Case Report

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Eosinophilic gastroenteritis with multiple serous membrane effusion as the first sign: a case report and literature review

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Abstract

Multiple serous membrane effusion (MSSE) as the first sign of eosinophilic gastroenteritis is extremely rare, and its clinical features and treatment methods have not been well described. The clinical characteristics, diagnosis, and treatment methods of MSSE in a 44-year-old woman were retrospectively reviewed. Laboratory testing revealed an elevated eosinophil count and serum immunoglobulin E level. The levels of all tumor markers were normal, but the CA125 level in serum and ascitic fluid was significantly increased. Ultrasonography showed a large amount of ascites and a moderate amount of pleural effusion. Echocardiography showed a small amount of pericardial effusion. Chest and abdominal computed tomography showed gastrointestinal wall thickening. Moreover, eosinophilic infiltration was detected in duodenal and rectal biopsy samples that had been collected during endoscopic examination of the upper gastrointestinal system. The patient was treated with 30 mg of prednisolone, and seafood was excluded from her diet for 4 weeks. The prednisolone was tapered over 8 weeks and continued at 5 mg prednisolone daily thereafter. The MSSE and peripheral eosinophilia showed a dramatic response to the steroid treatment. This case indicates that we should be highly aware of MSSE as the first clinical manifestation of eosinophilic gastroenteritis.

Keywords

Eosinophilic gastroenteritis, multiple serous membrane effusion, diagnosis, treatment, prednisolone, ascites

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Introduction

Eosinophilic gastroenteritis (EGE) is an extremely rare disease of unknown etiology characterized by infiltration of eosinophils within the gastrointestinal (GI) tract.[1] EGE is histopathologically classified into three distinct types: that predominantly affecting the mucosal layer, muscular layer, and subserosal layer.[2] Patients with the subserosal type, which is the rarest form, often have serous membrane effusions that may lead to a missed diagnosis of EGE because of the unusual clinical manifestation. Although a few case reports have described EGE in patients with MSSE, there are no systematic reports on the clinical features and treatments.

In this case report, we retrospectively studied the clinical presentation, imaging features, endoscopic findings, and treatment effects in a patient with EGE who exhibited MSSE as the first sign. We also herein review the patient outcomes described in the published literature.

Case report

This study was approved by the Ethics Committee of the First People's Hospital of Changzhou. Written informed consent was obtained from the patient for publication of this case report and accompanying images.

A 44-year-old woman presented with a 6-week history of nausea and vomiting accompanied by progressive painless abdominal distention. She was admitted to the inpatient service of the Department of Gastroenterology, the First People's Hospital of Changzhou. She had no history of liver or heart disease except for bronchial asthma during childhood. Prior to this admission, she was not on any medications. She denied alcohol use. Physical examination revealed decreased breath sounds bilaterally, abdominal distention, and hypoactive bowel sounds. Notable laboratory abnormalities on admission were a high eosinophil count (1.31×10^9/L) and a remarkably high level of CA125 in the serum and ascetic fluid. The alpha-fetoprotein, carcinoembryonic antigen, CA199, CA153, and beta-human chorionic gonadotropin levels were all within normal limits. The nature of the patient's ascites was exudative as indicated by a serum-to-ascites albumin gradient of >11 g/L. Parasitic infestation was excluded by negative stool studies and negative serology for *Strongyloides* and *Toxocara*. Moreover, as listed in Table 1, all other laboratory data were unremarkable (including serum electrolytes, coagulation parameters, tuberculin purified protein derivative, and thyroid, kidney, and liver test results). Antinuclear antibody was negative and bone marrow biopsy showed no abnormalities. Ultrasonography showed a large amount of ascites and a moderate amount of bilateral pleural effusion. In addition, echocardiography showed only a small amount of pericardial effusion without cardiac disease. Chest and abdominal computed tomography (CT) showed diffuse thickening of the gastric antrum and duodenum, mild edema of the small bowel loops, and large amounts of abdominal ascites, bilateral pleural effusion, and pericardial effusion (Figure 1); however, no ovarian masses were present. Esophagogastroduodenoscopy showed extensive congestion and edema in the duodenum and antrum. Colonoscopy revealed no abnormalities (Figure 2). Biopsies demonstrated significant eosinophilic infiltration in the duodenum and rectum (Figure 3). In addition, gastric mucosal biopsies displayed mucosal eosinophilic infiltration (18–20 cells/mm^2), but there was no evidence of *Helicobacter pylori*-associated gastritis. The patient was treated with 30 mg of prednisolone, and seafood was excluded from her diet for 4 weeks. She was also treated with 600 mg of calcium–vitamin D3 chewable tablets and 40 mg of oral

