

Clinical features and treatment outcomes of eosinophilic gastroenteritis : an analysis of 28 cases

X.-M. Yang¹, S.-Q. He¹, H. Yang³, H.-H. Zheng⁴, L.-H. Zhu², S.-K. Zhou⁵, Y. Zhang¹

(1) Department of Gastroenterology, Taizhou Hospital of Zhejiang Province, Wenzhou Medical College, 150 Ximen Street, Linhai, Zhejiang Province, China ; (2) Department of Medical Administration, Taizhou Hospital of Zhejiang Province, Wenzhou Medical College, Linhai, China ; (3) Department of Radiology, Enze Hospital, Wenzhou Medical College, 1th Tongyang East Road, Taizhou city, Zhejiang Province, China ; (4) Department of Pathology, Taizhou Hospital of Zhejiang Province, Wenzhou Medical College, 150 Ximen Street, Linhai, Zhejiang Province, China ; (5) Department of Gastrointestinal Surgery, Taizhou Hospital of Zhejiang Province, Wenzhou Medical College, 150 Ximen Street, Linhai, Zhejiang Province, China.

Abstract

Background : Eosinophilic gastroenteritis (EG) is uncommon disease, and the pathogenesis of this disease have yet to be fully clarified.

Aim : This study was to describe the clinical manifestations, endoscopic features and treatment outcomes of a cohort of patients with EG.

Method : This retrospective study was included 28 consecutive patients who were diagnosed EG between January 2011 and December 2015 in Taizhou Hospital. The patients' clinical manifestations, endoscopic features and treatment outcomes were reviewed from a prospectively maintained database.

Results : Twenty-eight patients with EG were enrolled in the study (median age 54 years). The main symptoms were abdominal pain (78.6%), abdominal distension (50.0%), nausea and vomiting (28.6%) and diarrhea (25.0%). Laboratory examinations showed the elevation of blood eosinophil count (85.7%), serum IgE (71.4%). Endoscopic findings included small patchy mucosal erythema or erosions (75.0%), mucosal fold thickening (17.9%), submucosal nodules (21.4%), small gastroduodenal ulcers (14.3%). Twenty patients were treated and responded to prednisolone but five patients (25.0%) relapsed during the follow-up. The other 8 patients were treated with loratadine, proton pump inhibitors and dietary modification, 5 patients had clinical resolution during the follow-up. The other 3 patients did not achieve clinical remission, and then were given prednisone treatment.

Conclusion : For some patients with gastrointestinal symptoms and peripheral eosinophilia, a high suspicion of EG is necessary and multiple endoscopic examinations might be helpful in diagnosis of EG. Most patients with EG could achieve remission after with the treatment of steroid or dietary elimination therapy. (*Acta gastroenterol. belg.*, 2019, 82, 5-10).

Introduction

Eosinophilic gastroenteritis (EG) is uncommon disease, which is characterized by eosinophilic infiltration into one or more layers of the gastrointestinal tract. Although EG was firstly described in 1937 by Kaijser, the pathogenesis of the disease have yet to be fully clarified (1-3). EG may involve anywhere in the gastrointestinal tract from the esophagus to the rectum, but is most commonly affected in the stomach and proximal small bowel. It may discovered at any age, but is usually presents in the third to fifth decades of life, with a slight male preponderance (3).

In 1970, based on the depth of tissue involvement, Klein et al. classified this disorder into three subtypes: mucosal, muscular, and subserosal (4, 5). Each subtype shows distinct clinical manifestations based on the site and depth of eosinophilic intestinal infiltration. The clinical manifestations which might overlap with other

common gastrointestinal disorders such as irritable bowel syndrome (IBS). And imaging tests may show irregular thickening of the folds, but these imaging features might also be found in other disorders such as lymphoma or Crohn's disease (6, 7). The endoscopic performance is also nonspecific. Thus, the diagnosis of EG in the clinical practice remains a challenge for the physicians, and the current literature is limited to single case reports or small case series (6, 8, 9). In this study, we aimed to describe the clinical, endoscopic, and histopathologic features and treatment outcomes of a cohort of patients with EG.

