Conservative management of eosinophilic enteritis presenting with acute abdominal syndrome

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ABSTRACT

Eosinophilic enteritis, an increasing recognized condition, is rare and often presents with non-specific symptoms. We report a case of a 46-year old female who presented with acute onset abdominal pain and nausea associated with ascites, small bowel thickening and peripheral eosinophilia. Diagnosis was confirmed by biopsies taken at esophagogastroduodenoscopy demonstrating diffuse infiltration by inflammatory cells, mainly eosinophils. Appropriate therapy was instituted. The patient recovered well and was symptom-free at 1-month follow up. In this report, we discuss the clinical presentation and the diagnostic criteria of the eosinophilic enteritis, and examine the pathophysiological theories and therapeutic strategies. The relevant literature on eosinophilic enteritis is summarized.

Introduction

Eosinophils were first described over a century ago as granular white blood cells that stained readily with eosin. These acidophil granulocytes have pro-inflammatory functions and are involved mainly in protecting against parasites and allergies.[1]

However, only a small number of mature eosinophils are normally present in the peripheral blood. These granulocytes are predominantly tissue-dwelling cells with particular affinity for epithelial surfaces that interact with the external environment (*e.g.* skin, lung, gastrointestinal tract). Within the *lamina propria*, eosinophils are situated to protect against parasitic infection and in normal circumstances do not evoke either inflammatory reaction or tissue damage. When provoked by a number of stimuli, including non-specific tissue injury, allergens or infections, eosinophils become activated to degranulate various cytotoxic agents and to stimulate immunoglobulin E (IgE) production, resulting in local tissue damage and dysfunction.[2]

Eosinophilic enteritis (EE), a distinctive pathologically-based disorder characterized by an eosinophil-predominant inflammatory process, is rare. Its etiology is still unknown.[3]

Diagnostic criteria include demonstration of eosinophilic infiltration in the bowel wall, lack of evidence of extraintestinal disease, and exclusion of various disorders that mimic a similar condition.[4]

EE is an uncommon disease and, as such, no prospectively performed therapeutic studies are available. While patients with the serosal type respond dramatically to steroid therapy, optimal treatment is yet to be found for other EE forms. Despite the fact that EE is likely to be a chronic disorder, its natural course has still not been defined.[5]

Case Report

A 46-year old Caucasian woman was admitted to our hospital complaining of acute-onset right-lower quadrant pain and nausea. She had not undergone any abdominal operation and denied having taken any drugs. She had a history of an allergy to seafood and

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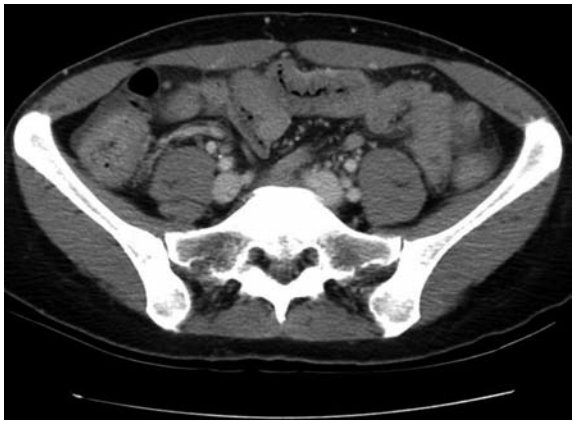

Figure 1. Computed tomography image of diffuse thickening of the small intestine with dilation of the jejunum and ascites.

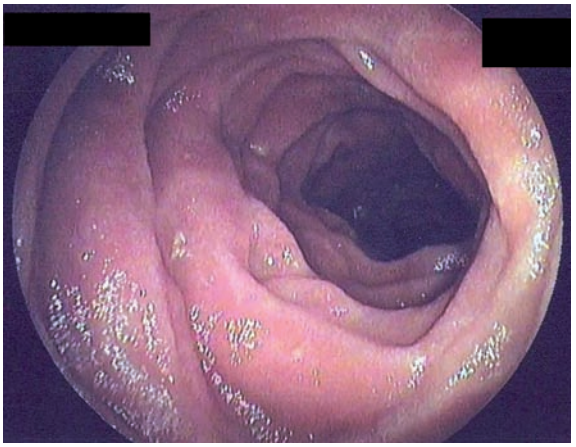

Figure 2. Endoscopic image of erythematous areas of distal duodenum and proximal jejunum.

