

Eosinophilic gastroenteritis, eosinophilic cystitis, and ascites: A case report and review of the literature

Eozinofilik gastroenterit, eozinofilik sistit ve assit: Olgu sunumu ve literatürün gözden geçirilmesi

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Eosinophilic gastroenteritis is a rare disorder characterized by eosinophilic infiltration of the gastrointestinal tract. The organ most often involved is the stomach, followed by the small intestine and colon. The involvement of the bladder in eosinophilic gastroenteritis is extremely rare. In the literature, only six cases of eosinophilic gastroenteritis with associated eosinophilic cystitis have been reported. Cases who had peripheral hypereosinophilia, abdominal pain, diarrhea, and ascites were effectively treated with steroids after other systemic disorders associated with peripheral eosinophilia were ruled out.

Key words: Eosinophilic gastroenteritis, eosinophilic cystitis, eosinophilia

Eozinofilik gastroenterit gastrointestinal sistemin eozinofilik infiltrasyonu ile karakterize nadir bir hastalıktır. En sık tutulan organ midedir ve takiben ince barsak ve kolon tutulur. Ancak, eozinofilik gastroenteritte mesane tutulumu çok nadirdir. Literatürde şu ana kadar yalnızca eozinofilik sistit ile ilişkili eozinofilik gastroenterit tanısı konulan 6 vaka yayınlanmıştır. Periferik hipereozinofili, karın ağrısı, diyare ve assit ile başvuran bu vakaların hipereozinofili yapan diğer hastalıklar dışlandıktan sonra steroid ile efektif olarak tedavi edildiği bildirilmiştir.

Anahtar kelimeler: Eozinofilik gastroenteritis, eozinofilik sistit, eozinofili

INTRODUCTION

Eosinophilic gastroenteritis (EGE) is a rare disease characterized by eosinophilic inflammation in one or more organs of the gastrointestinal (GI) tract with or without peripheral hypereosinophilia. The etiology and pathogenesis of EGE are not well understood (1). It was first described by Kaijer in 1937 (2). To date, only 300 cases have been reported in the literature. EGE may affect both genders and all age groups, but it is more prevalent between the ages of 30 and 50 years. The Klein classification divides EGE into mucosal, muscular, and serosal types, based on the layer(s) involved (3,4). The serosal form, which is the least common, usually presents as eosinophilic ascites (5).

The stomach is the organ most commonly affected, followed by the small intestine, colon, and esophagus (1,3). However, EGE is rarely associated with widespread gastrointestinal and bladder involvement. To date, only six cases of EGE with associated eosinophilic cystitis (EC) have been reported (6,7). Here, we report a rare case of

EGE complicated by EC and ascites who presented with dysphagia, abdominal pain, diarrhea, and peripheral hypereosinophilia. The association of EGE and EC will be discussed.

CASE REPORT

A 22-year-old woman was admitted to the hospital with complaints of dysphagia, abdominal pain, and diarrhea lasting 2 weeks. Her medical history was unremarkable. She denied any of history drug intake or travel. Physical examination revealed abdominal distention and ascites. There was no organomegaly or abdominal mass. Laboratory tests results were as follows: white blood cells (WBC): 22.900/mm³; eosinophils 51%; alanine aminotransferase (ALT) level was 65 U/L (normal, 5-37); and aspartate aminotransferase (AST) level was 86 U/L (normal, 5-37). Her erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and total immunoglobulin E (IgE) level were normal. Repeated examinations of stool and urine for ova

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and parasites were negative. In addition, serologic tests for Schistosomiasis, Echinococcosis, Toxocara, and Fascioliasis were negative.

Thorax computerized tomography (CT) showed marked esophagus wall thickening of up to 11 mm and luminal narrowing. Abdominal ultrasound examination showed bladder wall thickening and moderate ascites. Abdominal magnetic resonance (MR) showed moderate ascites with diffuse stomach, small intestine, and bladder wall

thickening (up to 11 mm) and the presence of mural stratification in the bladder (Figure 1A, 1B).