Materials and methods

Patient

This retrospective study was approved by the ethics committee of Taizhou Hospital, Wenzhou Medical College. The analysis included consecutive patients who were diagnosed EG between January 2011 and December 2015 in Taizhou Hospital.

The diagnostic criteria of EG in this study were performed according to Klein's criteria, as follows : 1) The presence of gastrointestinal symptoms including abdominal pain, abdominal discomfort nausea, vomiting, diarrhea, ascites, etc. ; 2) The pathological confirmation of eosinophilic infiltration into gastrointestinal tissues (esophagus, ≥ 15 eosinophils/HPF ; stomach, duodenum and small intestine, ≥ 20 eosinophils/HPF ; colon and rectum, ≥ 30 eosinophils/HPF) (10, 11) ; 3) Patients were excluded if they were diagnosed as follows : eosinophilic esophagitis, parasitic infestation or clinical response to empirical anti-parasitic agents if stool tests for ova cysts and parasites were negative, hypersensitive reaction to drugs, inflammatory bowel disease, malignancy, lymphoma, autoimmune disease and hypereosinophilic syndrome.

Correspondence to : Shen-Kang Zhou, Department of Gastrointestinal Surgery, Taizhou Hospital of Zhejiang Province, Wenzhou Medical College, 150 Ximen Street, Linhai, Zhejiang Province, China. Tel :+86 13736249308, Fax : +8657685199171.

E-mail:zhouk80@163.com

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From January 2011 to December 2015, a total of 28 consecutive patients with EG were included in this study. Patients' demographics, clinical symptoms, allergy history, absolute eosinophil counts, serum albumin, IgE, radiology examination, endoscopy examination and pathology report, treatment, the response to treatment and other parameters, were reviewed and analyzed. Data for analyses were collected from a prospectively maintained database.

The number of infiltrating eosinophils on the biopsy slide was recalculated under microscopy with maximum 400 magnification ($\times 400$) by two pathologists. "Sweeping" technique was applied, which refers to count downward, then upward and finally from left to right. Two pathologists performed this analysis independently. In this study, the mean number of eosinophils was the final number of infiltrating eosinophils.

Allergy testing was examined on a detector (XD236, Xunda, China) by immunoblotting method, which includes food allergy (egg, milk, sea food [fish, shrimp, crab], beef, mutton, peanut, mango, wheat, etc..) and aeroallergens (dust mites, animal dander, mold spores, ragweed, pollens, etc..).

Subtype

According to the predominantly involved gastrointestinal layers, EG was categorized into three disease subtypes: mucosal, muscular, and subserosal. In this study, if patients with muscular disease or subserosal disease had mucosal eosinophil infiltration, they were categorized as having muscular disease or subserosal disease. And Patients with hypereosinophilia in ascites were also categorized as subserosal disease (6, 12).

Results

In this study, 28 patients with EG were enrolled in the study, and the clinical data of these patients are showed in Table 1. Of whom 15 patients were male (53.6%). The median age of the patients was 54 years (range 18-73 years). Nine out of 28 patients (32.1%) had clear allergy history, including 5 who had positive reaction to shrimp >3 had allergic asthma and one had positive reaction to sulfa drugs. The median duration from onset of symptoms to diagnosis was 1.5 month (range, 0.5-33 months). The disease duration was range five days to two years. The main symptoms were abdominal pain (78.6%, 22/28), abdominal distension (50.0%, 14/28), nausea and vomiting (28.6%, 8/28) and diarrhea (25.0%, 7/28).

Laboratory and imaging examinations

In this study, blood routine test showed eosinophilia (above $500 \times 10^6/L$) in 24 cases (85.7%). The median eosinophil count was $1495 \times 10^6/L$ (interquartile range $820-5990 \times 10^6/L$), and the median of the eosinophil percentage was 28.2% (interquartile range 17.1-49.0%).

