Three case reports of eosinophilic gastroenteritis with milk, wheat, and peanut food allergy

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ABSTRACT

Eosinophilic gastroenteritis (EGE) is an uncommon disease that can affect one or more organs of the digestive tract. EGE has a very low incidence rate and its diagnosis is challenging for any clinician. We report a case series of three cases of EGE who were evaluated for non-specific gastrointestinal symptoms and presented with an increase in eosinophils and total immunoglobulin E. The diagnosis of EGE was confirmed by histopathological findings. The causative food allergens were identified by provocation and elimination tests. The relevance of our case series lies in concomitant food allergy with the atopic constitution and the improvement of symptoms after the elimination of specific food is the mainstay for the management of EGE.

Key words: *Eosinophilic colitis, Eosinophilic enteritis, Eosinophilic esophagitis, Eosinophilic gastroenteritis, Food allergy*

Eosinophilic gastrointestinal disorders are an abnormal immune-mediated response to an allergic reaction determined by both an immunoglobulin E (IgE)-mediated and TH2-mediated (type IV) eosinophilic delayed hypersensitivity process. The exact incidence is unknown, but it is estimated to be around 1–30/100,000 [1]. Eosinophilic gastroenteritis (EGE) more commonly affects Asians while eosinophilic esophagitis (EE) is more common in Caucasians [2]. According to the affected site(s), eosinophilic gastrointestinal disorders are subclassified into three types as EE, eosinophilic gastritis (EG), eosinophilic enteritis (EE), and eosinophilic colitis (EC).

Most of the patients are sensitized to environmental allergens and up to 62% of cases are sensitized to food [3]. As per a theory, food allergens cross- intestinal mucosa and trigger an inflammatory response which includes mast cell degranulation and recruitment of eosinophils and can be associated with other atopic diseases [4]. The associated allergic disorders are asthma, allergic rhinitis, and atopic eczema and are found in 45–63% of reported cases of EGE [5]. Elevated IgE levels are reported in patients with EGE [6]. Cow's milk, wheat, and peanut are the main allergenic food items, which may cause EE [7]. The diagnosis is based on history, high eosinophil count, and histopathological biopsy with atopic sensitization.

CASE REPORT

We report a case series of three cases that presented with relevant findings of gastrointestinal symptoms with increased peripheral blood eosinophils. The patients were evaluated further by histopathological findings and the diagnosis of EE/colitis was confirmed. One of our patients was asked to stop milk products and the second patient was asked to stop wheat while the third was asked to stop peanuts for 6 weeks. The diagnosis was confirmed after diet elimination for 6 weeks and provocation test of causative food following which they again developed gastric symptoms (abdominal cramps, pain, dyspepsia, etc.)

Case 1 (EE)

A 29-year-old female presented with complaints of lower abdomen pain and nausea with on and off loose stools, weight loss, and loss of appetite for 1.5 years. She had similar complaints in her childhood as well. She was admitted to a gastric center for the same. Her general examination was unremarkable and vitals were normal. Blood investigations showed total IgE – 419 IU/ml, specific IgE to *Dermatophagoides pteronyssinus* – 16.30 kU/L, *Dermatophagoides farinae* – 23.30 kU/l, milk – 0.10 kU/l, blood eosinophil – 41%, and absolute eosinophil count (AEC) – 3310 cells/ul (Table 1). Her colonoscopy was normal, random biopsies were taken from the terminal ileum and colon. Ileum biopsy showed normal tall villi with maintained crypt-villous ratio, the lamina propria showed inflammation, including numerous eosinophils (>20/high-power field [HPF]). Intraepithelial eosinophilic infiltration was also present. Deeper tissues also showed sheets of eosinophils. No parasite identified. These features were consistent with EE.

Section from colon biopsy showed preserved crypt architecture. The lamina propria shows mild-to-moderate inflammation, including lymphocytes, plasma cells, and few eosinophils. There was no increase in epithelial lymphocytes. No thickening of the basement membrane was seen. No granuloma

or neoplastic pathology seen. Based on clinical, endoscopic, and histological findings, the patient was diagnosed as EE. The patient was advised to take a milk-free diet and was followed up for 3 years during which her symptoms improved.

Case 2 (EE)

A 19-year-old male presented with complaints of epigastric pain for 1 month which was aggravated on taking meals. He also complained of frequent bloating and dyspepsia after taking meals. On general examination, tenderness was present in the epigastrium. Vitals were all normal. Blood investigations showed total IgE – 522 IU/ml, specific IgE to wheat – 0.32 ku/l, peanut – 0.27 ku/l, soybean – 0.19 ku/l, and egg white – 0.15 ku/l. Allergic skin (Fig. 1) and blood tests were positive. Blood eosinophil count was 24.30% and AEC was 2430 cells/ul (Table 1). Contrast-enhanced computed tomography (CECT) abdomen was normal.