Upper endoscopy and colonoscopy showed erythematous mucosal changes in the stomach and bulbous mucosa of the esophagus, but portion 2 of the duodenum were normal. Colonoscopy was normal. Further, cystoscopy was performed, and it showed a diffuse hyperemic and edematous bladder mucosa. Biopsies from the esophagus, stomach, duodenum, terminal ileum,

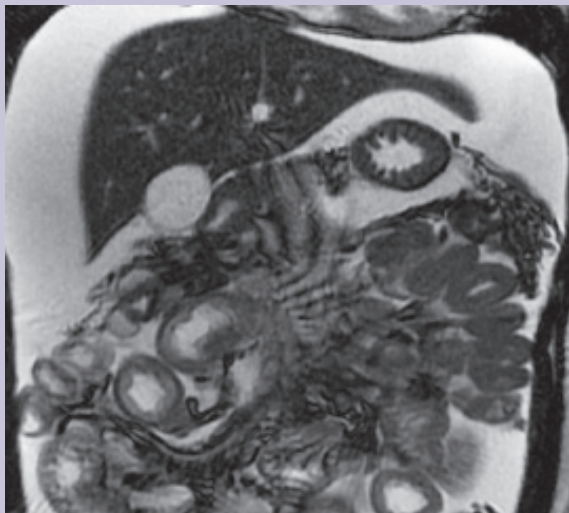


Figure 1A. Scan of the abdomen shows moderate ascites with diffuse stomach and small intestine thickening (up to 11 mm).

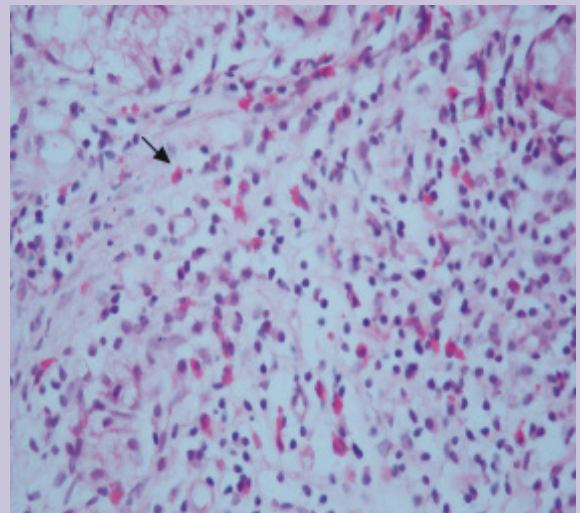


Figure 2A. Microscopic findings of the esophagus show a heavy eosinophilic infiltration (>20 eosinophils per high-power field (H&E, ×200).

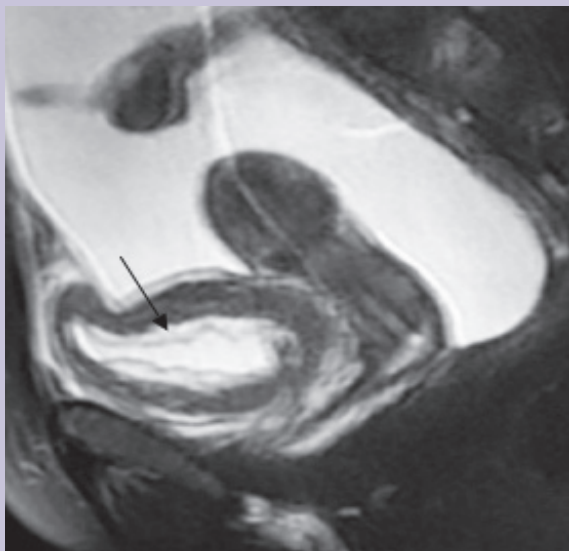


Figure 1B. Scan of the abdomen shows diffuse thickening (up to 11 mm) and the presence of mural stratification in the bladder.

