ANCA-Negative Eosinophilic Granulomatosis With Polyangiitis Presenting With Severe Diarrhea: A Case Report

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Abstract
Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare form of systemic vasculitis affecting small to medium-sized blood vessels. The presence of GI involvement is considered a poor prognostic factor in the Five-Factor Score (FFS), and is associated with lower long-term survival rates and higher relapse rates.. In this report, we present a case of EGPA-related duodenitis that was successfully treated with rituximab.
Keywords: EGPA, Mesenteric Vasculitis

Background

Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare systemic vasculitis targeting small to medium vessels. Typically, the disease presents with a triad of asthma, allergic rhinitis, and elevated peripheral blood eosinophil count. EGPA can affect multiple organ systems, including the lungs, heart, kidneys, nervous system, skin, and gastrointestinal tract.
GI involvement occurs in approximately 8% to 60% of all EGPA patients, with a higher incidence in ANCA-negative cases.
ANCA-negative EGPA is generally associated with an "eosinophilic phenotype," characterized by a higher likelihood of tissue infiltration by eosinophils in organs like the heart and GI tract. In contrast, ANCA-positive patients tend to exhibit a more systemic "vasculitic phenotype," often involving the kidneys and peripheral nerves.
The most frequent GI symptoms include abdominal pain (up to 90.5% of affected patients) and diarrhea (up to 42.9%), along with nausea, vomiting, and GI bleeding or perforation in severe cases.
Approximately 40% of EGPA patients are ANCA-positive, indicating that B cells may play a role in the disease's pathogenesis. B cell-depleting therapy with rituximab (RTX) has shown effectiveness in ANCA-positive EGPA, but published data are limited. The efficacy of RTX in the treatment of ANCA-negative EGPA remains unclear. Here, we describe a patient with EGPA-related gastrointestinal involvement—specifically duodenitis and ileitis—who was ANCA-negative and responded successfully to rituximab treatment.

Case Presentation

A 29-year-old Saudi man presented with recurrent abdominal pain, bloating, bloody diarrhea, and weight loss. He also reported joint pain affecting his ankles and feet, as well as a skin rash. His medical history was significant for bronchial asthma since childhood, with increased severity and exacerbations in recent years, and nasal polyps. He previously underwent nasal polypectomy one year prior. Family history was unremarkable.
Initial laboratory investigations revealed leukocytosis (WBCs: 13.76 x 109/L), an eosinophil count of 3.7 x 103/μL, a lymphocyte count of 4.7 x 103/μL, and an elevated erythrocyte sedimentation rate (ESR: 83 mm/h).

The patient's history of adult-onset asthma progression, joint pain, and gastrointestinal symptoms raised suspicion of EGPA. Further serological testing showed a positive antinuclear antibody (ANA), negative P-ANCA, positive C-ANCA (48), and normal immunoglobulin E (IgE) levels. Colonoscopy revealed friable mucosa with aphthous ulcers in the descending and sigmoid colon as well as the terminal ileum. Biopsies demonstrated eosinophil-rich active chronic duodenitis (up to 70 eosinophils per high-power field), active chronic colitis, and active moderate ileitis with ulceration and granulation tissue.

The combination of clinical history, laboratory findings, and colonoscopy results supported a diagnosis of eosinophilic granulomatosis with polyangiitis with gastrointestinal involvement (eosinophilic duodenitis), as per ECR/EULAR 2022 criteria, for which the patient scored 11. Induction therapy was initiated with oral prednisolone 60 mg for one month, followed by a tapering dose (reduced by 5 mg every two weeks). In addition, the patient received four doses of intravenous rituximab 360 mg at one-week intervals and was subsequently maintained on oral azathioprine 100 mg orally daily. The patient reported significant symptomatic improvement following treatment.

DISCUSSION

Eosinophilic granulomatosis with polyangiitis (EGPA), first described in 1951 by Churg and Strauss, is a vasculitis of small- and medium-sized vessels characterized by asthma, allergic rhinitis, and elevated peripheral blood eosinophil counts. The incidence ranges from 0.5 to 2.3 cases per 1 million person-years, with a prevalence of 2 to 22.3 cases per 1 million persons. The typical age of onset is between 38 and 54 years.

Gastrointestinal (GI) involvement is relatively common in EGPA and is more frequently seen in ANCA-negative patients compared to those who are ANCA-positive. The small intestine is the most frequently affected site of GI involvement, followed by the stomach and colon. Pathological findings in the small bowel—such as ulceration, perforation, and obstruction with eosinophilia and granulomas—are rarely reported in the literature.

When the gastrointestinal tract is involved, eosinophilic gastroenteritis and mesenteric vasculitis often coexist. These conditions typically cause nonspecific symptoms like abdominal pain, nausea, vomiting, and diarrhea but may also lead to severe complications, including bleeding or intestinal obstruction due to submucosal nodular masses. Mesenteric vasculitis increases the risk for ischemic bowel, mucosal ulceration, and even perforation, which may require surgical intervention. Serosal involvement can cause eosinophilic ascites and peritonitis, while rare manifestations include necrotizing acalculous cholecystitis, pancreatitis, and eosinophilic liver disease.

Histological diagnosis of EGPA using endoscopic biopsies can be challenging, as the samples are often too superficial to assess the submucosal vessels adequately. This case is unique in demonstrating histological evidence of intestinal EGPA with a negative p-ANCA and documenting a favorable clinical response to rituximab.

Treatment options depend on disease severity and include immunosuppressants such as methotrexate (MTX) or azathioprine (AZA), often used alongside glucocorticoids for maintenance therapy. There is currently no standardized therapy regimen for remission induction or maintenance. The substantial side effects associated with high-dose glucocorticoids or cyclophosphamide, high relapse rates with standard regimens, and the occurrence of non-responsiveness to cyclophosphamide highlight the need for alternative therapies.

Recent case reports have shown a beneficial effect of the B cell-depleting agent rituximab (RTX) in EGPA. The rationale for using B cell-depleting therapy in EGPA relates to the presence of myeloperoxidase (MPO)-specific ANCA in about 40% of patients, though the role of B cells in ANCA-negative EGPA is less clear. Th2 cells, through the production of IL-4 and IL-13, may support activation of both eosinophils and B lymphocytes and promote B-cell class switching to IgE. Eosinophilic granulocytes can perpetuate T-cell activation by secreting IL-25. Increased serum IgG4 levels have also been described in EGPA. While RTX can induce remission, current knowledge about its role in EGPA is based on a small number of case reports—fewer than 15 EGPA patients treated with RTX have been reported to date. In this case, the patient was started on rituximab and exhibited significant clinical improvement after the first cycle.

CONCLUSION

ANCA status distinguishes two phenotypes of EGPA that differ in organ involvement: renal and peripheral nervous system manifestations are more common in ANCA-positive patients, while cardiac and gastrointestinal involvement and pulmonary infiltrates are more frequently seen in ANCA-negative cases. The higher incidence of GI involvement in ANCA-negative patients highlights the importance of vigilant screening for GI symptoms in this subgroup. The pathology often involves eosinophilic infiltration of the mucosal layers, but vasculitis can also occur and lead to severe, life-threatening complications like intestinal perforation. Studies report good remission rates in ANCA-negative patients treated with rituximab.