

A Childhood Case of Eosinophilic Gastritis and Protein-Losing Enteropathy

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Eosinophilic gastrointestinal (GI) conditions are becoming more prevalent in pediatrics.¹ One of the most common allergic GI conditions is eosinophilic esophagitis (EoE), which can present with vomiting, dysphagia, food impaction, or esophageal stricture.² In allergic eosinophilic gastroenteritis (AEG), eosinophilic inflammation can be found throughout the GI tract. It is rare, with only a handful of cases reported in the literature. AEG can present with abdominal pain, failure to thrive, vomiting, or diarrhea.³ In this report, we describe a unique case of a child who presented with edema and was found to have protein-losing enteropathy (PLE) from AEG. The primary site of AEG was the stomach, making this the first reported pediatric case of eosinophilic gastritis.

Case Report

A 2.5-year-old girl presented with facial and abdominal swelling for 10 months. She was being managed by rheumatology for right knee swelling and carried a diagnosis of juvenile rheumatoid arthritis. She failed nabumetone, so was switched to adalimumab, with mild improvement of the knee swelling. The patient had no other medical history or medications, and family history was only significant for an uncle with rheumatoid arthritis. The patient had a good appetite, without vomiting, diarrhea, or abdominal pain. She had hair thinning and was at the 10th percentile for weight and 50th percentile for height, with a normal body mass index (BMI). Her initial evaluation revealed a normal white blood cell count with elevated eosinophil count (9.8%; normal = 0%–6%), low albumin (2.6 g/dL), and negative rheumatologic laboratories.

The patient's GI evaluation included an abdominal ultrasound, which revealed minimal ascites and elevated stool α -1 antitrypsin (>1.33 mg/g; normal < 0.62), confirming PLE. An endoscopy (EGD) revealed only friability of her gastric mucosa. Histology revealed severe gastric eosinophilic inflammation with 55 eosinophils per high-power field on biopsies taken throughout the stomach. The esophagus, duodenum, terminal ileum, and colon appeared grossly normal, and only minimal eosinophilia was found. The patient underwent allergy

testing: radioallergen sorbent test (RAST) was positive for milk, eggs, sesame, apples, corn, wheat, and nuts. These foods were eliminated from the patient's diet in addition to soy, fish, peanuts, and seafood, as is commonly done for the treatment of EoE and AEG.³ She was started on lansoprazole 2 mg/kg daily. Then, 5 months later, a repeat EGD and sigmoidoscopy revealed unchanged and severe eosinophilic gastritis in the gastric antrum, body, and fundus. No eosinophilia was seen in the esophagus, duodenum, or recto-sigmoid. Duodenal fluid and stool were sent for ova and parasite testing and were negative. Unfortunately, the patient's arthritis and edema persisted. Her 24-hour stool α -1 antitrypsin level remained elevated (130 mg/dL; normal <55 mg/dL). It therefore appeared that the patient had a partial response to the restrictive diet as demonstrated by resolution of her mucosal eosinophilia outside of the stomach. However, her gastric eosinophilia remained robust and unchanged.

The patient was then started on prednisolone 1 mg/kg daily. Soon after initiating steroids, the patient's edema and arthritis resolved. An EGD performed after 1 month demonstrated complete resolution of gastric eosinophilia. Stool α -1 antitrypsin normalized, as did serum albumin (3.7 g/dL). Cromolyn 100 mg, 4 times daily, was then added for maintenance therapy, and the steroids were tapered off over 1 month. Adalimumab was discontinued. An EGD 1 month after completing steroids showed only a few scattered eosinophils within the stomach. As the patient was asymptomatic at this time with normal laboratories, eggs were added to her diet. It became protocol during food reintroduction to obtain albumin and stool fecal α -1 antitrypsin levels at the time of EGD. One month after introducing eggs, the EGD and laboratories remained normal, so wheat was added to her diet. (It should be noted that the order of the food additions was guided by the patient's allergy testing.) After the patient had been on wheat for 10 weeks, a

