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CASE REPORT | SMALL BOWEL

Cryptogenic Multifocal Ulcerative Sclerosing Enteritis: A Curious Case of Intestinal Obstruction in the Setting of Human Immunodeficiency Virus

Kelly Hathorn, MD[1,2], Taha Qazi, MD[1,2], Michael Travis Caton, MD[2,3], and Jessica R. Allegretti, MD, MPH[1,2]

[1]*Division of Gastroenterology, Brigham and Women's Hospital, Boston, MA*
[2]*Harvard Medical School, Boston, MA*
[3]*Division of Radiology, Brigham and Women's Hospital, Boston, MA*

ABSTRACT

Cryptogenic multifocal ulcerative sclerosing enteritis (CMUSE) is a rare clinical entity characterized by chronic, relapsing episodes of ileus and obstruction resulting from superficial ulcerating lesions of the small intestine with a clinical course that responds favorably to corticosteroids. We report a case of CMUSE arising in a patient with a history of human immunodeficiency virus infection. This case highlights the unique pathology of CMUSE as well as the potential pathogenesis of this atypical clinical entity.

INTRODUCTION

Cryptogenic multifocal ulcerative sclerosing enteritis (CMUSE) was first described by Debray et al. in 1964.[1] The authors noted episodic obstructions related to ulcerative stenosis of the small intestine. The condition was characterized by relapsing–remitting courses with improvement following corticosteroids. We present a complicated case of a patient with persistent worsening obstructive symptoms.

CASE REPORT

A 55-year-old man with well-controlled human immunodeficiency virus (HIV) on highly active antiretroviral therapy was evaluated for abdominal pain. He was diagnosed with HIV several years before the setting of *Pneumocystis jirovecii* pneumonia (PJP). During PJP treatment, he developed significant watery, nonbloody diarrhea that was attributed to sulfamethoxazole/trimethoprim. It persisted, so abdominal computed tomography scan was taken, which demonstrated diffuse bowel wall thickening of the small intestine and colon (Figure 1). Extensive infectious stool evaluation was negative; however, he was found to have cytomegalovirus (CMV) viremia, with a CMV polymerase chain reaction greater than 1,000 U/mL. Esophagogastroduodenoscopy (EGD) was notable for Los Angeles (LA) grade D esophagitis with pathology consistent with severe active esophagitis. Colonoscopy revealed diffuse, severely congested mucosa, with similar findings in the terminal ileum (Figure 2). Pathological examination confirmed active ileitis and colitis with ulceration, with multiple CMV inclusions identified. The patient was treated with a prolonged course of intravenous ganciclovir.

He began complaining of solid food dysphagia. EGD revealed sloughing, and pathological examination was positive for CMV (Figure 3). He was restarted on valganciclovir, until biopsies cleared. He ultimately developed severe esophageal stenosis from the chronic inflammation and required 7 esophageal dilations, leading to symptom resolution.

Unfortunately, several months later, he developed abdominal pain, nausea, and worsened vomiting approximately 1 hour after eating, prompting gastrointestinal workup. Vital signs were within normal limits. On physical examination, he was thin, but well appearing. His abdomen was soft, nontender, and nondistended with normoactive bowel sounds. There was no rebound tenderness

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Correspondence: Jessica R. Allegretti, MD, MPH, Brigham and Women's Hospital, Boston, MA 02115 (jallegretti@bwh.harvard.edu).

