactions, gold salts, azathioprine, gemfibrozil, enalapril, carbamazepine, clofazimine and cotrimoxazole
9.	Parasitic infections (the most common cause of gastrointestinal eosinophilia in developing countries)
10.	*Helicobacter pylori*

In regards to the laboratory findings, the main pathological result consists of peripheral blood eosinophilia (>500/mm^3), which was discovered in 70% of the patients and was fleeting and corresponded to the EoN flare ups. Because EoN can manifest itself with intestinal inflammation, malabsorption or protein losing enteropathy, the peripheral blood may also show iron deficiency, an increase in C-reactive protein or hypoalbuminemia. Additionally, a lack of eosinophilia may be discovered (which was the case in 25% of the cases), but that should not exclude the EoN diagnosis [15-17]. Reporting back to the presented patient, in support of the EoN diagnosis, he presented inflammatory syndrome, peripheral eosinophilia and a malabsorption syndrome which is consistent with the main findings for the mucosal form of EoN.

Regarding imaging, EoN has nonspecific characteristics. Upper gastrointestinal endoscopy may show no macroscopic changes or only light mucosal modifications such as edema, erythema, erosions, or nodules. The wireless endoscopy capsule reveals different lesions. CT and MRI scans are useful in EoN patients since they can describe the depth of the eosinophilic infiltration within the intestinal wall and the presence of free fluid in the abdomen (ascites). However, only small bowel biopsies can definitively diagnose EoN [18-20]. The imaging criteria was also proved in our case, the patient presenting atypical characteristics, the most noteworthy ones being hypoperistaltic small intestine loops dilated up to 40 mm in the hypochondrium and the left flank, thin layer of fluid in the hypogastrium, between the loops.

The main branches of the approach to the EoN treatment are: dietary strategies, steroids, azathioprine, biologic agents, and anti-inflammatory medication (Table 2). Budosonide, with lower intestinal absorption, can be used to avoid the side effects of the systemic steroids, with good results [21-25] and it showed a satisfactory response in our 42-year-old patient.

CONCLUSIONS

Eosinophilic enteritis is a rare ailment defined by the eosinophilic infiltration in the small intestinal wall. Our case report, together with the literature, emphasizes the variability and atypical clinical and paraclinical findings of this disease, which makes its diagnosis a difficult one. The pathological mechanisms are still relatively unknown, though there are some risk factors and pathological pathways being discussed. Corticosteroid therapy is currently the most common course of action for EoN, having good results in most patients. The natural evolution of EoN is for the most part benign, with few flare ups, however, left untreated can have very damaging effects, depending on the intestinal segment affected.

Table 2. Treatments used in EoN [15].

Dietary changes	1st line treatment strategy, according to the food allergy tests
Prednisone/Budesonide	1st line treatment used in remission induction Low dosages for maintenance in steroid dependence cases
Montelukast/ Sodium cromoglycate/ Ketotifen	1st line treatment strategy Agent used for the sparing of steroids
Azathioprine	Agent used for the sparing of steroids
Mepolizumab/ Omalizumab/ Infliximab/Adalimumab	Agent used for the refractory cases

Conflicts of interest and funding

No conflicts of interest and no funding to declare.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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