Eosinophilic Gastroenteritis Associated with Rheumatoid Arthritis

Eozinofilik Gastroenterit ile Romatoid Artrit Birlikteliği

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Abstract: This article evaluated the relationship between eosinophilic gastroenteritis and peripheral eosinophilia in patients with rheumatoid arthritis. A 71-year-old female patient presented with gastrointestinal symptoms and peripheral eosinophilia. Gastrointestinal endoscopy, ultrasonography, computed tomography, stool analysis, and biochemical analysis were performed. The patient was diagnosed with eosinophilic gastroenteritis with esophageal dysmotility, pangastritis, and duodenal erythema. The patient was treated with immunosuppressive therapy, and follow-up showed improvement.

Keywords: Eosinophilia; gastrointestinal involvement; rheumatoid arthritis.

Eosinophilic gastroenteritis (EG) is a rare gastrointestinal disorder that can present with various gastrointestinal manifestations, depending on the specific site of the affected gastrointestinal tract and specific layer of the affected gastrointestinal wall. The pathogenesis and etiology of EG remain
unclear. Diagnostic criteria include demonstration of eosinophilic infiltration of the bowel wall, lack of evidence of extra-intestinal disease, and exclusion of various disorders that could mimic a similar condition. This rare disease should be considered during the differential diagnosis of unexplained gastrointestinal symptoms, especially when they are associated with peripheral eosinophilia.[3]

Rheumatoid arthritis (RA) is a chronic disease that can cause irreversible joint damage and significant disability. Even with a prevalence of only 1%, there is a considerable impact on the community. Diagnosis is based on a combination of clinical and laboratory features. Patients typically present with a symmetrical polyarthritis of the small joints of the hands and feet accompanied by early morning stiffness and possible occasional, constitutional symptoms.[2]

The relationship between EG and RA is, however, unclear. Until now, there have only been three published reports in the literature concerning their coexistence, but there was no clarification to explain it.[3-5] Therefore, we aimed to present the coexistence of EG and RA in relation to its contribution to the literature while also seeking to determine whether it can be used in the detection of overlooked diseases.

CASE REPORT
A 71-year-old female presented with a history of generalized aches, nausea, upper abdominal tenderness and swelling along with pain and limited movement of the left knee. Her constitutional symptoms had worsened over the previous year, and she had lost eight pounds. She had used ranitidine and omeprazole without benefit. She had an eight-year history of seropositive RA, and her medications had included methotrexate and nonsteroidal antiinflammatory drugs (NSAIDs), but she rarely took the NSAIDS. She had no personal or family history of allergic reactions. A clinical examination revealed a mildly distended, tender abdomen, signs of active arthritis of the left knee joint, and chronic deformities of the hands caused by RA. Stool samples were negative for ova, parasites, and common pathogens. A complete blood count revealed a white blood cell (WBC) count of 7360/mm³ with an eosinophil count of 23.2% (normal 0 to 4%). The erythrocyte sedimentation rate (ESR) was 64 first hour, and the C-reactive protein level was 161 g/dl. Other laboratory tests and tumor markers were unremarkable. Computed tomography (CT) scans and ultrasonography of the abdomen were normal. Esophagogastroduodenoscopy (EGD) revealed esophageal dysmotility. Pangastritis and erythema of the duodenal bulb were also noted. Histological examination and biopsies from the gastric antrum and duodenum demonstrated subacute and chronic inflammation with distinct eosinophilic infiltration of the submucosa and muscularis. Therefore, the diagnosis of EG was confirmed. Because of the symptoms of RA and EG, we started treatment with prednisone 60 mg/day. Her eosinophil count normalized after the steroid treatment. However, her abdominal pain recurred, and she reported worsening nausea, postprandial fullness, and bloating. For this reason, sodium cromoglycate 200 mg three times a day (TID) was added to her treatment with modest improvement of her symptoms. However, during hospitalization follow-up, she developed nosocomial pneumonia and died due to sepsis.

DISCUSSION
Eosinophilic gastroenteritis is a rarely diagnosed inflammatory bowel disease that is defined by the presence of nonspecific gastrointestinal symptoms, histologic infiltration of the gastrointestinal wall by eosinophilic granulocytes in a diffuse or segmentary manner, and exclusion of parasitic and extraintestinal diseases.[6] Although the etiology of eosinophilic gastroenteritis is still undefined, autoimmune mechanisms may play an important role in the development of this disease.[7]

Rheumatoid vasculitis is a relatively uncommon complication of RA. It shows a wide variety of extra-articular features, including skin and neurologic involvement, but rarely shows gastrointestinal involvement. Several studies suggest that RA may affect the gastrointestinal system. Intestinal ischemia, rectal bleeding, hemorrhage, multiple small bowel ulcerations, obstruction, infarction, and perforation are seen in the course of RA. A pathological examination of these studies showed multiple lesions of the small intestine were caused by rheumatoid vasculitis. Also, histologic changes were characterized by partial or complete loss of superficial epithelium, lymphocytes, plasma cells, granulocytes, and the presence of vasculitic lesions.[8-12] In these reports, no eosinophilic cells were seen in the histologic examination; however, in our case, we detected distinct eosinophilic infiltration on the bowel wall.

While the association between RA and peripheral blood eosinophilia is well recognized, the link
between tissue eosinophilia and RA is less well established. Eosinophilic pneumonia, eosinophilic fasciitis, hypereosinophilic syndrome, and cutaneous eosinophilic vasculitis have been described in patients with RA.\[3\] In our patient, there was no evidence of other systemic tissue eosinophilic infiltration outside the gastrointestinal tract.

Steroids are the mainstay of treatment in EG, and about 90% of patients respond to this therapy. Patients with serosal disease usually show a dramatic response to steroids. Sodium cromoglycate is a mast cell stabilizer that prevents release of toxic mediators such as histamine, platelet activating factors, and leukotrienes from mast cells. Ketotifen is similar to sodium cromoglycate in its biological profile and may be useful in some cases. The elimination of presumed dietary articles is unhelpful in most cases. Successful treatment of EG with montelukast, a leukotriene modifier, has been reported. Suplatast tosilate is a new IL-4 and IL-5 inhibitor which has proven to be effective in treating asthma and has been reported to be useful in the treatment of EG.\[13\] In our case, the patient was given a steroid and sodium cromoglycate. There was no benefit of the steroid therapy, and no response was observed to the sodium cromoglycate because of early death due to sepsis.

In conclusion, EG is a blood disorder which damages the mucosa of the gastrointestinal tract, and gastrointestinal involvement occurs in patients with RA due to vasculitis. Symptoms are related to the layer of bowel mucosa involved. To our knowledge, there have only been three published reports on clinically manifested eosinophilic enterocolitis in a patient with RA.\[3-5\] and the relationship between EG and RA is unclear. It is a rare and heterogeneous disease that is probably misdiagnosed in clinical practice because it encounters a high degree of suspicion. Peripheral eosinophilic counts should be performed in RA patients with nonspecific abdominal complaints. When these counts are elevated, an endoscopic investigation of the upper gastrointestinal tract should be performed, and biopsies of both abnormal and normal mucosa should be taken.

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**REFERENCES**