Table 1. Laboratory parameters upon admission

Parameters	Index	Reference range
Blood		
WBC ($\times 10^9$/L)	8.74	4.0–10.0
EO ($\times 10^9$/L)	1.31	0.02–0.52
EO (%)	15.0	0.4–8.0
RBC ($\times 10^{12}$/L)	4.65	3.5–5.5
Hb (g/L)	144	120–155
PLT ($\times 10^9$/L)	478	100–300
TP (g/L)	55.3	60–82
ALB (g/L)	24.6	35–55
cTnI (ng/mL)	0.0078	0–0.04
AFP (ng/mL)	3.56	0–8
CEA (ng/mL)	0.7	0–5
CA199 (U/mL)	11.8	0–37
CA125 (U/mL)	193.3	0–35
ESR (mm/h)	20	<38
CRP (U/L)	30	30–110
IgE (kU/L)	868	<60
IgG (g/L)	11.2	7.23–16.8
IgM (g/L)	2.78	0.63–2.77
IgA (g/L)	1.35	0.69–3.82
Anti-ANA	(−)	–
T-spot	(−)	–
Peritoneal fluid		
WBC ($\times 10^6$/L)	597	–
EO (%)	82.7	–
TP (g/L)	40.0	63–82
LDH (U/L)	274	313–618
ADA (U/L)	10.8	–
CRP (mg/L)	9.6	–
CEA (ng/mL)	0.2	–
CA125 (U/mL)	1108.0	–

WBC, white blood cells; EO, eosinophils; RBC, red blood cells; Hb, hemoglobin; PLT, platelets; TP, total protein; ALB, albumin; cTnI, cardiac troponin I; AFP, alpha-fetoprotein; CEA, carcinoembryonic antigen; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; Ig, immunoglobulin; ANA, antinuclear antibodies; T-spot, T-SPOT.TB test; LDH, lactate dehydrogenase; ADA, adenosine aminohydrolase.

omeprazole to prevent the occurrence of prednisolone-induced osteoporosis and upper GI bleeding. Her symptoms improved immediately, and her eosinophil count normalized within 3 weeks. Prednisolone was tapered over 8 weeks and continued at 5 mg prednisolone daily. The serum level of CA125 dropped to the normal range, and her MSSE was in complete remission throughout the 2-month follow-up period. Follow-up esophagogastroduodenoscopy after 3 months showed normal mucosa of the gastric antrum and duodenum.

Discussion

EGE is a rare disease characterized by eosinophil-rich inflammation of the GI tract that affects both the pediatric and adult populations.[3,4] However, the precise process of the development of EGE remains obscure. The current hypothesis of an immunoglobulin E-mediated immune response to various food allergens has long been widely accepted.[5,6] Food allergens may stimulate the transformation of lymphocytes in the GI lymphoid tissue to cytokine-secreting T helper type 2 effector cells, which produce interleukin 5.[7,8] Interleukin 5 functions as a key mediator, activating the expansion of eosinophils and their migration from bone marrow.[8] Therefore, eosinophils are considered an important hallmark of the pathology of EGE. The patient in the current case had peripheral blood eosinophilia at presentation and a history of asthma.

