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CASE REPORT | INFLAMMATORY BOWEL DISEASE

Saddle Nose Deformity in a Patient With Crohn's Disease

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ABSTRACT

Crohn's disease is a chronic inflammatory disorder of the gastrointestinal tract, frequently presenting with extraintestinal manifestations. Granulomatosis with polyangiitis is a systemic vasculitis primarily affecting the respiratory tract and kidneys. Extraintestinal Crohn's disease and granulomatosis with polyangiitis may have similar clinical presentations and, in rare occurrences, can coexist. This case report highlights the diagnostic and therapeutic complexities of this uncommon overlap syndrome.

KEYWORDS: Crohn's disease; granulomatosis with polyangiitis; extraintestinal manifestations; saddle nose deformity

INTRODUCTION

Extraintestinal manifestations (EIMs) are common in Crohn's disease (CD), affecting up to 40% of patients.[1] Granulomatosis with polyangiitis (GPA) is a systemic vasculitis primarily affecting the upper and lower respiratory tract and kidneys.[2] The overlap of CD and GPA is extremely rare, with few cases reported in the literature.[3,4]

CASE REPORT

A 37-year-old man with biopsy-confirmed ileocolonic CD diagnosed 8 years earlier (Montreal Classification: A2, L3, B3), refractory to multiple biologics, was evaluated for oral pain, stridor, new nasal deformity, and bloody diarrhea.[5] Physical examination revealed multiple oral ulcerations on the soft palate, perforation of the right tympanic membrane, saddle nose deformity, and nasal ulcers with extensive crusting (Figures 1 and 2). Laboratory evaluation revealed a high C-reactive protein at 127 mg/L and fecal calprotectin at 1,058 mcg/g. Serologies for myeloperoxidase, proteinase 3, and syphilis IgG were negative. Flexible laryngoscopy and tracheoscopy to evaluate the patient's stridor revealed subglottic and laryngeal stenosis. Maxillofacial computerized tomography demonstrated bilateral maxillary and sphenoid sinusitis (Figure 3).

The presence of nasal crusting, septal deformity, and tracheal stenosis prompted a differential diagnosis of CD-GPA overlap vs EIMs of CD. Nasal septum and oral ulcer biopsies revealed mucosa with acute and chronic inflammation without evidence of vasculitis, granulomas, or dysplasia. Colonoscopy revealed severe pancolitis. Colonic biopsies showed moderate active, chronic colitis with extensive ulceration without signs of vasculitis, granulomas, or mycobacterial organisms. Based on these findings, along with the negative anti-neutrophil cytoplasmic antibodies serologies, the overall presentation was deemed secondary to EIMs of CD.

The patient had improvement of symptoms and inflammatory markers with a diverting loop ileostomy, intravenous methylprednisolone transitioned to a prolonged oral steroid taper, and outpatient initiation of certolizumab pegol (CTZ). Unfortunately, the patient was rehospitalized after a single CTZ dose because of sigmoid perforation and underwent partial sigmoidectomy with primary end-to-end anastomosis. Flexible sigmoidoscopy of the diverted colon revealed large pancolonic ulcers with a simple endoscopic score for CD of 36. Biopsies were negative for cytomegalovirus. Given the ongoing severe colonic inflammation, he was started on cyclosporine at 2 mg/kg as a continuous 24-hour infusion. He had a clinical response characterized by improved abdominal cramping and was transitioned to oral therapy within 72 hours. CTZ was also restarted, and he continued oral steroids. At