Table 1. — Clinical data of the 28 patients with eosinophilic gastroenteritis

Age, median (range), years	54	(18-73)
Gender, n (%)		
Male	15	(53.6)
Female	13	(46.4)
Allergy history, n (%)	9	(32.1)
Presenting symptoms, n (%)		
Abdominal pain	22	(78.6)
Abdominal distension	14	(50.0)
Nausea and vomiting	8	(28.6)
Diarrhea	7	(25.0)
Ascites	7	(25.0)
Peripheral eosinophilia count, median, $\times 10^6/L$ (IQR)	1495 (82-5990)	
Peripheral eosinophilia percentage, median, % (IQR)	28.2 (17.1-49.0)	
Serum IgE, median, IU/ml (IQR)	391	(118.5-689.3)
C-reactive protein, median, mg/dl (IQR)	5.3 (2.8-9.0)	
Blood sedimentation, median, mm/h (IQR)	12	(6-25)
Fecal occult-blood, n (%)	8	(28.6)
Hypoalbuminemia, n (%)	7	(25.0)
Multiple allergen simultaneous test, n (%)	1	(3.6)
Type of endoscopy examination, n (%)		
Gastroscopy, colonoscopy and enteroscopy	3	(10.7)
Gastroscopy and colonoscopy	19	(67.9)
Gastroscopy	4	(14.3)
Colonoscopy	2	(7.1)
Endoscopic detection, n (%)		
Patchy mucosal erythema/erosions	21	(75.0)
Mucosal fold thickening	5	(17.9)
Submucosal nodules	6	(21.4)
Ulcers	4	(14.3)
no abnormal findings	5	(17.9)

The median of serum IgE was 391.1 IU/ml (interquartile range 118.5-689.3 IU/ml), and 20 out of them (71.4%) had elevated levels ranging from 207 to 1428 IU/ml. C-reactive protein and blood sedimentation rate elevation was observed in 14.3% and 32.1% of the patients, respectively. Seven patients (25%) had hypoalbuminemia, and one patient had a positive reaction for shrimp in food multiple allergen simultaneous test (MAST). Fecal occult-blood testing showed 8 patients (28.6%) with a positive reaction. Seven out of 28 (25.0%) patients had ascites, including mild ascites 5 cases and massive ascites 2 cases, and ascites routine test was performed in 7 patients with ascites and showed the eosinophil count was range 690 to 2900/ul.

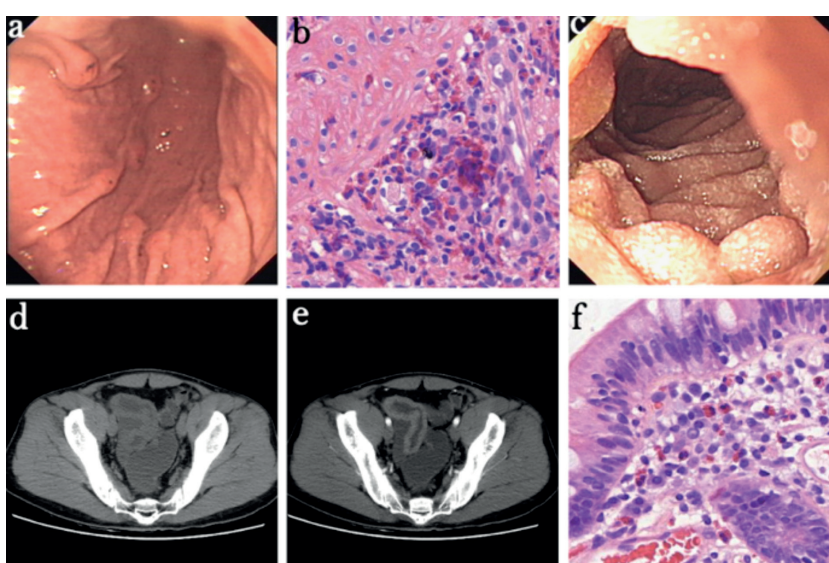


Figure 1 (a-f). A patients with eosinophilic gastroenteritis : (a) endoscopic view of small protruding lesions patchily distributed in the stomach ; (b) Massive infiltration of eosinophils in the gastric mucosa ; (c) Enteroscopic view of small protruding lesions found in the small intestine ; (d) Computed tomography (CT) showed a segment of the distal ileum was diffused thickness ; (e) Contrast-enhanced CT showed the segment of the distal ileum had homogeneous density ; (f) Massive infiltration of eosinophils in the intestinal mucosa.