Clinical manifestations of EGE are diverse depending on the affected layers of the GI tract and range from barely perceptible symptoms to intestinal obstruction or ascites.[2,9] Mucosal involvement, the most common manifestation, may result in abdominal pain, vomiting, nausea, and weight loss. Muscularis involvement results in gut wall thickening, which may lead to symptoms of GI obstruction. Serosal involvement, the rarest manifestation, often causes pleural effusion and ascites.[10] These three types may also exist together. Given its wide array of nonspecific symptoms and relatively low prevalence, the diagnosis of EGE requires a high index of suspicion. In our case, the main symptoms

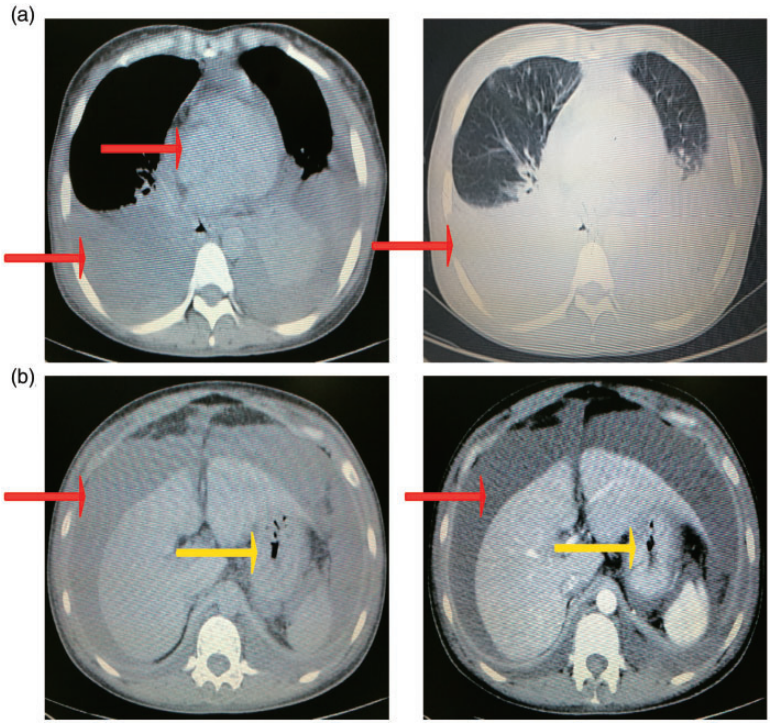

Figure 1. Conventional and enhanced computed tomography images. (a) Chest and abdominal computed tomography demonstrated a large amount of ascites and a moderate amount of pleural effusion and pericardial effusion (red arrowhead). (b) Imaging study shows multiple segments of small bowel wall thickening (yellow arrowhead).

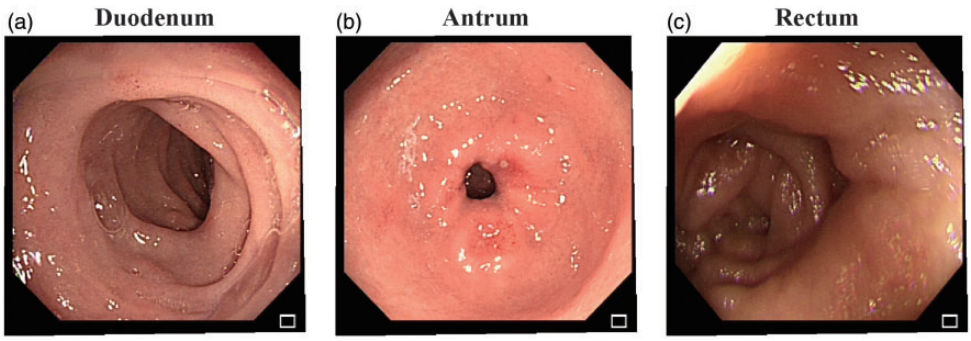

Figure 2. Endoscopic appearance. Endoscopy showed extensive congestion and edema in the (a) duodenum and (b) antrum. (c) Colonoscopy revealed no abnormality.

of EGE were painless abdominal distention accompanied by atypical symptoms of nausea and vomiting. Therefore, we consider that our patient might have had a hybrid type of EGE because of the concurrent presence of eosinophilic infiltration of the GI tract and MSSE. Although exactly how the accumulation of eosinophils in