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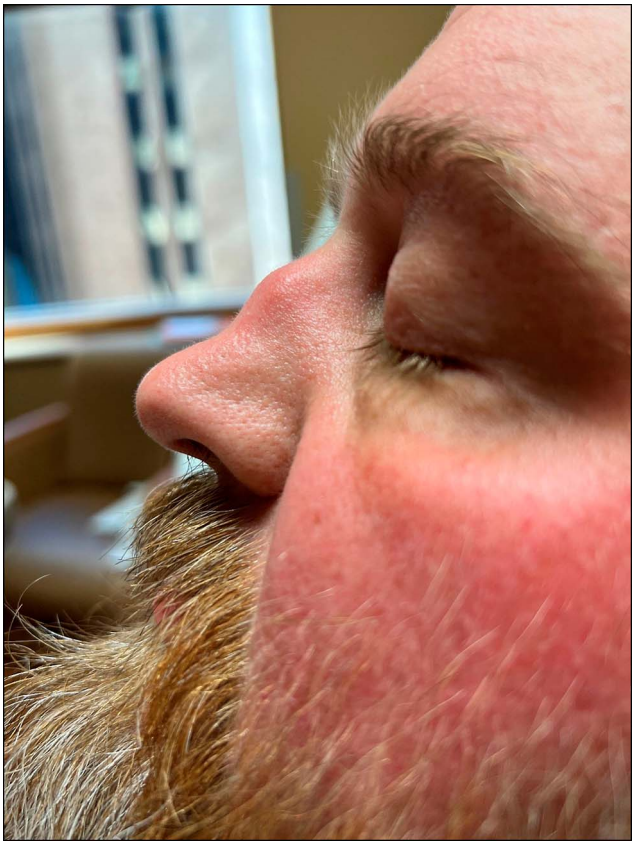

Figure 1. Saddle nose deformity.

the follow-up, he reported significant reduction in frequency and intensity of abdominal symptoms, but no reduction in upper respiratory tract symptoms.

A few months later, he was admitted for abdominal pain with increased ostomy output and bright red blood per rectum. Sigmoidoscopy revealed mucosal healing with chronic sigmoid colitis, but no signs of acute inflammation on pathology. A

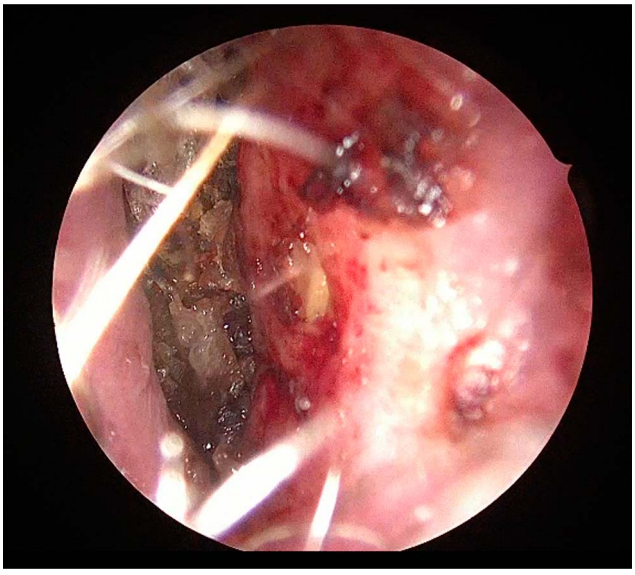

Figure 2. Rhinoscopy demonstrating nasal ulcer with crusting.

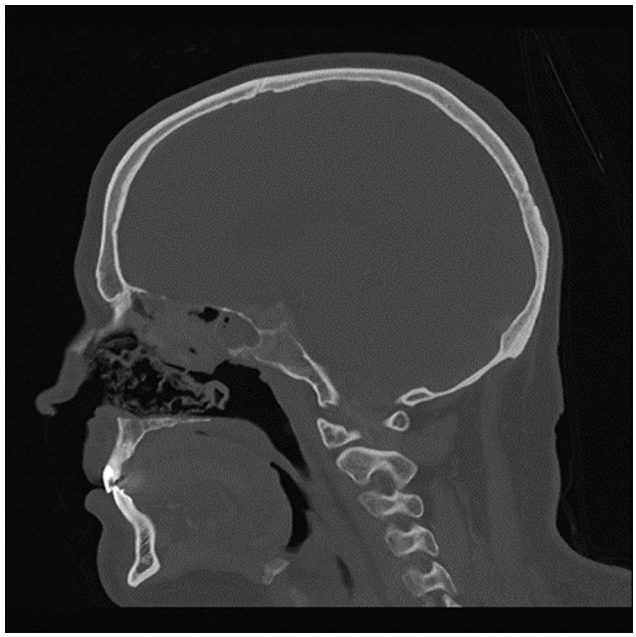

Figure 3. Maxillofacial computed tomography showing septal deformity and sinusitis.