Endoscopy examinations

In this study, all 28 patients were examined with gastroscopy and/or colonoscopy. Twenty-two patients underwent gastroscopy and colonoscopy, including 3 patients underwent the double-balloon push enteroscopy examination. The other 6 patients were given only one type endoscopy examination, including 4 gastroscopy and 2 colonoscopy. Endoscopic examinations showed small patchy mucosal erythema or erosions (21/28 ; 75.0%), mucosal fold thickening (5/28 ; 17.9%), submucosal nodules (6/28, 21.4%), small gastroduodenal ulcers (4/28 ; 14.3%), and no abnormal endoscopic findings (5/28 ; 17.9%).

In this study, all 28 patients were performed endoscopic biopsy, 23 out of them (82.1%) were detected significant eosinophilic infiltration in the mucosa. Twenty-six patients underwent gastroscopy biopsy, and 8 out of 26 patients (30.7%) were detected significant eosinophilic infiltration, including 6 patients with gastric eosinophilic infiltration and 2 with duodenal eosinophilic infiltration. Twenty-four patients underwent colonoscopy biopsy, 11 out of 24 patients (45.8%) were detected significant eosinophilic infiltration. And 3 patient underwent biopsy by double-balloon enteroscopy, all of them were detected significant eosinophilic infiltration.

Treatments and follow-up

According to the examinations of endoscopic biopsy and ascites, 21 patients were classified with mucosal disease, and the other 7 patients were classified with subserosal disease. After diagnosed as EG, 20 out of 28 patients were treated with prednisone with doses ranging from 20 to 40 mg daily. As evidenced by

the improvement of gastrointestinal symptoms and eosinophilic infiltration on repeat endoscopic biopsy, prednisone was tapered gradually over 1 to 3 months. During the follow-up (median 26 months ; range 9-62 months), 5 patients relapsed following tapering-off of prednisolone. However, prednisone was still effective in these 5 patients with disease recurrence.

Eight out of 28 patients were not treated with corticosteroids when diagnosed as EG. These 8 patients were received dietary modification and treated with loratadine and proton pump inhibitors (PPI). Among them, 5 patients had clinical resolution during the follow-up (9-38 months). The other 3 patients did not achieve clinical remission, and then were given prednisone treatment. The application of prednisone was aforementioned. These 3 patients showed symptom relief and no relapse during the follow-up. The clinical outcomes of treatments were showed in Table 2.

Discussion

EG is a rare condition, and its pathogenesis have yet to be fully clarified. Some scholars believe that there is a correlation between EG and allergic conditions. Before this study, several studies reported that 20%-50% of EG patients had allergy-related conditions such as asthma and atopy (1, 2, 13). In this study, 32.1% of patients had allergy history, which was within the reported range. Thus, when a patients with allergy history suffers from gastrointestinal symptoms, he should be highly suspected as EG. In this study, the main clinical manifestations of EG were abdominal pain, abdominal distension, nausea and vomiting and diarrhea. Such clinical manifestations were similar to those previously reported. Compared to other gastrointestinal disease, these manifestations of

Table 2. — Clinical features and treatment outcomes of 28 patients with eosinophilic gastroenteritis