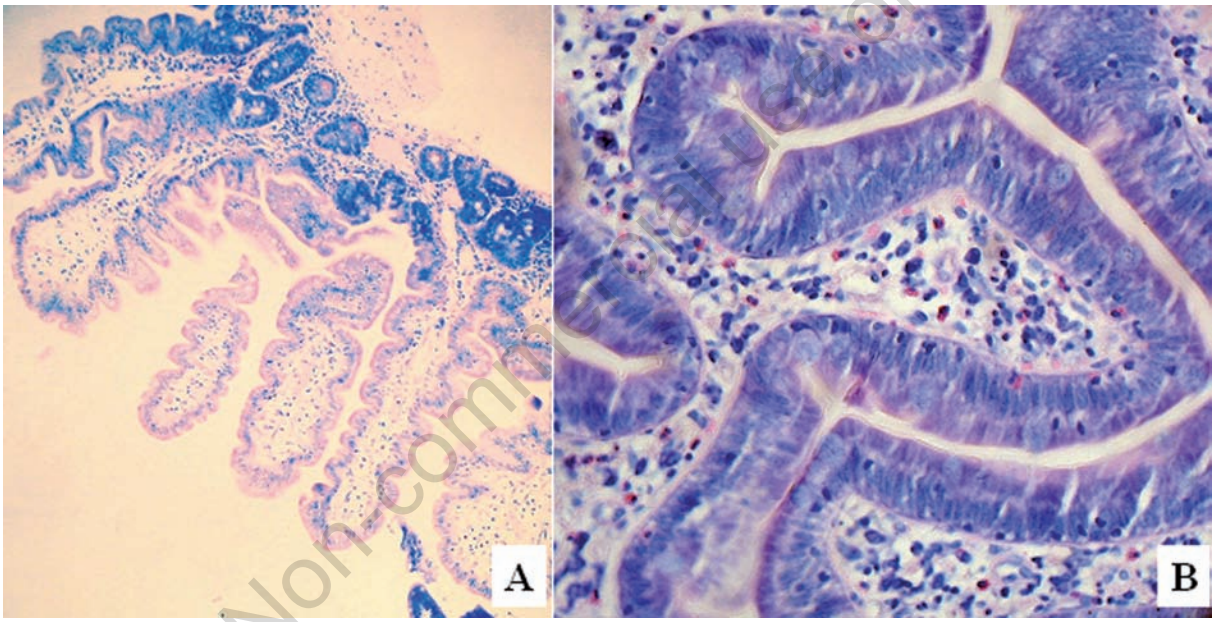

Figure 3. Histological images showing edema, normal villous architecture (A) and eosinophilic infiltration (B) (×40 high power field).

atopic dermatitis. Recently, she had been subjected to skin prick test; this had resulted negative. There was no associated diarrhea, melena or change in bowel habits.

Physical examinations revealed diffuse direct tenderness and involuntary guarding of the entire abdomen; this improved with intravenous fluids.

Laboratory data showed a white cell count of 12.3×10^9/L with 21.2% eosinophils; all other relevant blood parameters were within normal limits (including lactate dehydrogenase and serology for celiac disease). Stool cultures and parasitological examinations were negative.

An abdominal ultrasound revealed a diffuse thickening of the small intestine with dilation of the jejunum and ascites; this was confirmed by computed tomography (Figure 1).

An endogastroduodenoscopy was performed showing a multiple erythematous area of the distal duodenum and of the proximal jejunum (Figure 2).

Histologically, diffuse infiltration by inflammatory cells, mainly eosinophils, was observed (Figure 3).

Colonoscopy with distal ileoscopy revealed a resected sub-centimetric sessile colonic polyp and this resulted in a tubular adenoma with low-grade dysplasia.

The patient was treated with oral budenoside 9 mg/day and discharged. At 1-month follow up, the patient remained symptom free with no evidence of white blood cell abnormalities, and disappearance of ascites and bowel thickening.