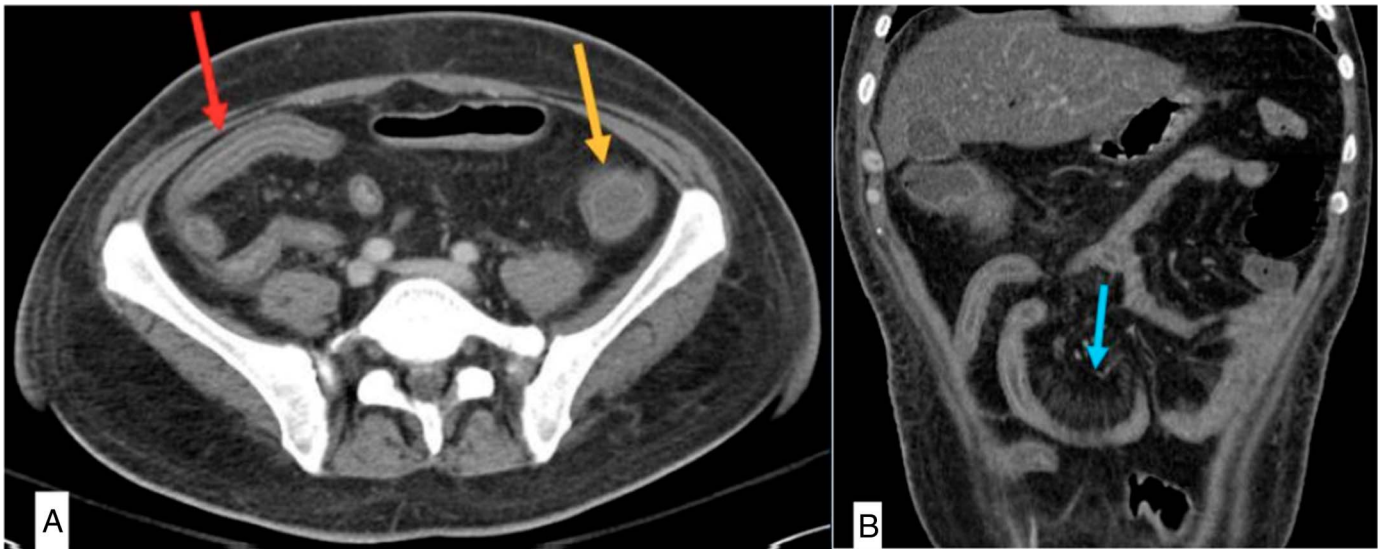

Figure 1. Contrast-enhanced abdomen and pelvic computed tomography (A) axial images demonstrating colonic inflammation (yellow arrow) and ileal inflammation (red arrow) and (B) coronal images demonstrating "teeth of comb" appearance of engorged mesenteric veins (blue arrow).

nor guarding. Examination was otherwise unremarkable. His medical history was notable only for his HIV, well controlled on highly active antiretroviral therapy; he had no other chronic medical conditions or systemic illnesses. Given the severity of his symptoms, repeat abdomen computed tomography was performed, which demonstrated multiple areas of small bowel wall thickening in a discontinuous pattern as well as narrowing and upstream small bowel dilatation. Infectious workup, including tuberculosis testing, was negative. Colonoscopy was grossly normal. Biopsies demonstrated focal active colitis and ileitis, without viral cytopathic changes, and CMV immunostain showed negative results. Symptoms were therefore felt to be inflammatory. Biopsies were not consistent with Crohn's disease, and thus, they were felt to be related to HIV/immune reconstitution inflammatory syndrome. He was empirically started on prednisone 40 mg daily. He noted mild improvement in his symptoms; however, several weeks later, symptoms returned with severe postprandial pain, anorexia, nausea, and emesis.

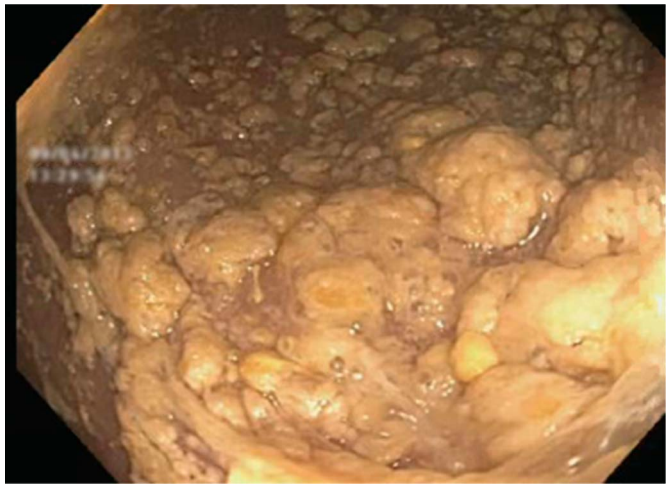

Figure 2. Colonoscopy with diffusely congested, friable, granular mucosa in the descending colon.

