

Eosinophilic gastroenteritis and colitis related to cow's milk allergy: A case report

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Summary

Objective: To provide evidence on clinical, laboratory, histopathological features, diagnostic and treatment of primary eosinophilic gastroenteritis in children. **Case presentation:** A 7-year-old boy admitted to the 108 Military Central Hospital with symptoms of abdominal pain, nausea and vomiting, recurrent diarrhea related to cow's milk intakes. The child was diagnosed with eosinophilic gastroenteritis, combined with increased serum IgE. The disease was stabilized with corticosteroids, oral proton pump inhibitors (PPIs) combined with the elimination of cow's milk from the daily diet. **Conclusion:** Primary eosinophilic gastroenteritis in children was definitively diagnosed based on exclusion of other causes of eosinophilia and 3 features: Gastrointestinal symptoms, endoscopy showed gastrointestinal eosinophilic infiltration, peripheral eosinophilia. Corticosteroids are the most effective and useful symptom control drugs in most cases in combination with a diet, eliminating the allergic component.

Keywords: Gastroenteritis, eosinophilia, cow's milk allergy.

1. Background

Eosinophilic gastroenteritis (EGE) is a rare inflammatory disorders characterized by eosinophilic infiltration of the stomach, small intestine and colon without any other cause such as renal failure, hypersensitivity reactions with drugs, collagen vascular disease, malignancies or parasitic infections number has to be confirmed by further studies in children. The prevalence of EGE is approximately 5.1 per 100,000 individuals. EGE is more common among children of age < 5 years. Furthermore, an association with documented allergic conditions was reported in 58.9% of children [1], [2]. The pathophysiology of EG is still unknown. EG is thought to be a disorder of immunoglobulin E (IgE) and delayed allergic response via immunoglobulin E (IgE) through Th2 cells (T-helper

cell type 2) [3]. Children with eosinophilic gastroenteritis have many different clinical manifestations, depending on age and degree of target organ involvement such as nausea, vomiting, abdominal pain, diarrhea, anemia, malabsorption and losing weight. There is no gold standard for the diagnosis of eosinophilic gastrointestinal disease and the currently accepted approach is based on three characteristics [3], [4]: gastrointestinal symptoms, endoscopic biopsy showing EGE infiltrates and the diagnosis excludes various pathologies causing peripheral and/or tissue eosinophilia. This poses many obstacles for doctors as well as children themselves in the process of diagnosis, treatment and eosinophilic gastroenteritis. We would like to present a case of such a patient with abdominal pain, loose stools, nausea and vomiting with repeated episodes, related to eating cow's milk products.

2. Case presentation

A 7 years-old boy, admitted to the hospital in January, 2021 with abdominal pain, no fever,

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accompanied by nausea and vomiting, loose stools 4-5 times/day, stools without bloody mucus. History of having episodes of rhinitis when changing weather. The feeding history of the child was not special, except that gastrointestinal symptoms such as abdominal pain, nausea, and loose stools often appear and worsened when the child drank more cow's milk. The child was admitted to the Pediatric Department-108 Military Central Hospital for treatment. The examination showed that the child had no fever, no skin rash. Examination of the abdomen was soft, the liver and spleen were not enlarged. Tests at the time of admission showed an elevated white blood cells (WBC): 26.20G/L, elevated eosinophils: 41.1% (10.80G/L), neutrophils: 43.5% (normal); C-reactive protein (CRP): 2.5mg/l. The initial diagnosis was an intestinal infection, *Helicobacter pylori* gastritis (negative). This patient was treated with antibiotic ceftriaxone 1g x 2g/day IV combined with oral probiotics, and feeding a hospital diet. After 3 days of treatment, the child still had abdominal pain, and no fever.

The results of the tests were further investigated: serum IgE > 2000IU/ml; fecal examination for worm eggs and parasites was negative. Therefore, the diagnosed eosinophilic syndrome, increased serum IgE was made. Solumedrol 40mg/day IV was added to the 5-day regimen. Gastrointestinal symptoms subsided thereafter. However, the symptoms of abdominal pain, nausea, and loose stools recurred 2 weeks after the child was discharged from the hospital.

