Use of Montelukast as Steroid-Sparing Agent for Recurrent Eosinophilic Gastroenteritis

D.A. SCHWARTZ, MD, D.S. PARDI, MD, and J.A. MURRAY, MD

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Eosinophilic gastroenteritis is an uncommon chronic disease of the gastrointestinal tract that is characterized by abdominal pain, nausea, and diarrhea. Eosinophilic infiltration of the gut wall is pathognomonic of the disease. Eosinophilic gastroenteritis can be classified into three types (mucosal, muscular, and subserosal) based on which level of the gut wall is predominantly involved. (1). The presentation is dependent on the form of eosinophilic gastroenteritis. Patients with primarily mucosal disease tend to present with nonspecific gastrointestinal symptoms, while those with primarily serosal disease can present with severe abdominal pain and eosinophilic ascites (2). There have been approximately 300 cases described in the literature since it was first reported in 1937 (1–17).

In general, patients respond well to corticosteroids, but relapses are common. Other authors have described the use of oral cromolyn as a steroid-sparing agent with varying success (13, 18–20). Patients with relapsing disease are usually placed on long-term low-dose prednisone or immunosuppressive therapy (21). Here we report a patient with severe steroid-dependent eosinophilic gastroenteritis who was able to successfully taper off steroids and maintain remission after starting montelukast.

CASE REPORT

A 27-year-old man presented with a history of recurrent flares of eosinophilic gastroenteritis. He had no history of seasonal or food-related allergies. His symptoms had begun approximately two years earlier when he developed severe abdominal pain, nausea, vomiting, and diarrhea. On admission at another institution, he was found to have diffuse abdominal tenderness without peritoneal signs and significant ascites. His white blood cell count (WBC) was $8200 \times 10^9$/liter with an eosinophil count of $2900 \times 10^9$/liter (35%). His serum albumin was 2.9 g/dl. The remainder of his laboratory studies, including amylase and lipase, were unremarkable. A CT scan showed several thickened loops of small bowel and a large amount of ascites (Figure 1). A diagnostic paracentesis was performed. The ascitic fluid contained 2980 nucleated cells of which 76% were eosinophils. His stool had no ova or parasites present. A barium swallow demonstrated several thickened small bowel folds. An upper endoscopy showed edematous mucosa with erythematous stippling in the postbulbar duodenum. Small bowel biopsy from the third portion of the duodenum demonstrated nonspecific chronic inflammation. The patient was started on 40 mg of prednisone per day for the diagnosis of serosal eosinophilic gastroenteritis. His symptoms resolved within 48 h of starting the prednisone, and he was discharged on a slow steroid taper.

Four months later, the patient had completed the steroid taper and his peripheral eosinophil count was $90 \times 10^9$/liter. One month later, the abdominal pain and diarrhea returned. At this time, his eosinophil count had risen to $578 \times 10^9$/liter. Prednisone was restarted and again the abdominal pain and diarrhea promptly resolved. After two months on prednisone, the eosinophil count had fallen to $209 \times 10^9$/liter. The steroids were tapered this time over six months. Three months after stopping prednisone, symptoms returned and the eosinophil count rose to $1514 \times 10^9$/liter. Prednisone was restarted and the patient’s abdominal pain resolved. The steroids were tapered over the next five months. Abdominal pain returned six weeks later and prednisone was restarted.

It was at this point that we became involved in the patient’s care. He was symptom free on 20 mg of prednisone a day and was interested in alternatives to steroid therapy but was not interested in beginning immunosuppressive therapy. Allergy skin testing failed to reveal any
suspect foods. Thus, we decided to begin montelukast therapy at 10 mg/day.

After beginning montelukast, the patient was able to taper off prednisone within four weeks. Currently, he remains off steroids and has been symptom free for the last 20 months on daily montelukast.

**DISCUSSION**

Montelukast (montelukast sodium, manufactured by Merck, tradename Singulair) is a selective and competitive leukotriene receptor antagonist that is used primarily to treat asthma. Its mechanism of action for asthma is based on its ability to block the leukotriene receptor Cys-LT1 that is present on bronchial smooth muscle cells (22).

Leukotrienes are potent mediators of inflammation that are released from eosinophils and mast cells. Their presence causes increased vascular permeability, smooth muscle contraction, and the attraction of inflammatory cells, especially eosinophils. Specifically, leukotriene D₄ (LTD₄) has been shown to be a very powerful chemoattractant for eosinophils (23). In addition, leukotrienes have been shown to enhance the proliferation of bone marrow eosinophils and basophil precursors (24). Thus, by blocking the Cys-LT1 receptor, montelukast prevents bronchoconstriction, the further release of inflammatory mediators, and the recruitment of additional proinflammatory cells.

Extrapolating what is known about eosinophils and asthma to eosinophilic gastroenteritis is challenging. The eosinophil’s role in inflammatory conditions of the gut, including eosinophilic gastroenteritis, inflammatory bowel disease, and celiac disease, remains controversial and is just beginning to be elucidated. Of these disease processes, the eosinophil’s role in eosinophilic gastroenteritis is the best studied.

Keshavarzian et al. demonstrated that the amount of the activated degranulated eosinophils in the gastrointestinal mucosa correlated with the severity of eosinophilic gastroenteritis (25). In addition, they showed that histologic improvement following steroids was accompanied by a decrease in the number of activated eosinophils present on biopsy. Desreumaux et al. demonstrated that eosinophil che-