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CASE REPORT | PATHOLOGY

Gastrointestinal Hemorrhage With Gastritis and Pancolitis as the Sole Presentation for Granulomatosis With Polyangiitis Flare

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ABSTRACT

Granulomatosis with polyangiitis (GPA), previously known as Wegener granulomatosis, is a rare small vessel vasculitis affecting mainly Whites. The prevalence of GPA in the United States is estimated to be 3 of 100,000 individuals. Classically, GPA affects upper airways, lungs, and kidneys, with the upper airways being the most common site. Occasionally, other organs affected by GPA include eyes, skin, joints, and the nervous system. The gastrointestinal system is rarely affected; however, some cases have been reported. In this case report, we present a patient with hemorrhagic gastritis and pancolitis consistent with GPA and discuss features from the literature of gastrointestinal manifestations in patients with GPA.

INTRODUCTION

Granulomatosis with polyangiitis (GPA) is a rare small vessel vasculitis affecting mainly Whites. The prevalence of GPA in the United States is estimated to be 3 of 100,000 individuals.[1] Classically, GPA affects upper airways, lungs, and kidneys, with the upper airways being the most common site.[2] Occasionally, other organs affected by GPA include eyes, skin, joints, and the nervous system. The gastrointestinal (GI) system is rarely affected; however, some cases have been reported.[3] In this case report, we present a patient with hemorrhagic gastritis and pancolitis consistent with GPA, and we discuss features from the literature of GI manifestations in patients with GPA.

CASE REPORT

A 28 year-old man with a medical history of GPA presented with 2 weeks of bloody diarrhea characterized by 6–8 loose black bowel movements, epigastric pain, and coffee-ground emesis. He reported self-discontinuation of his mycophenolate 5 months earlier. Physical examination was notable for abdominal tenderness to deep palpation in the epigastrium and lower quadrants. He was diagnosed with GPA during childhood with involvement of sinuses, ears, and lungs (pulmonary nodules) and rapidly progressive crescentic glomerulonephritis on renal biopsy. Although he was initially managed with rituximab, because of relapse with unknown symptoms, he was transitioned to mycophenolate maintenance therapy. Aside from baseline persistent tinnitus, he denied respiratory or urinary symptoms on current presentation.

Initial laboratory analysis demonstrated leukocytosis to 13.6 k/μL, elevated C-reactive protein (2.5 mg/dL on admission), and elevated Cr (1.47 mg/dL; baseline 1.07 mg/dL). An abdominal-pelvic computed tomography scan with intravenous contrast revealed thickening and edema of the walls of the gastric antrum, suggestive of gastritis, without evidence of vasculitis on imaging. Stool testing was positive for fecal calprotectin and lactoferrin. Infectious workup of the stool for common bacterial pathogens causing

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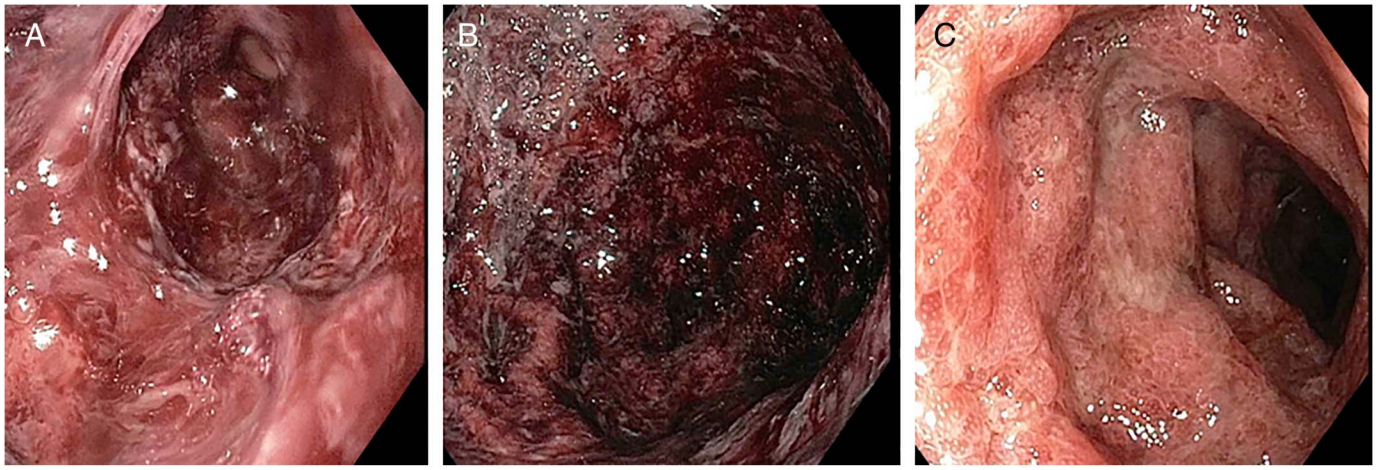