The child was referred to the national children's hospital, where the child was performed gastroscopy under anesthesia and biopsies were

taken for pathology; tests for antibodies to the parasite; result of abdominal CT scans showed that the last segment of small intestine was thick and light around the circumference, the thickest part was 6mm. There was a lot of peritoneal fluid in the pelvis, 12mm thick, clear fluid; endoscopy results of esophagus, stomach, duodenum, colon and ileum with biopsies for HE staining pathology showed that children with gastroenteritis had eosinophilic infiltrates, *H.pylori* (negative) and there was no granulomatous lesion. The ileal mucosa was not ulcerated, the epithelium was clear, the stromal tissue had moderate inflammatory infiltrate, inflammatory cell diversity. There was a strong proliferation of eosinophils, there were places where eosinophils were concentrated in clusters, the number was 50 eos/hpf (Figure 1A). Infiltrating colonic mucosa with moderate inflammation, increased eosinophils, number 40/hpf (Figure 1B). No malignancy was seen; abdominal ultrasound results: Thickened into loops of intestine, fluid between loops of intestine.

We used prednisolone 1mg/kg/day combined with nexium 20mg, and completely removed cow's milk and cow's milk products from the children's diet for treatment. Digestive symptoms were completely improved after 4 weeks of treatment. The dose of prednisolone was gradually reduced and discontinued, which was then tapered over 6- 8 weeks. As a result, after 6 months of treatment stopping prednisolone treatment, the child did not show any recurrence of gastrointestinal symptoms, and the peripheral blood eosinophil and WBC counts remained within normal limits.

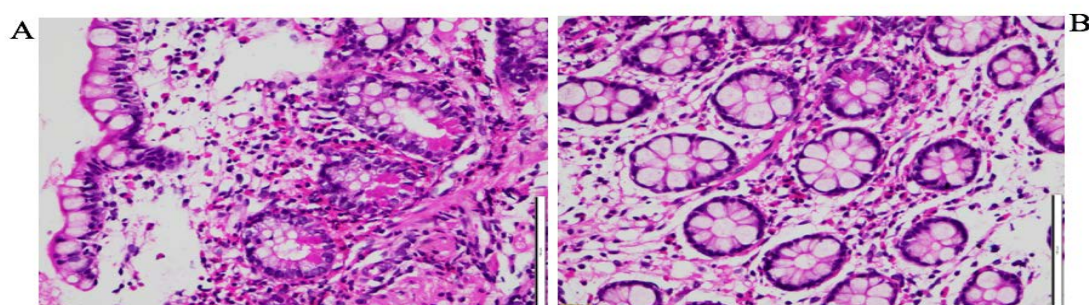


Figure 1. Histopathological Imaging of Stomach, Duodenum (A) and Conlon (B) Biopsy showed Eosinophilic infiltrate

3. Discussion

Eosinophilic gastrointestinal diseases (EGIDs) comprise a group of chronic, inflammatory diseases of the gastrointestinal (GI) tract that are characterized by symptoms related to the dysfunction of the involved segment(s) of the GI tract and histologically, by dense eosinophilic inflammation, in the absence of an identifiable secondary cause. The group of EGIDs comprises eosinophilic esophagitis (EoE), eosinophilic gastritis (EG), eosinophilic gastroenteritis (EGE), and eosinophilic colitis (EC) [2], [3]. The clinical presentation of the EGIDs differs depending on the location and the extent of the eosinophilic infiltration in the GI tract, as well as its depth through the bowel wall. With the lining of the stomach and colon, the most common symptoms are abdominal pain, nausea, vomiting, bloating, indigestion, and diarrhea. Conversely, if the duodenum is dominant, it may present with malabsorption, protein-losing enteropathy and failure to develop [2]. Patients with eosinophilic gastritis and enterocolitis may develop focal ascites, causing abdominal distension and discomfort. In the case of our patient, there was an eosinophilic infiltrate of the gastric mucosa, duodenum, and colon, possibly also the small intestine, which was also affected, often presenting with abdominal pain, nausea, vomiting, Abdominal bloating and loose stools.

The pathogenesis of eosinophilic gastroenteritis is still unknown, but patients with eosinophilic gastroenteritis is thought to be the result of a combination of IgE-mediated dysregulation and a Th2 cell-dependent immune response, leading to elevated eosinophilic, antigen-specific IgE activation and production [4], [5]. Patients with eosinophilic gastroenteritis are often associated with and/or a history of allergic conditions such as asthma, rhinitis, food, drug, urticaria, or eczema [6]. This explained why the clinical manifestations in our patient tend to worsen or recur when the child ate cow's milk and cow's milk products. Cow's milk might be the

cause of this child's illness. Our assertion was further reinforced when the child's serum IgE concentration was very high ($>2000\text{IU/ml}$), the peripheral eosinophil count was increased, and the child had a history of allergic rhinitis. We also performed analysis of hematological, immunological, biochemical, microbiological, and imaging tests to rule out other causes of eosinophilic gastroenteritis, both negative results. Furthermore, the gastrointestinal symptoms such as abdominal pain, vomiting, diarrhea and peripheral eosinophilia in the pediatric patient were significantly improved after treatment with oral corticosteroids combined with component removal of cow's milk out of the daily diet.