No.	Sex/age	Allergy History	PE,(%)	Serum IgE	CT examination	Type of Endoscopy	Site of positive histology	Treatment	Remission	Relapse	Follow-up
1	F/56	No	32.5	1305.0	local thickening of sigmoid	gastroscopy colonoscopy	sigmoid	Prednisolone +PPI	Yes	No	62
2	M/60	No	12.2	90.0	no evident abnormality	olonoscopy	transverse colon	Prednisolone +PPI	Yes	No	57
3	F/59	Sulfa drugs	13.2	50.8	no evident abnormality	gastroscopy	gastric antrum	Prednisolone +PPI	Yes	No	52
4	M/62	No	13.2	98.0	no evident abnormality	olonoscopy	transverse colon	Prednisolone +PPI	Yes	No	50
5	F/43	No	50.1	1015.7	local thickening of gastric body	gastroscopy colonoscopy	gastric body	Prednisolone +PPI	Yes	Yes	47
6	M/73	No	15.7	258.0	mild ascites	gastroscopy	-	Dietary, loratadine and PPI	Yes	No	42
7	F/73	Allergic asthma	48.1	207.6	no evident abnormality	gastroscopy colonoscopy	gastric body	Prednisolone +PPI	Yes	No	40
8	M/57	No	23.9	361.9	no evident abnormality	gastroscopy colonoscopy	ascending colon	Prednisolone +PPI	Yes	No	38
9	F/59	No	70.5	401.1	mild ascites	gastroscopy colonoscopy	-	Prednisolone +PPI	Yes	No	36
10	M/34	Shrimp	28.9	526.2	part thickening of small intestine, mild ascites	gastroscopy colonoscopy	No	Dietary, loratadine and PPI	Yes	No	31
11	F58	No	12.7	42.8	no evident abnormality local	gastroscopy	gastric antrum second	Prednisolone +PPI	Yes	No	30
12	F/36	Shrimp	32.0	731.7	thickening of gastric body local	gastroscopy colonoscopy	part of duodenum	Loratadine and PPI	(prednisolone + PPI)	No	28
13	M/54	No	61.8	467.0	thickening of terminal ileum	gastroscopy colonoscopy	ascending colon	Prednisolone +PPI	Yes	Yes	28
14	F/36	Shrimp	32.0	887.7	local thickening gastric body	gastroscopy colonoscopy	second part duodenum	dietary, loratadine and PPI	No (prednisolone + PPI)	No	26
15	F/39	Allergic asthma	16.2	82.0	no evident abnormality	gastroscopy colonoscopy	gastric antrum	Prednisolone +PPI	Yes	No	24
16	M/54	No	21.2	87.0	no evident abnormality	gastroscopy colonoscopy enteroscopy	small intestine	Prednisolone +PPI	Yes	No	24
17	F/59	No	22.5	985.0	local thickening of rectum	gastroscopy colonoscopy	rectum	Prednisolone +PPI	Yes	No	23
18	M/32	Allergic asthma	25.9	561.9	no evident abnormality	gastroscopy colonoscopy	ascending colon	Dietary, loratadine and PPI	Yes	No	21
19	M/48	No	29.2	377.0	mass ascites	gastroscopy colonoscopy enteroscopy	small intestine	Prednisolone +PPI	Yes	No	19
20	M/62	No	61.8	477.0	local thickening terminal ileum	gastroscopy colonoscopy	terminal ileum	Prednisolone +PPI	Yes	Yes	17
21	M/62	No	17.5	72.0	no evident abnormality	gastroscopy colonoscopy	gastric body	Prednisolone +PPI	Yes	No	16
22	M/35	Shrimp	16.9	179.9	mild ascites	gastroscopy colonoscopy	-	Dietary, loratadine and PPI	Yes	No	15
23	F/47	No	36.7	232.6	part thickening of small intestine	gastroscopy colonoscopy enteroscopy	small intestine	Prednisolone +PPI	Yes	No	12
24	M/18	Shrimp	57.0	1428.0	no evident abnormality	gastroscopy colonoscopy	rectum	Dietary, loratadine and PPI	Yes	No	11
25	M/56	No	24.9	381.1	no evident abnormality	gastroscopy colonoscopy	ascending colon	Prednisolone +PPI	Yes	Yes	11
26	F/49	No	55.5	525.1	mass ascites	gastroscopy colonoscopy	-	Prednisolone +PPI	Yes	No	10
27	F/38	No	49.3	926.7	local thickening of gastric antrum, mild ascites	gastroscopy colonoscopy	-	Prednisolone +PPI	Yes	Yes	9
28	M/55	No	27.5	541.9	no evident abnormality	gastroscopy colonoscopy	ileum terminal	Dietary, loratadine and PPI	No (prednisolone + PPI)	No	9

EG were lack of specificity. The clinical manifestations of EG is related to the clinical types of EG. According to Klein classification, the clinical symptom of EG depends primarily on the gastrointestinal tract involvement. Patients with mucosal disease is associated with nonspecific gastrointestinal symptoms, such as abdominal pain, abdominal distension and diarrhea. Those with muscular disease might present with bowel thickening and stenosis and show severe abdominal pain (6, 12, 14).