Figure 1. Endoscopic findings on endoscopy and colonoscopy. (**A** and **B**) Hemorrhagic gastritis found on endoscopy. Diffuse severe hemorrhage with adherent blood and clots was found on the entire examined stomach. (**C**) Colitis found on colonoscopy. The entire examined colon was characterized by diffuse severe inflammation with adherent blood, edema, erosions, erythema, and granularity.

inflammatory diarrhea was negative, as was testing for *Yersinia*, *Aeromonas*, and *Plesiomonas*. He had a rising white blood count level with white blood cells of 19.66 k/μL. C-antineutrophil cytoplasmic antibodies (ANCAs) and P-ANCAs were negative, both acutely and during routine follow-up before hospitalization, including testing for proteinase-3 and myeloperoxidase antibodies. It is unknown whether ANCAs were positive on diagnosis during childhood. Serum C3 and C4 levels remained within normal limits.

Endoscopy and colonoscopy revealed striking hemorrhagic inflammation of the stomach; copious irrigation and suction was attempted to clear the hemorrhage, without success (Figure 1). Similarly, colonoscopy revealed diffuse inflammation throughout the entire examined colon (Figure 1). Biopsies demonstrated gastritis and colitis with acute inflammation of mucosa and non-necrotizing vasculitis, without granulomas (Figure 2). The patient's symptoms worsened with up to 20 bloody bowel movements a day; therefore, he was started on intravenous methylprednisolone for GI vasculitis, with rapid resolution of his symptoms starting within a day of initiation. His creatinine normalized with hydration. Subsequently, he was transitioned to a prednisone taper on discharge and later started on azathioprine, with improvement in hematochezia on outpatient follow-up.

DISCUSSION

Now widely known as proteinase-3-associated ANCA vasculitis, GPA presents rarely with GI manifestations. The prevalence is estimated to be 6%–7% among severe cases.[4,5] We report a 28-year-old man who presented with severe hemorrhagic gastritis and pancolitis and biopsy evidence of acute mucosal inflammation and vasculitis and who responded well to steroids.

GI vasculitis induces inflammation of the vascular wall, causing thickening and increased thrombosis, compromising blood flow, and inducing end-organ damage. Patients present with a spectrum of symptoms, including abdominal pain, vomiting, diarrhea, and bleeding. Cases of liver and pancreas involvement have been described, although they are exceedingly rare.[6–8]