Patients with eosinophilic gastroenteritis present differently on laboratory findings. Serum eosinophil counts are usually elevated, but may be normal in about 20% of patients, and counts are often higher in patients with mucosal and submucosal gastroenteritis. Diagnosis of primary eosinophilic gastroenteritis is diagnostic of excluding secondary causes and including three signs: gastrointestinal symptoms, peripheral eosinophilia, and gastrointestinal eosinophilic infiltration on biopsies [6], [7]. In the case of our pediatric patient showed gastrointestinal symptoms; peripheral eosinophilia and histopathological findings of dense eosinophilia in the gastrointestinal mucosa.

Currently, the treatment of eosinophilic gastroenteritis in children is mainly based on case reports and expert opinion. There are no guidelines for the treatment of primary eosinophilia with elevated serum IgE in children. In general, treatment is based on the presence and stability of symptoms. Elimination diets, remove allergenic ingredients from food ingredients. Steroids are the most effective symptom control tool, useful in most cases. The efficacy of steroids on eosinophilic disorders is largely mediated by inhibition of eosinophils growth factors such as IL-3, IL-5 and the granulocyte macrophage-stimulating factors may play an important role in the infiltration of eosinophils into the gastrointestinal tissue [8]. Steroids therapy are

usually recommended, with most patients responding within two weeks at a dose of 0.5-1 mg/kg daily. This was demonstrated by our patient who responded after 2 weeks of 1mg/kg/day prednisolone therapy. Symptoms of abdominal pain, vomiting, loose stools, and eosinophilia improved with steroids. The clinical symptoms were remised and did not relapse even after 6 months of steroid discontinuation. Doses of steroids higher than 2 mg/kg/day have also been reported in some reports [6]. Recurrence of the disease can be so frequent that the patient may be dependent on steroids. In addition, other causes of eosinophilic gastroenteritis should be ruled out as steroids therapy may exacerbate certain conditions. Other medications include leukotriene receptor antagonists (Montelukast), antihistamines and mast cell stabilizers (Ketotifen, Sodium cromoglicate), biologics (Omalizumab, Mepolizumab), and IL-4 inhibitors. Surgery was indicated if bowel obstruction or perforation. Current trends in the clinical use of biologics for the treatment of eosinophilic dyspepsia [2], [3]. Treatment with proton pump inhibitors (PPIs) and diet: even in the absence of GERD, neutralizing gastric acidity with PPIs was believed to be effective in improving symptoms and pathological level. However, some studies had shown that treatment of PPIs with lansoprazole (10mg/day) improved eosinophil infiltration in pediatric patients with eosinophilic gastroenteritis. The mechanism was thought to involve blockade of IL-4 and IL-13 activity, as well as acid suppression, shortening the viability of eosinophils by increasing pH [4]. Therefore, the use of PPIs should not be underestimated. Identifying the food allergens and taking an eliminated dietary can alleviate the symptoms of the disorder. However, complete remission is usually achieved with cow milk proteins-based elemental diets.

Finally, patient tolerance and adherence to such strategies were difficult to track, particularly when applying empiric or high-component diets [5]. Therefore, eosinophilic gastroenteritis in children

with a high risk of recurrence is very high when completely eliminating the triggering of the eosinophilic immune response from the daily food for a child is difficult task. The case report illustrated the results and difficulties in diagnosis, evaluation, and long-term follow-up of eosinophilic gastrointestinal disorders. It also highlights the importance of clinical and laboratory associations, the need to identify biomarkers for monitoring disease activity.

4. Conclusion

We reported a rare and followed-up case of a 7 years-old boy with eosinophilic gastroenteritis (EGE) increased blood IgE levels. The diagnosis was confirmed based on excluding other causes of eosinophilia and including three features: Gastrointestinal symptoms, biopsy showing eosinophils infiltrating gastrointestinal tissue, and increased peripheral acidophilic. Steroids in combination with diet, eliminating allergens are the most effective and useful method of symptoms control in most cases of eosinophilic gastroenteritis associated with cow's milk allergy.

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