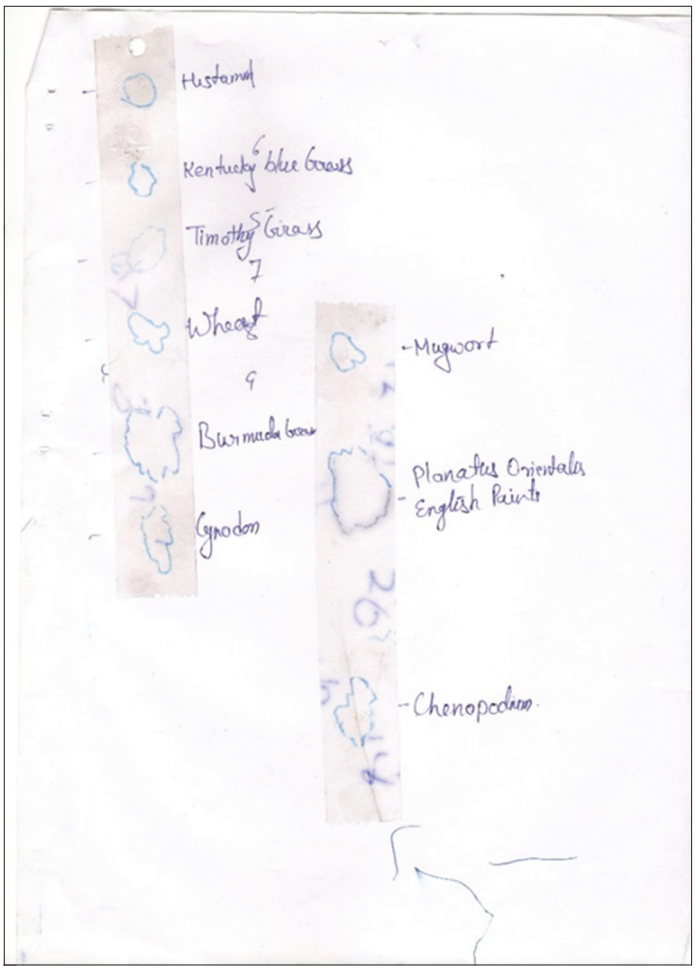


Figure 1: Skin prick test of case 2 showing various positive allergens

In view of a typical clinical picture associated with peripheral blood eosinophilia, the patient underwent upper gastrointestinal endoscopy along with multiple biopsies from gastric and duodenal mucosa. Upper gastrointestinal endoscopy was unremarkable (Fig. 2). Gastric biopsy showed superficial fragments of the gastric mucosa. Lamina propria showed mild chronic inflammation composed chiefly of lymphocytes. No granuloma or parasites were seen. Duodenal biopsy showed multiple fragments of duodenal mucosa with normal crypt villous architecture with many eosinophils. Occasional small aggregates of eosinophils were seen. No intraepithelial lymphocytes, parasites, or granulomas seen. Chronic duodenitis with increased eosinophils was suggestive of EE. The patient was followed for 2 years and he showed improvement with the elimination of milk and wheat from his diet.

Case 3 (EC)

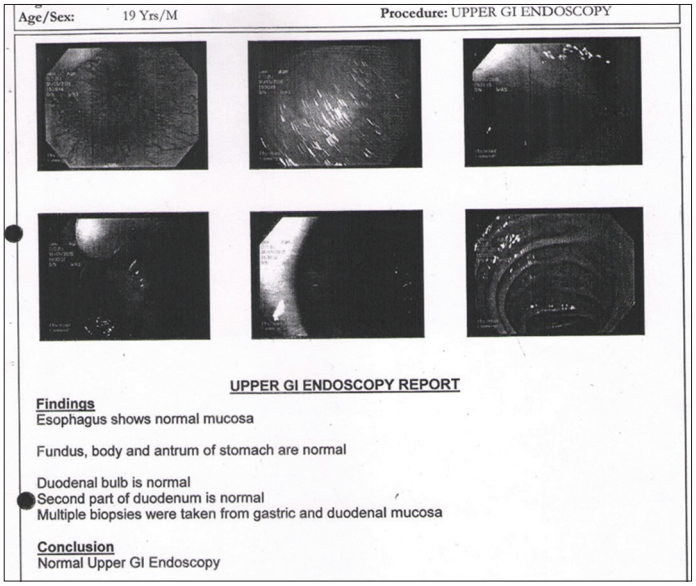
A 44-year-old male, known case of allergic asthma and hypertension, had a history of drug allergy to various antibiotics. The patient underwent a small surgical procedure of hemorrhoidectomy following which he developed severe rectal bleeding. On general examination, the nose was pale and boggy. Chest examination showed bilateral rhonchi and vesicular breath sounds were present. Vitals were normal. His blood investigations showed: Total IgE-1426 IU/ml, specific IgE to *D. pteronyssinus*-12.3 ku/l, *D. farinae*-15.5 ku/l, peanut-0.07 ku/l. Allergic skin test was positive for *D. pteronyssinus*, *D. farinae*, egg, and peanut (Fig. 3).

