

Case Report

Malabsorption Syndrome and Leukotriene Inhibitor

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Summary

Previously described treatments used for eosinophilic diseases of the gastrointestinal tract have included dietary restrictions primarily of cow milk protein, anti-inflammatory therapy utilizing suplatast, budesonide and corticosteroids, cromolyn sodium, anti-histamines and oral inhalable steroids. We describe a 12-year-old girl with diarrhea and malabsorption, who was later diagnosed to have eosinophilic gastroenteritis, was unresponsive to standard therapies, but exhibited marked improvement with use of montelukast.

Key words: montelukast, diarrhoea, endoscopy, eosinophilia.

Introduction

Eosinophilic gastroenteritis (EGE) is a distinct eosinophil-predominant inflammatory process in gastric or small intestinal mucosal biopsies. Although the endoscopic changes are non-specific, chronic or recurring symptoms are present and other causes of intestinal eosinophilia require exclusion (e.g. parasitic infections, medications) [1–3]. EGE has been considered an uncommon, even rare disorder but this may well depend on its definition as well as the method of detection. We describe a 12-year-old girl with diarrhea and malabsorption, who was later diagnosed to have EGE, was unresponsive to standard therapies, but exhibited marked improvement with use of montelukast.

Clinical Report

A 12-year-old female child presented with complaints of intermittent pain abdomen, loose stools, non-productive cough and hyper pigmentation of skin for last 2 months. This was accompanied by vomiting since last 20 days. There was associated history of poor appetite and progressive weight loss. At admission, the child was in shock for which she received fluid boluses followed by ionotropes. Antibiotic was started in view of suspected sepsis (gastrointestinal focus). General physical examination revealed moderate pallor with skin hyperpigmentation. Anthropometry showed; weight = 25 kg (<5th centile), height = 135 cm (<5th centile). There was no dysmorphic features. Abdominal examination revealed mild hepatomegaly (liver 2 cm below costal margin) without any other organomegaly or ascites. Rest of the systemic examinations were within normal limits.

The shock gradually got passive and ionotropes tapered and stopped. Antibiotic was stopped after 5 days as work up was normal [total leucocyte counts (TLC), blood culture, stool routine and culture]. On enquiry there was past history of snake (viper) bite 1 year back. There was no other significant past or family history of similar complaints. There was no history of any atopic disorders.

In view of gastrointestinal complaints, with malnutrition and progressive weight loss, as well as respiratory symptoms, tuberculosis, HIV and malabsorption syndrome were kept as possibilities and the child was investigated accordingly. Hemogram done showed hemoglobin = 11.5 g%, TLC = 8400 cu mm⁻¹ and marked eosinophilia (differential count = 38% and absolute count = 3500 cu mm⁻¹), normal ESR (8 mm h⁻¹). Renal and liver function tests were within normal limits. Metabolic parameters (calcium/phosphate/alkaline phosphatase), blood sugar, urine and stool
examination were normal (no intestinal parasitic infection). Tuberculosis work up (chest X-ray, Mantoux test, sputum examination) and HIV test was negative. Ultrasonography of abdomen revealed mild hepatomegaly with normal echotexture. Upper GI endoscopy showed normal proximal and mid-esophagus, with multiple erosions which was whitish, with punctate hemorrhages, seen from distal 3rd of esophagus up to 2nd part of duodenum, with intense duodenitis. Biopsy of duodenal and gastric mucosa was taken during endoscopy and sent for biopsy. Histopathology was suggestive of eosinophilic gastroenteritis (Fig. 1). Child was treated with diethylcarbamazine (DEC), albendazole and ivermectin for 21 days in keeping the possibility of tropical eosinophilic syndrome. After treatment, there was mild symptomatic improvement, but absolute eosinophil count did not show any significant improvement (decreasing only to 2600 cu mm\(^{-1}\)). After 1 month, the absolute eosinophil count again increased to 3600 cu mm\(^{-1}\), with symptom recurrence. Then the child was treated with montelukast (Lasma\textsuperscript{TM}, Valencia, CA, USA) 10 mg OD, which lead to total symptom resolution with normal eosinophil count after 1 month of starting montelukast. In the last follow-up, the child was asymptomatic with weight gain and is off the drug. Repeated upper GI endoscopy showed complete resolution of the enteritis (Fig. 2).

**Discussion**

Most often, the diagnosis of EGE is defined by histological evaluation of endoscopic biopsies. There are some potential diagnostic issues and pitfalls and these include: eosinophils may normally be detected in the gastric and intestinal mucosa and only limited numbers of studies have tried to quantify normal compared to abnormal numbers in health and different inflammatory disease states, e.g. ulcerative colitis [4, 5]; fixation methods may be critical in the definition of eosinophils in gastric and intestinal biopsies [e.g. Bouin’s solution (often used for gastric or intestinal biopsies), can result in ‘bleaching’ of eosinophil granules making detection much more difficult. If EGE is suspected, routine formalin fixation is useful] [6].

Common presentations include abdominal pain and diarrhea. Other features are: weight loss, iron deficiency, obstruction or, even an acute abdomen and ascites. Peripheral blood eosinophilia has been recorded in up to 70%, but this is not specific for EGE and should lead to exclusion of other disorders, specifically parasitic infections [2]. In some with EGE, increased serum IgE levels may be seen, but this is also not specific. Endoscopic evaluation might permit definition of the extent of the inflammatory process in the upper gastrointestinal tract. Treatment is largely aimed at resolving symptoms. Medications used in EGE are largely based on empirical observation and experience. Because of the rarity of EGE, there are no controlled treatment trials available. Steroids have been used as a traditional form of therapy to reduce the inflammatory process [1–3]; however, these may cause

**Fig. 1.** Histopathology suggestive of eosinophilic gastroenteritis (hematoxylin and eosin stain).

**Fig. 2.** Repeat biopsy showing resolution of the eosinophilic gastroenteritis (hematoxylin and eosin stain).
steroid-related effects, especially because of their recurring need over prolonged periods. Other remedies have been used but their effectiveness still requires definition. These include: mast cell stabilizers, ketotifen, leukotriene antagonists, etc. [7–9]. This lengthening therapeutic list might be construed as a clear reflection of the limited forms of effective therapy that are currently available.

Our decision to use montelukast in index case was based largely on the demonstrated efficacy of this agent in other eosinophilic conditions such as asthma [10]. Cysteinyl leukotrienes (LTC4, LTD4 and LTE4) are products of arachidonic metabolism released from mast cells and eosinophils and selective antagonists, such as montelukast, inhibit physiologic actions of LTD4 without any agonist activity. Therefore, one could postulate a variety of abnormalities that occur in eosinophilic disorders in both the respiratory and GI tract that could be alleviated with the use of montelukast. The exact role of montelukast in the treatment of patients with gastrointestinal symptoms and gut eosinophilia cannot be determined from patients so far treated with this agent and variable dose and duration has been used.

In the index case, there was complete clinical as well as pathological/histological improvement with use of montelukast as shown by repeat endoscopic biopsy. A carefully designed and conducted double-blind, placebo-controlled study of montelukast for treating gastrointestinal eosinophilic disorders in children should be the next step to verify the excellent clinical response so far witnessed.

References