3-day course of methylprednisolone 60 mg IV was administered, followed by daily oral prednisone 40 mg with a slow taper. Genetic testing for 118 autoinflammatory genes, including Yao syndrome, was negative. Rheumatology recommended rituximab initiation for likely CD and GPA overlap, given the persistence of upper respiratory symptoms, but rituximab was deferred because of the rare but known increased risk of colonic perforation with this drug in the setting of this patient's multiple previous perforations. Ultimately, because of his refractory CD, he underwent elective total proctocolectomy with end ileostomy. Surgical pathology revealed active colitis without evidence of vasculitis or IgG4-related disease. He is currently being monitored for the resolution of his EIM of CD after bowel resection before consideration of further immunosuppressive therapy to target respiratory tract manifestations.

DISCUSSION

CD and GPA overlap is extremely rare and presents unique diagnostic and therapeutic challenges. This patient presented with oral ulcerations, hearing loss, tracheal stenosis, and a saddle nose deformity, all of which can be hallmarks of GPA or present in severe cases of extraintestinal CD.[6,7]

To definitively diagnose GPA, histopathological evidence of vasculitis is needed. Biopsies should target areas of active disease because histopathological characteristics differ based on biopsy site. In general, diagnostic yield increases with progression from the upper to lower respiratory tract. One study demonstrated that 91% of lung biopsies showed histological evidence of vasculitis compared with 16% with upper airway biopsies.[8] Tissue from the upper respiratory tract usually shows nonspecific inflammatory changes, as seen in this case.[9] Nasal

biopsies in particular are of low diagnostic yield, with solid organ biopsies being preferred.

Given the difficulty of diagnosing vasculitis, the classification criteria based on clinical, laboratory, and imaging factors were created to guide evaluation. The most recent criteria state that anti-neutrophil cytoplasmic antibodies (myeloperoxidase/proteinase 3) positivity is no longer needed to diagnose GPA.[10] Although the negative serologies and absence of vasculitis on biopsies in this case suggested against a diagnosis of GPA, neither of these factors are sufficient to rule out GPA.[11]

When considering treatment for patients with CD-GPA overlap syndrome, many of the medications used for CD will not treat GPA. For patients with new-onset GPA, a combination of glucocorticoids with either cyclophosphamide or rituximab is recommended for induction, whereas remission maintenance requires a combination of low-dose glucocorticoids with either azathioprine, rituximab, methotrexate, or mycophenolate mofetil.[11,12]

By comparison, the treatment of CD varies based on the severity of disease. In patients with mild-to-moderate ileocecal disease, controlled ileal-release budesonide is the primary treatment. In patients with moderate-to-severe symptoms, addition of azathioprine, 6-mercaptopurine, methotrexate, or anti-tumor necrosis factor therapy is recommended. In severe or fulminant disease, IV corticosteroids and anti-tumor necrosis factor agents are considered.[13–16]

Despite targeted CD therapies, the patient's EIMs did not improve. If EIMs do not improve on CD-targeted treatment, it is worth considering the escalation of immunosuppressive therapy to target an overlap with GPA. Previous cases of CD-GPA overlap treated with a combination of steroids, cyclophosphamide, and mesalazine have led to a resolution of intestinal and pulmonary manifestations.[17,18]

This case highlights the complex diagnostic and therapeutic decision-making in patients with CD-GPA overlap. Many therapeutics targeting EIM of CD differ from those used in overlap syndromes, reinforcing the need for close monitoring and flexibility in treatment plan. Further research is needed to understand the pathophysiology of this overlap syndrome, which will help guide effective treatment strategies and assist with timely diagnosis.

DISCLOSURES

Author contributions: BJ Gawey: conceptualization, data curation, formal analysis, investigation, methodology, resources, writing–original draft preparation, and is the article guarantor. D Guerrero Vinsard, M. Own, and SV Kane: conceptualization, data curation, formal analysis, investigation, methodology, resources, supervision, writing–original draft preparation, writing–review, and editing.

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Informed consent was obtained for this case report.

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