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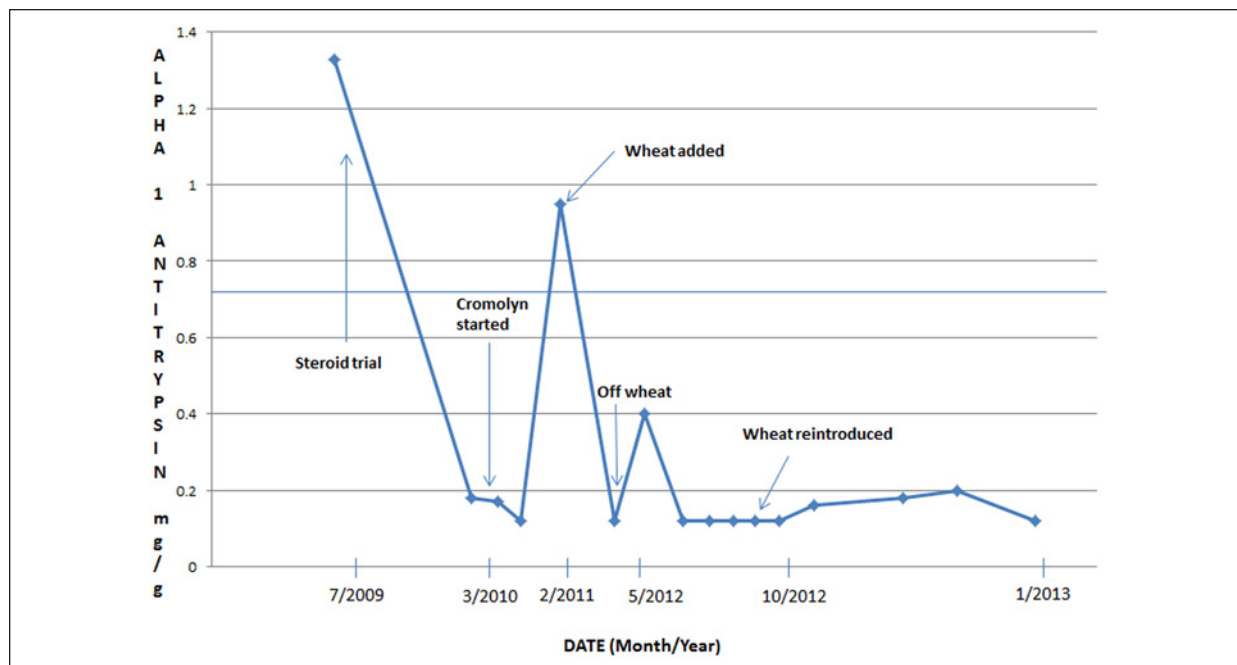


Figure 1. Stool α -1 antitrypsin (in mg/g) over time in our patient, showing when steroids and cromolyn were started and how this number increased after the addition of wheat. Levels below the blue line are considered normal.

repeat EGD was again normal; however, she was noted to have an elevated stool α -1 antitrypsin despite having a normal albumin (Figures 1 and 2). Although the patient was asymptomatic without eosinophilia on biopsies, wheat was removed from her diet as a precaution. Follow-up EGD and laboratories 12 weeks later were normal.

Gradually, the patient's diet was liberalized, and corn, milk and soy were added one at a time every 1 to 3 months with repeat EGDs to confirm histological remission. She remained asymptomatic during the serial reintroductions with no to rare eosinophilia on all gastric, duodenal, and esophageal biopsies. Her albumin and stool α -1 antitrypsin also remained normal. Wheat was then reintroduced, and the patient's subsequent stool α -1 antitrypsin and pathology remained normal. We continued to add foods: sesame, peanuts, tree nuts, and finally, fish. Since the reintroductions, the patient has had no recurrence of her presenting symptoms; her albumin and stool α -1 antitrypsin have remained normal; and her duodenal, gastric, esophageal, and rectosigmoid biopsies have all remained normal with no or rare eosinophils. She remains on lansoprazole 2 mg/kg daily and cromolyn therapy.

On her most recent EGD (8 months after the last food introduction), the patient ate an unrestricted diet except for shellfish (which she had no interest in trying) and

had no eosinophilia on all biopsies. At her last clinical visit (4 years after her diagnosis), the patient had a weight in the 25th percentile and height in the 50th percentile with a normal BMI. She continued to have no arthritis, facial or abdominal swelling, or GI symptoms, and her hair was no longer thinning. We plan to continue her cromolyn at 100 mg 4 times daily and have decreased her lansoprazole to once daily. We will check her laboratories every 6 months and repeat an EGD in 1 year.

Discussion

AEG has been described in the pediatric literature and is a rare cause of PLE.⁴ The mechanism of PLE in AEG is thought to be secondary to an increase in intestinal permeability as a result of inflammation. This leads to serum protein loss, resulting in low plasma oncotic pressures and edema.⁴ This patient only had evidence of severe eosinophilic inflammation in the stomach, and the mild mucosal eosinophilia in other areas of the GI tract resolved on a hypoallergenic diet. Only after the eosinophilic gastric inflammation disappeared with oral steroids did we see any evidence of clinical improvement and resolution of the PLE, indicating that the eosinophilic gastritis was the most likely cause of PLE.