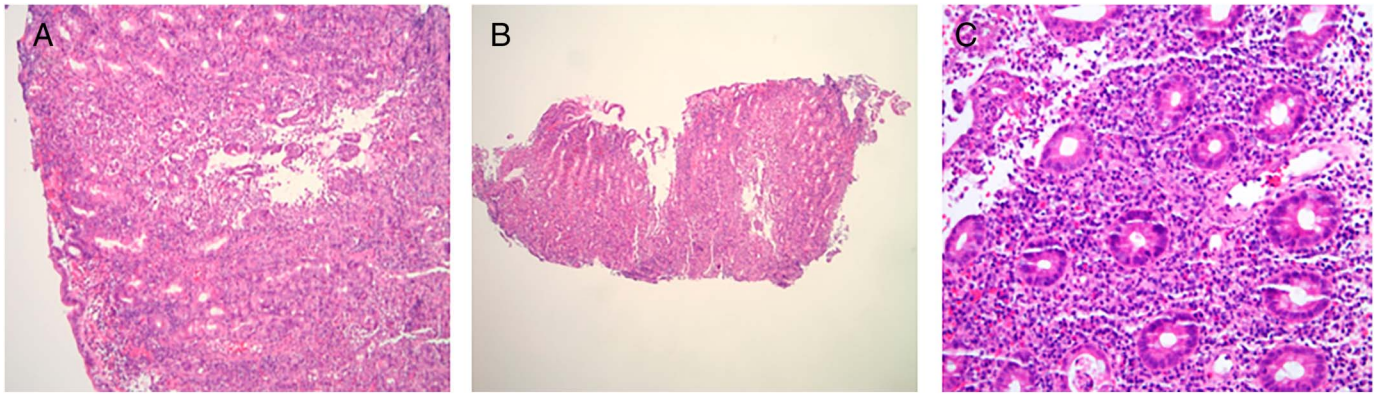

Figure 2. (**A** and **B**) Gastric mucosa. (**C**) Colonic mucosa. The gastric oxyntic-type and colonic mucosae revealed an unusual pattern of chronic active gastritis and colitis with neutrophilic-mediated epithelial injury in the form of glandular microabscesses, cryptitis, crypt abscesses, and vasculitis. No granulomas were identified. A *Helicobacter pylori* immunostaining was negative on the gastric biopsy.

Intestinal involvement has comparatively been described more frequently, often with mesenteric ischemia, ulceration, bleeding, or abdominal perforation.[3,9,10]

Similar to previous case reports, our patient's GI bleeding due to significant inflammation was the predominant symptom.[11] Although our patient lacked granulomas on pathology, a review of the literature demonstrates that this is not atypical. Reports have shown some patients on histology to have only signs of ischemia, thrombotic necrosis with perivasculitis, or ulceration.[9,12] One report found that only 1 of 2 patients had granulomatous colitis on histologic analysis.[12]

GI involvement in GPA has been associated with more severe cases of vasculitis. Patients have higher Birmingham Vascular Assessment Scores and increased need for surgery with GI GPA, often because of acute abdomen or intractable bleeding.[9,10] One review found 54.5% mortality with GI involvement, and all cases reviewed required surgery.[13] Furthermore, GI GPA has been associated with higher mortality.[11] GI manifestations occur late in the disease course of GPA.[14] Although some studies have explored endoscopic findings of GI disease in other vasculitides, because of the rarity of GPA in the GI tract, most of the work in this area has focused on the widely varying GI manifestations of GPA.[15] Currently, neither the American College of Rheumatology nor the American College of Gastroenterology has guidelines on the endoscopic diagnosis or medical management of GI manifestations of GPA.[16]

Our patient's young diagnosis age, ANCA negativity, and GI manifestations are unusual for GPA.[1] In our case, the diagnosis is confounded by the absence of other organ involvement on acute presentation. An important differential diagnosis is Crohn's disease, considering the absence of currently active vasculitis in other typically affected organs (upper airways, lung, and kidneys). However, our patient's upper airway involvement with ongoing tinnitus is supportive of a diagnosis of GPA. Pulmonary and upper respiratory tract involvement (eg, stenosis of nasal passages, pansinusitis) in Crohn's disease is rare, although it has been described.[17–19] In a single-center experience, of 3,626 patients with Crohn's disease, the incidence of pulmonary manifestations was 0.1%.[17] According to the 2017 classification of ANCA-associated vasculitis, including GPA, negative ANCA testing should not exclude diagnosis if there is a strong clinical suspicion, such as in our case.[20] According to 2021 classification criteria endorsed by the American College of Rheumatology, only 73.3% of patients with GPA had cytoplasmic-antineutrophil cytoplasmic antibody (C-ANCA) positivity while only 9.8% had perinuclear-antineutrophil cytoplasmic antibody (P-ANCA) positivity.[21]

Although coexistence of GPA and inflammatory bowel disease has been described, it is very rare.[22–24] Association has been shown between Crohn's disease and GPA.[22] Theories have been proposed that this association may lie in the similar granulomatous Th-1-mediated pathophysiology of both conditions, with Th-1 and Th-17 predominance in peripheral blood. Our patient's previous classic initial presentation during childhood (pulmonary nodules, nasal inflammation, and hematuria) and the presence of vasculitis on pathology are supportive of GPA vasculitis, although he may be a rare case of coexistent Crohn's disease and GPA. Despite diagnostic challenges, his gastroenterologist and rheumatologist comanaged his illness with azathioprine with a good response.[25] Unfortunately, he later underwent nephrectomy for resection of clear cell renal carcinoma diagnosed incidentally. Interestingly, reports have described an association between GPA and clear cell cancer, possibly because of the oncogenicity of maintenance immunosuppression drugs.[26–28]

DISCLOSURES

Author contributions: All authors contributed significantly as per ICMJE criteria. M. Alkhayyat is the article guarantor.

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