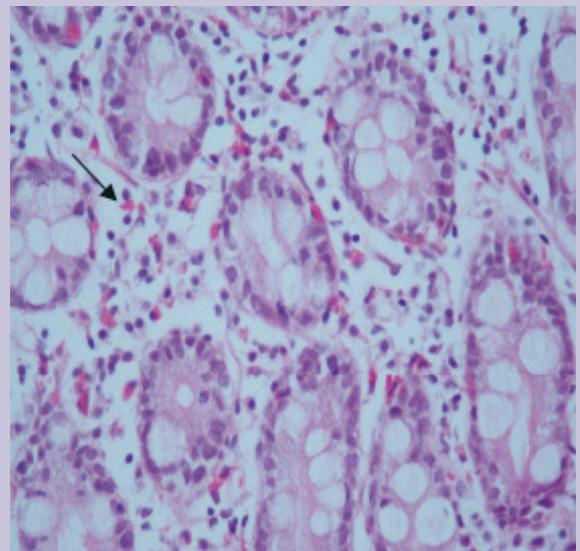


Figure 2B. Duodenal submucosal eosinophilic infiltration [>20 eosinophils per high-power field (H&E, ×200)]

and bladder showed marked increased mucosal and submucosal eosinophilic infiltration [hematoxylin and eosin (H&E) stain, $\times 200$, Figure 2A and 2B].

Examination of ascitic fluid revealed a high total leukocyte count ($11 \times 10^3/\text{mm}^3$, 90% eosinophils) and a serum ascites albumin gradient (1.1 g/dL). Cytology of the ascitic fluid also showed chronic inflammation with increased eosinophils and was negative for malignant cells. Ascites culture was sterile. Bone marrow aspiration and biopsy showed hypercellularity with a marked increase in mature eosinophils without blasts. BCR-ABL fusion gene, FIP1-like-1 gene, platelet-derived growth factor receptor-alpha gene, and Janus kinase-2 (JAK-2) mutations were negative. Echocardiographic findings were normal.

After ruling out of parasite infection and malignancy, a diagnosis of EGE associated with EC was considered. The patient was initially treated with prednisolone (40 mg/day) for 2 weeks, then its dose was tapered and stopped over 8 weeks. Her symptoms improved quickly, and her eosinophil count and abnormal radiologic imaging normalized within 1 week.

DISCUSSION

Eosinophilic gastroenteritis is a rare disease of known etiology, pathologically characterized by eosinophilic infiltration of the GI tract (3,4). The diagnosis of EGE require three criteria: (1) presence of GI symptoms; (2) histologic evidence of eosinophilic infiltration in one or more areas of the GI tract; and (3) exclusion of other causes of tissue eosinophilia such as parasitic infection, drugs, lymphoma, leukemia, hypereosinophilic syndrome, autoimmune disease, vasculitis, and inflammatory bowel disease (8). In our patient, the diagnosis of EGE was based on clinical findings, histological evidence of eosinophilic infiltration, and the exclusion of the disorders listed above.

EGE can affect any part of the GI tract from the esophagus to the rectum, but the stomach and proximal small intestines are the most affected organs. A proportion of 30% and 28% of patients with EGE also have concomitant involvement of the esophagus and colon, respectively (1,2). EGE can rarely be associated with extraintestinal manifestations such as eosinophilic pancreatitis, eosinophilic cholecystitis, eosinophilic cholangitis, and eosinophilic cystitis (7,9). There are few reports of cases involving the bladder in patients with EGE. Its prevalence was found to be 4.5% of patients with EGE (6,7,10). The present case had extensive gastrointestinal tract involvement, excluding the colon and bladder.

In 1970, Klein et al. reported that this disorder could be pathologically classified into three major types: mucosal,

muscle, and subserosal. The mucosal type (57.5% of cases) may cause abdominal pain, diarrhea, vomiting, gastrointestinal bleeding, iron deficiency anemia, malabsorption, and weight loss. The mural type (30% of cases) may cause a partial or total intestinal obstruction. The serosal type is the rarest presentation of EGE (9% of cases), causing eosinophilic ascites. Furthermore, the involvement of the esophagus may cause complaints such as dysphagia, heartburn, and chest pain (4,11). Involvement of the bladder may cause dysuria, hematuria, suprapubic pain, and urinary retention (6,7). The patient in our case had presenting symptoms of abdominal pain, diarrhea, and ascites, which were features of the mucosal and subserosal type, and dysphagia. She had no urinary symptoms.

There are no specific laboratory tests for diagnosing EGE and EC. Hypereosinophilia has been recorded in approximately 80% of EGE cases and 50% of EC cases. Hypereosinophilia is more severe in EGE cases with serosal involvement, as was seen this patient. The ESR and CRP can be elevated in few cases. In approximately two of three EGE cases, elevated IgE levels are detected (11). Paracentesis often reveals exudative fluid rich in eosinophils. In the patient in our case, the IgE level and ESR were normal on presentation, and her ascites was of the exudative form with an increased eosinophil count (80%).