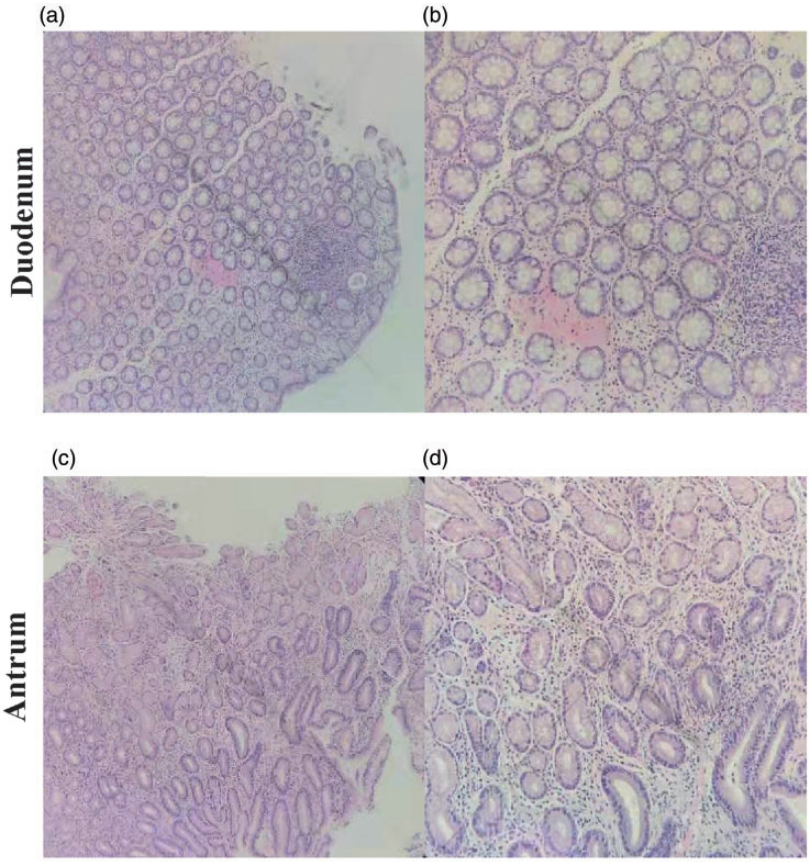

Figure 3. Histological examination. Histological sections of the (a, b) duodenum and (c, d) antrum demonstrated eosinophilic infiltration within inflammatory cells in the lamina propria and submucosa (hematoxylin and eosin stain). (a, c) Magnification, 20×. (b, d) Magnification, 40×.

the intestinal tissue causes MSSE is unknown, eosinophil degranulation leads to a severe inflammatory response in the mucosa via the formation of reactive oxygen species, eosinophil-derived neurotoxins, and halide acids, all of which might contribute to the development of MSSE.[11]

There are no strict or uniform diagnostic criteria that directly point to the presence of EGE in patients with MSSE. However, the differential diagnoses of eosinophilia, such as a parasitic infestation, hypereosinophilic syndrome, and intestinal lymphoma,[12,13] must be excluded prior to diagnosing EGE. In addition, endoscopic ultrasound and CT examinations can reveal the presence of not only localized or general thickening of the GI wall but also pleural effusion and ascites. Hence, the presence of serous membrane effusion is an important clue to the diagnosis of EGE. Moreover, pathologic examinations based on endoscopy and biopsy are playing an increasingly important role in the diagnosis of EGE. Although the endoscopic appearance is not characterized by specific lesions, and although pathological biopsies have the chance of negative results, multiple biopsies should be performed to avoid missing the diagnosis.

In our case, congestion and edema of the duodenal and antrum mucosa were observed during endoscopy, and eosinophilic infiltration of biopsy specimens was detected.

Although a few reports have described the spontaneous resolution of EGE without treatment,[14,15] most patients require medical therapy. At present, corticosteroid treatment and avoidance of food antigens are the major form of therapy.[14,15] Fortunately, most patients typically respond to steroid therapy quite rapidly. However, some cases may relapse after the discontinuation of steroid treatment. Moreover, steroid treatment in the presence of occult parasitic infection may result in catastrophic disease dissemination. Therefore, to avoid the adverse effects of long-term use of steroids, multiple novel therapeutic strategies have been used to treat patients with EGE and concurrent MSSE.[5,16,17] These treatments include budesonide and steroid-sparing agents, such as leukotriene inhibitors, immunomodulators, antihistamines, and mast cell stabilizers. Furthermore, some biological therapies with monoclonal antibodies to inflammatory cytokines (immunoglobulin E and interleukin 5) have recently been successfully used in the treatment of EGE.[5,17,18] We successfully treated our patient with steroids. Subsequent continuous low-dose therapy maintained her state of remission.