Blood eosinophil count was 8% and AEC was 510 cells/ul (Table 1). The CECT abdomen was normal. Upper gastrointestinal endoscopy showed erosive gastropathy. Colonic biopsy revealed

Table 1: Investigations done for the three cases

Investigations	Case 1		Case 2		Cases 3	
Total IgE	419 (<158 IU/ml)		522 (<158 IU/ml)		1426 (<158 IU/ml)	
Peripheral blood eosinophils	41 (0.0–7.0%)		24.3 (0.0–7.0%)		8 (0.0–7.0%)	
Absolute eosinophil count	3310 (15–550 cells/ul)		2430 (15–550 cells/ul)		510 (15–550 cells/ul)	
Skin prick test	Histamine	5 mm	Histamine	10 mm	Histamine	5 mm
	D. ptero.	20 mm	*Platanus orientalis*	21 mm	Peanut	6 mm
	D. farina.	20 mm	*Cynodon dactylon* (Bermuda)	20 mm	*D. ptero.*	14 mm
	Milk	4 mm	*Chenopodium album*	20 mm	*D. farina.*	14 mm
			Wheat	12 mm	*Prosopis juliflora*	6 mm
			Histamine	10 mm		
Specific IgE	*D. ptero.*	16.3 ku/l	Wheat	0.32 ku/l	*D. ptero.*	12.3ku/l
	D. farina.	23.3 ku/l	Peanut	0.27 ku/l	*D. farina.*	15.5ku/l
	Milk	0.10 ku/l	Egg	0.15 ku/l	Peanut	0.07 ku/l

D. ptero.: *Dermatophagoides pteronyssinus*, *D. farina.*: *Dermatophagoides farinae,* IgE: Immunoglobulin E


Age/Sex: 19 Yrs/M Procedure: UPPER GI ENDOSCOPY

UPPER GI ENDOSCOPY REPORT

Findings
Esophagus shows normal mucosa

Fundus, body and antrum of stomach are normal

Duodenal bulb is normal
Second part of duodenum is normal
Multiple biopsies were taken from gastric and duodenal mucosa

Conclusion
Normal Upper GI Endoscopy

Figure 2: Normal upper gastrointestinal endoscopy of case 2

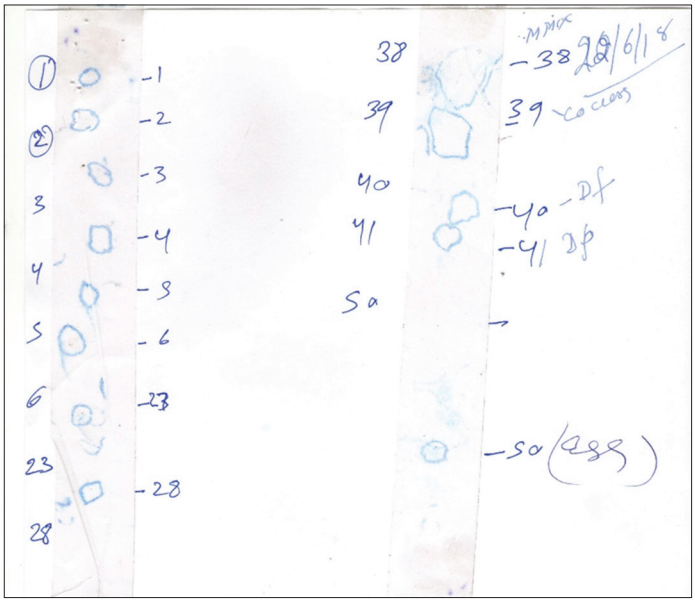


Figure 3: Skin prick test of case 3 showing various positive allergens

mucosa with infiltrates of lymphocytes, plasma cells, and eosinophils. These features were suggestive of EC. He was followed up for 3 years and showed improvement with peanut elimination from his diet.