The endoscopic findings of EGE and EC are nonspecific. The endoscopic finding of EGE and EC includes normal aspects or mucosal erythema, edema, enlarged mucosal folds, erosions, and tumor-like appearance. Thus, endoscopic biopsies play an essential role in diagnosis. A common histological feature includes an increase in the number of eosinophils in the mucosa and lamina propria (≥ 15 eos/hpf in the esophagus, $\geq 20-25$ eos/hpf in the stomach and small bowel, and ≥ 50 eos/hpf in the colon). It is necessary to obtain multiple biopsies (at least six) from normal and abnormal mucosa, because eosinophilic infiltration is often patchy. Sometimes, full-thickness biopsies may be required for the diagnosis of EGE, especially in cases of the mural and serosal types (4,8). Our patient's endoscopic and cystoscopic findings were also nonspecific and detected increased eosinophilic infiltration in the mucosa and lamina propria of the bladder wall, esophagus, stomach, and duodenum and terminal ileum.

Radiologic images are valuable for evaluating the location and extent of EGE. Ultrasound can detect ascites and intestinal wall thickening. Computed tomography (CT) scan can detect enlarged gastric folds, intestinal wall thickening, ascites, and obstruction. The most common CT findings are intestinal wall thickening with layering (halo sign) and the "araneid-limb-like sign," which is characteristic of inflammatory diseases (12). The CT

finding of EC is a normal or diffuse/asymmetric bladder wall thickening and a local mass mimicking a tumor, and a mucosal lining on postcontrast CT is the characteristic sign (10). Knoshito et al. evaluated the CT findings of 111 patients with EGE and reported that thickened gut walls and ascites were detected in 75% and 56% of those cases, respectively. In this study, except thickened esophago-gastrointestinal walls, no radiologic finding was specific to the diagnosis of EGE (13). In our case, thorax CT also detected esophageal wall thickening (up to 10 mm) and luminal narrowing. Abdominal CT was not performed.

There is limited information about magnetic resonance imaging (MRI) findings in patients with EC and EGE. To date, there has been one adult patient in whom the MRI characteristics of EC associated with EGE have been described in the literature (7). This patient's MRI revealed asymmetric thickening of the bladder wall (up to 18 mm). This thickened bladder wall appeared hyperintense on T1-weighted images (T1WI), isointense on T2-weighted images (T2WI), and enhanced after administration of contrast material. In our patient, abdominal magnetic resonance (MR) revealed moderate ascites with diffuse stomach, small intestine, and bladder wall thickening (up to 11 mm) showing a distinct hyperintensity on T1WI and a low signal intensity on T2WI.

There is no standard therapy for EGE and EC. Corticosteroids are frequently used as the first line of therapy

and provide effective relief of symptoms within a few days to weeks. The duration of steroid therapy reported is variable. Relapse is frequent after withdrawal of therapy. A patient with refractory or relapsing disease may require long-term, low-dose steroids or immunosuppressive therapy (azathioprine and 6-mercaptopurine) (12). If food allergies are identified, an elemental diet can be recommended to reduce the symptoms of EGE. In the literature, there are reported cases who remained in remission with an elemental diet (14). Other treatment options include mast cell stabilizers, antihistamines, leukotriene antagonists (montelukast), mepolizumab (IL-5 antibody), and IgE monoclonal antibody (omalizumab) (14,15). Surgery may be required in cases with perforation or obstruction. Our patient was also treated with prednisolone for 2 months. Her abnormal laboratory and radiological findings were quickly improved after steroid therapy.

As a conclusion, EGE associated with EC is a rare condition. It should be considered in cases who have hyper-eosinophilia and one or more imaging features of EGE such as mucosal fold thickening, bowel wall thickening with layering, luminal narrowing, ascites, combined with excessive bladder wall thickening, and enhancement of the bladder on CT or MRI. Currently, steroids are the primary drugs for therapy, but in most patients, symptoms relapse after withdrawal of treatment. Therefore, these patients should be closely followed up.

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