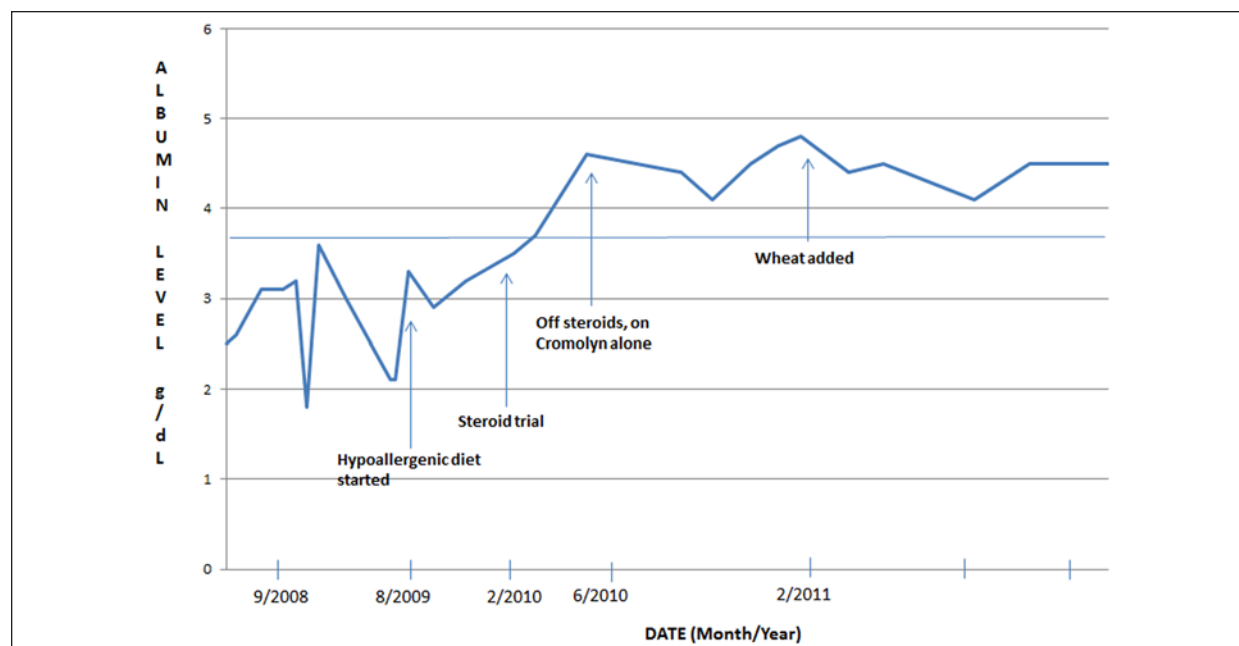


Figure 2. Albumin level (in g/dL) over time in our patient, showing when the hypoallergenic diet was started, what occurred during the steroid trial, and that wheat had no effect on decreasing the albumin level significantly. Values above the blue line are considered normal.

The diagnosis of AEG can be suspected in those with a variety of chronic GI symptoms, including abdominal pain, vomiting, and diarrhea. Our patient's symptoms, however, were confined to persistent edema and arthritis. We speculate that given the resolution of the arthritis immediately after treatment, her arthritis may have been related to her AEG. It is well known that chronic inflammation of the GI tract in inflammatory bowel disease is associated with arthritis/arthralgias. However, there are no reports of an association between arthritis and EoE or AEG. An increase in peripheral eosinophilia is often seen in AEG,⁵ as it was with this patient, but the diagnosis is confirmed histologically. The differential diagnosis for GI eosinophilia includes infection, hyper-eosinophilic syndrome, celiac disease, autoimmune disorders, food allergy, and medications.³

Treatment of AEG is typically with steroids and/or dietary therapy with a hypoallergenic diet or elemental formula. Compliance with these diets can be challenging, and the success rate with diet therapy alone is less successful in AEG than in EoE.⁶ Allergy testing, including RAST and skin patch or prick testing, has not been shown to reliably determine the cause of allergic GI disease.⁷ Steroids have good efficacy in treating allergic eosinophilic conditions, but their side effects discourage long-term use. Because the initial hypoallergenic diet was not effective in our patient, we elected to induce

remission with steroids. As described in the treatment protocols for EoE, eliminated foods were gradually added back into the diet, with repeat EGDs after each reintroduction to document continued remission.⁸ Given the rarity of AEG, treatment is largely based on expert opinion and case reports. Cromolyn, which is a mast cell stabilizer, has been used alone and in combination with acid suppression, with good success for mucosal eosinophilia; it is generally well tolerated with a low side effect profile.⁹ We decided to include cromolyn in our patient's therapy to help her maintain remission during food reintroductions. Eventually, we were able to reintroduce almost all foods, including those that were RAST positive.

As is the case with many eosinophilic conditions, including EoE and AEG, our patient has undergone numerous procedures under anesthesia. In this report, normalization of stool α -1 antitrypsin and albumin levels correlated with endoscopic and clinical remission, with the exception of a single elevation in the stool α -1 antitrypsin at the time of the first introduction of wheat into the diet (which possibly represented a false-positive result, given the lack of clinical symptoms and other pathological and laboratory abnormalities). Stool α -1 antitrypsin, albumin, and peripheral eosinophilia may be useful as biomarkers of disease activity, though more studies are required to investigate this further.

Declaration of Conflicting Interests

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