DISCUSSION

The diagnosis of eosinophilic gastrointestinal disorders is based on eosinophilic infiltration of mucosa, exceeds 20 eosinophils/HPF with high AEC in blood in at least one sample with signs and symptoms of abdominal pain, nausea, vomiting, diarrhea, blood in stools, malabsorption, etc. [3]. To confirm the diagnosis of EGE, three following parameters are essential: (a) Gastrointestinal symptoms; (b) eosinophilic infiltration to one or more segments of the gastrointestinal tract, by measuring the number of eosinophils under HPF view, without established threshold ranging from >20 eosinophils/HPF to >50 eosinophils/HPF, EG: >30/HPF in >5 HPF or >70/HPF in >3 HPF [8]. EE: The presence of excess eosinophils in the small intestine could be considered a multiple of the maximum count in normal biopsies such as 2×26/HPF or 52/HPF in the duodenal mucosa and 2×28/HPF or 56/HPF in the ileum [9].

EC: Excess eosinophils in colonic mucosa could be considered as a peak count/HPF in normal biopsies, including 2×50/HPF or 100/HPF in the transverse and descending colon and 2×32/HPF or 64/HPF in rectosigmoid mucosa [9]. On the basis of histopathological findings, mucosal EGE is the most common, presenting with dyspepsia, abdominal pain, nausea, diarrhea, and vomiting rather than muscularis propria and serosal involvement [5]; and (c) exclusion of other causes that course with eosinophilic infiltration as hypereosinophilic syndrome, eosinophilic granulomatosis with polyangiitis, celiac disease, irritable bowel syndrome, polyarteritis nodosa, other connective tissue disorders, infection, and drug hypersensitivity.

In case one, cow's milk was considered as the main cause of EGE on the basis of skin prick test and provocation test. After discontinuation of milk products, she remained asymptomatic during 2 years follow-up. While in case two, wheat allergy was confirmed after provocation test, skin prick test, and specific IgE, and in case three, peanut allergy was confirmed by provocation and skin prick test, he also has had a history of rhinitis and asthma. Both cases two and three showed improvement after diet elimination of wheat and peanut, respectively. Our patients have a strong association of symptoms of EGE with milk (case 1), wheat (case 2), and peanut (case 3) and found concordance sensitization with skin prick test and specific IgE of dust mite, grass, and tree pollen (case 1 – dust mites and milk, case 2 – wheat and grass pollen, and case 3 – peanut, tree nut, and dust mites).

The six foods (soy/wheat/egg/milk/peanut/tree nuts/fish and shellfish) elimination diet consists of avoidance of food items, is based on empiric-based elimination and reintroduction of each food but has poor compliance, poor quality of life, and unpalatable diet. Our three cases were diagnosed after skin tests, blood tests, and provocation tests which support food allergy testing of the patients of EGE for clinical decision and maintenance therapy in a more consistent fashion.

In adults, the evidence of link between food hypersensitivity and EGE is limited. There are case reports about the effectiveness of diet avoidance in adults with EGE [10,11]. The literature shows that allergic clinical manifestation is associated with 64% of reported cases of EGE having frequent respiratory symptoms (allergic rhinitis 60% and allergic asthma 39%) and family history of atopic disease [12]. Two of our patients have high eosinophil count, case 1 (AEC-3310 cells/ul) and case 2 (AEC-2430 cells/ ul). The AEC is used to categorize the disease into mild (AEC: 600–1500 cells/ul, moderate (AEC: 1500–5000 cells/ul), and severe (AEC: >5000 cells/ul) [3].

High peripheral blood eosinophils are found in 20–80% of cases with an average count of 2000 cells/ul in patients with mucosal layer involvement, 1000 cells/ul in patients with muscular layer involvement, and 8000 cells/ul in patients with

serosal involvement [12]. All our cases belong to mucosal eosinophilia EGE. All the three cases have high levels of total IgE (total IgE 419, 522, and 1426 IU/ml in case 1, 2, and 3, respectively). It is said, total IgE > 100 IU/ml is increased in two-thirds of EGE cases. EGE could be IgE associated with Th2 cell-mediated eosinophilic delayed hypersensitivity reaction [13]. Skin tests and allergen-specific IgE are indicated in these patients. If immunologically positive, elimination of specific food should be the first approach for the management. Further studies are warranted to confirm these findings.

CONCLUSION

EGE is a rare disease, commonly underreported and needs good communication between clinical allergist, endoscopist, and pathologist. If there is a clinical suspicion of EGE, prompt histopathological evaluation followed by confirmation through the offending allergen/s should be done. We report a case series of three cases of EGE with a strong association with food allergy and there was an effective decrease in the abdominal symptoms after discontinuation of milk, wheat, and peanuts.

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