The clinical manifestations of EG lacks specificity, and might be range from mild IBS like symptoms to acute abdomen due to gastrointestinal perforation or obstruction. There are no significant difference between EG and other gastrointestinal disease, and diagnosis of EG requires histological evidence of significant eosinophilic infiltration of gastrointestinal tract (2). However, eosinophilic infiltration does not always exist in gastrointestinal mucosa with macroscopic abnormalities at endoscopy. On the contrary, it might be occurred in some normal appearing mucosa due to the patchy distribution of EG. In this study, gastroscopy biopsy was performed in 26 patients, and the detection rate of eosinophilic infiltration was only 30.7% (8/26). While combined biopsy examinations of gastroscopy, colonoscopy and/or double-balloon enteroscopy, the detection rate of eosinophilic infiltration was associated with a significant rise (82.1%). Therefore, endoscopic biopsy should be performed in multiple locations of the gastrointestinal tract, which might improve the detection rate of eosinophilic infiltration.

Peripheral eosinophilia is an important diagnostic clue of EG. In a previous study of 24 children diagnosed with EG, Choi JS et al reported 22 patients (91.7%) had peripheral eosinophilia (2). In another study, Wong GW et al reported that fifteen patients (83%) had peripheral blood eosinophilia (6). In this study, we found that 24 patients (85.7%) had peripheral blood eosinophilia. Although peripheral eosinophilia is not a universal feature of patients with EG and could be existed in other disorders such as parasitic infection, lymphoma or allergic disorders, it might be the first diagnostic clue for further evaluation of patients with suspected EG. Additionally, most patients with EG also showed the elevation of serum IgE level. Wong GW et al reported over 90% showed elevated levels in their study of 18 adult patients with EG (6). Reeda Craig et al also found that the serum IgE level increased markedly (12). In their study of 44 patients with EG, the median of serum IgE level was 188 IU/L (IQR: 24–467 IU/L). In our study, the median of serum IgE was 391.1 IU/ml (interquartile range 118.5–689.3 IU/ml), and 20 out of 28 patients (71.4%) had the elevation of serum IgE level. Therefore, serum IgE level also is another diagnostic clue for patients with suspected EG.

Currently, there is still no well-established consensus on the management strategy for EG (3, 15). Corticosteroids still is the basic therapeutic option for these patients

with EG. In this study, 20 patients were treated with prednisone and got relieved within a relatively short period of time after treated with prednisolone. The short-term efficacy of prednisolone for the treatment of EG has also been demonstrated in previous studies. However, the appropriate duration of steroid treatment is not well-established, and relapses are frequently noted when steroids are tapered or discontinued. Data on steroid-resistant EG and the treatment options remain nebulous. In this study, then five patients relapsed following tapering-off of prednisolone during the follow-up. However, prednisone was still effective in these 5 patients with disease recurrence. For steroid-dependent or steroid-resistant patients, Redondo-Cerezo et al reported that remission was induced by azathioprine (16). Yet, in another study of 3 steroid-resistant patients treated with azathioprine, Choi JS et al reported only one patient showed improvement after azathioprine treatment (2). Thus, the effect of azathioprine as a steroid-sparing treatment still need to be demonstrated. Diet control is another treatment for patients with EG (2, 12, 17–19). In this study, 8 patients were not treated with prednisone due to the worry medicine side effect. Among them, 5 patients had clinical resolution during the follow-up. Thus, for some EG patients with clear allergy history, dietary elimination therapy is another alternative therapeutic option.

There are several limitations in this study. First, this is a retrospective, single-center study and a selection bias may be existed, even though the clinical data were derived from a prospectively maintained database. Second, EG is a uncommon disease and the sample size was relative small. Other limitations in this study include the lack of randomization, and its relatively short follow-up period. Therefore, a randomized, multicenter prospective study is needed.

In conclusion, for some patients with gastrointestinal symptoms and peripheral eosinophilia, a high suspicion of EG is necessary. Endoscopic biopsy should be performed in multiple locations of the gastrointestinal tract, which might be helpful in the definite diagnosis of this disorder. Most EG patients could improved with steroid treatment or dietary elimination therapy, although a proportion of EG patients experienced relapse.

Disclosures

Xiao-Min Yang, Lin-Hong Zhu, Sai-Qin He, Hai-Hong Zheng, Shen-Kang Zhou and Yu Zhang have no conflicts of interest exist relating to this study.

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