In summary, EGE should be considered as a differential diagnosis in patients with MSSE. Peripheral eosinophilia is the main diagnostic clue. Further CT imaging and endoscopy can provide important help in the diagnosis of EGE. Steroid administration is the major therapeutic option, but relapses requiring retreatment can occur.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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References

1. Khan S and Orenstein SR. Eosinophilic gastroenteritis. *Gastroenterol Clin North Am* 2018; 37: 333–348.
2. Klein NC, Hargrove RL and Sleisenger MH. Eosinophilic gastroenteritis. *Medicine (Baltimore)* 1970; 49: 299–319.
3. Agrawal S, Vohra S and Rawat S. Eosinophilic ascites: a diagnostic and therapeutic challenge. *World J Gastrointest Surg* 2016; 8: 656–659.
4. Cheng LJ and Zhang SC. Abdominal ascites in children as the presentation of eosinophilic gastroenteritis: a surgeon's perspective. *Clin Res Hepatol Gastroenterol* 2018; 11: 3–9.
5. Foroughi S, Foster B and Kim N. Anti-IgE treatment of eosinophil-associated gastrointestinal disorders. *J Allergy Clin Immunol* 2007; 120: 594–601.
6. Cianferoni A, Spergel JM and Muir A. Recent advances in the pathological understanding of eosinophilic esophagitis. *Expert Rev Gastroenterol Hepatol* 2015; 9: 1501–1510.
7. Yoshikane H, Yatsuya H, Sakakibara A, et al. A case of eosinophilic peritonitis in which ascites interleukin 5 presented at a high level. *Hepatogastroenterology* 2000; 47: 1588–1589.
8. Bischoff SC. Food allergy and eosinophilic gastroenteritis and colitis. *Curr Opin Allergy Clin Immunol* 2010; 10: 238–245.
9. Le Connie D and Nguyen H. Eosinophilic gastroenteritis, ascites, and pancreatitis: a

case report and review of the literature. *South Med J* 2004; 97: 905–906.
10. Liu L, Liang XY and He H. Clinical features of eosinophilic gastroenteritis with ascites. *Zeitschrift Gastroenterologie* 2013; 51: 638–642.
11. Talley NJ, Shorter RG, Phillips SF, et al. Eosinophilic gastroenteritis: a clinicopathological study of patients with disease of the mucosa, muscle layer, and subserosal tissues. *Gut* 1990; 31: 54–58.
12. Daneshjoo R and Talley NJ. Eosinophilic gastroenteritis. *Curr Gastroenterol Rep* 2002; 4: 366–372.
13. Rothenberg ME. Eosinophilic gastrointestinal disorders (EGID). *J Allergy Clin Immunol* 2004; 113: 11–28.
14. Ingle SB, Patle YG and Murdeshwar HG. A case of early eosinophilic gastroenteritis with dramatic response to steroids. *J Crohns Colitis* 2001; 5: 71–72.
15. Tien FM, Wu JF and Jeng YM. Clinical features and treatment responses of children with eosinophilic gastroenteritis. *Pediatr Neonatol* 2011; 52: 272–278.
16. Urek MC, Kujund M, Bani M, et al. Leukotriene receptor antagonists as potential steroid sparing agents in a patient with serosal eosinophilic gastroenteritis. *Gut* 2006; 55: 1363–1364.
17. Maeyer ND, Kochuyt AM, Van Moerkercke W, et al. Montelukast as a treatment modality for eosinophilic gastroenteritis. *Acta Gastro-Enterologica Belgica* 2011; 74: 570–575.
18. Sunkara T, Rawla P, Yarlagadda KS, et al. Eosinophilic gastroenteritis: diagnosis and clinical perspectives. *Clin Exp Gastroenterol* 2019; 12: 239–253.