Discussion and Conclusions

EE is a rare disease of unknown etiology. It is characterized by eosinophilic infiltration of the bowel wall to a variable depth and symptoms associated with gastrointestinal tract.[4]

Since it was first described by Kaijer[6] in 1937, about 300 cases have been reported in the literature. It can affect any age group, but the peak of incidence is in the third to fifth decade of life, with a slight male predominance (1.4:1).[2]

EE was defined by the presence of gastrointestinal symptoms, biopsies showing eosinophilic infiltration of one or more areas of gastrointestinal tract, and no evidence of parasitic or extraintestinal diseases.[7]

Atopy and allergies are associated in 25-75% of cases.[8] However, IgE serum levels are not consistently elevated in patients.[9] Increased secretion of interleukins 4 and 5 by peripheral T cells, as a non-IgE-mediated pathophysiological mechanism, has also been reported in eosinophilic enteritis.[10]

Clinical features may reflect the extent, location and depth of infiltration of the eosinophilic inflammatory process in the intestinal tract.[1] According to Klein classification,[11] the disease is distinguished in the mucosal, muscular and serosal form.[7] Patients with mucosal disease (57.5%) present with symptoms similar to inflammatory bowel disease, including vomiting, abdominal pain, diarrhea, iron deficiency anemia, malabsorption. Disease involving the *muscolaris propria* (30%) typically presents with obstructive symptoms.[2]

Clinical features of serosal involvement (12.5%) are the presence of ascites and high peripheral eosinophil count.[1]

In our case, eosinophils infiltrated all layers of the intestinal wall, as confirmed by positive mucosal biopsies, thickening of the muscle layer and presence of ascites and peripheral eosinophilia.

The diagnosis of EE may be elusive because of non-specific symptoms and variable peripheral eosinophilia: a high eosinophil count is more likely to be associated with subserosal involvement rather than a mucosal and muscular subset.[7]

However, when ascites is found in association with serosal bowel disease with peripheral eosinophilia, a strong suspicion of EE must be taken into consideration.[9]

Radiographical studies help detect the muscular disease by finding stenosis or thickening of the bowel wall.[2]

Mucosal disease, in which endoscopy can directly visualize any mucosal changes and acquire biopsies, is the most readily diagnosed form of EE. However, endoscopic features are rather non-specific; thickened folds, erythema, friability, nodularity, abnormal persitalsis and brown-pigmented ulcer have been described.[2,5,12]

A new capsule endoscopy feature has recently been reported, showing dark blue coloration of the deeper layers of the small bowel in the absence of mucosal lesions, indicating a deep eosinophilic infiltration.[13]

Biopsies show increased eosinophils. However, no standards of diagnosis have been established. Indeed, the normal number of eosinophils has not been defined and criteria may differ between pathology departments, due to the fact that the healthy gastric and intestinal mucosa harbor eosinophils under physiological conditions.[5] Generally, diagnosis is based on the presence of eosinophilic infiltration in biopsy samples with 20 or more/high-power field.[7,13]

Most EE cases are diagnosed on surgical full-thickness biopsy or resection performed for obstruction or suspicion of malignancy. However, EE should be considered in the differential diagnosis of unexplained gastrointestinal symptoms, since most patients with EE can be treated successfully with medical therapy.[14]

The differential diagnosis of EE includes inflammatory bowel disease, peptic ulcer disease, lymphoma, amebiasis or other parasitic infections, protein-induced colitis.[9] In view of the close relationship between food allergy and EE, one of the most widely tested strategies in treating EE was based on controlling antigen exposure in the diet, although, when this presented later in childhood, the disease did not respond satisfactorily to dietary changes.[1]

The rarity of EE has limited any large prospective randomized therapeutic trials. However, the mainstay of obstructive disease is corticosteroid therapy. Prednisone or buodenoside, a steroid with fewer systemic side effects, can yield a good response.[2] Those with serosal disease appear to experience the greatest response to corticosteroids.[5,7]

Other therapies used with success include cromolyn,[15] montelukast,[16] ketotifen[17] and suplatast tosilate.[18]

The natural history of eosinophilic enteritis has not been well documented. When therapy ends, the disease tends to relapse, even when the diseased segment has been surgically resected.[14] Mild and sporadic symptoms can be managed with observation whereas drugs and steroid-sparing treatments such as montelukast are preferred maintenance strategies.[2,10]

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