Magnetic resonance enterography confirmed multiple segments of small bowel wall thickening and inflammation in a discontinuous pattern with persistent upstream small bowel dilation and fecalization (Figure 4). Given the concern for obstruction, the patient underwent a surgery, and a matted small bowel mass with massively dilated proximal small bowel was resected. A mesenteric lymph node testing was negative for lymphoproliferative disorder. His final pathological examination showed severe, chronic active enteritis and multifocal ulceration, neural hyperplasia, myointimal hyperplasia, and phlebitis of small-to-medium-sized blood vessels and serositis, with negative acid-fast bacilli and human herpesvirus 8, and ultimately revealed the final diagnosis of CMUSE. Postoperatively, all symptoms resolved. His appetite improved, and he had no further abdominal pain, nausea, or vomiting.

DISCUSSION

CMUSE was first described by Debray et al. in 1964.[1] The authors characterized a relapsing–remitting condition with episodic obstructions relating to ulcerative stenosis of the small intestine with characteristic improvement following corticosteroids. The clinical features of this condition in a case spanning 3 decades was previously described earlier in this journal.[2]

In the presented patient, alternative causes including Crohn's disease, tuberculous enteritis, nonsteroidal antiinflammatory drug-related ulcers, Bechet's disease, celiac disease, and malignancy were excluded through a review of the history, physical examination findings, endoscopic and serological evaluation, and pathology. The classically described features of ulcerations confined to the mucosa and submucosa on pathology, manifesting as

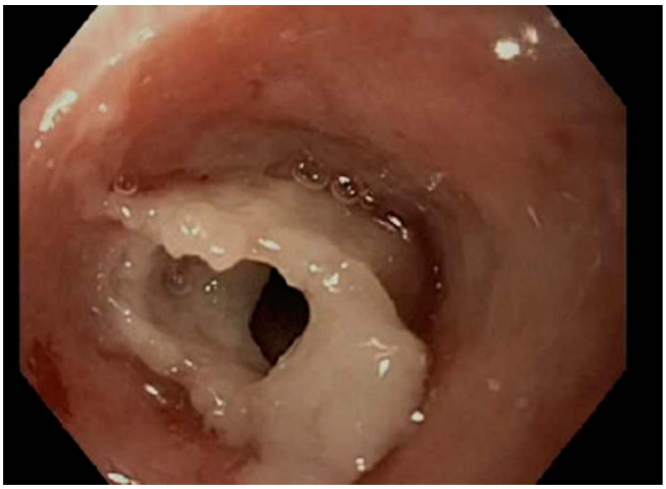

Figure 3. Esophagogastroduodenoscopy demonstrating esophageal ulceration and sloughing mucosal abnormality.

idiopathic strictures in the absence of other systemic inflammatory symptoms, suggested the diagnosis.

Several proposed mechanisms for the pathogenesis of CMUSE have been described, but the etiology for this extremely rare condition continues to be unknown. Implicated processes include a potential vasculitis, referenced in a case series demonstrating abnormal angiography and vascular pathology in a majority of reported subjects.[3] Complement deficiency has also been attributed to CMUSE in the context of a vasculitic process.[4,5] In our patient, there was evidence of venopathy, but testing including complement levels, markers of autoimmunity, imaging evaluations, and the lack of additional systemic manifestations did not suggest a vasculitic process.

To our knowledge, this is the first documented case of CMUSE in a patient with HIV. The gut contains high numbers of CD4+, CCR5+ T-cells that are profoundly depleted in HIV infection.[6,7] Despite anti-retroviral therapy, there is incomplete reconstitution within the gastrointestinal mucosa, and delays in reconstitution have been hypothesized to be related to collagen deposition resulting in the disruption of gut-associated lymphoid tissue.[8] Additionally, sustained immune activation related to bacterial translocation has been suggested as a potential etiology for gut-related fibrosis.[9] Specifically, uncontrolled, persistent activation of intestinal myofibroblasts have been shown to contribute to gut fibrosis through an imbalance in the pro-fibrogenic cytokine profiles.[10] In our patient, a pattern of chronic dysregulated immune activation in the context of not only HIV but also CMV infection may have provided the impetus for the development of CMUSE.

In conclusion, we present a case of CMUSE in the setting of HIV infection. In our patient, characteristics of both vasculitis and a dysregulated immune response potentially related to HIV may have contributed to the development of CMUSE. As such, our case highlights the unique and unfamiliar pathogenesis of this rare clinical disease.

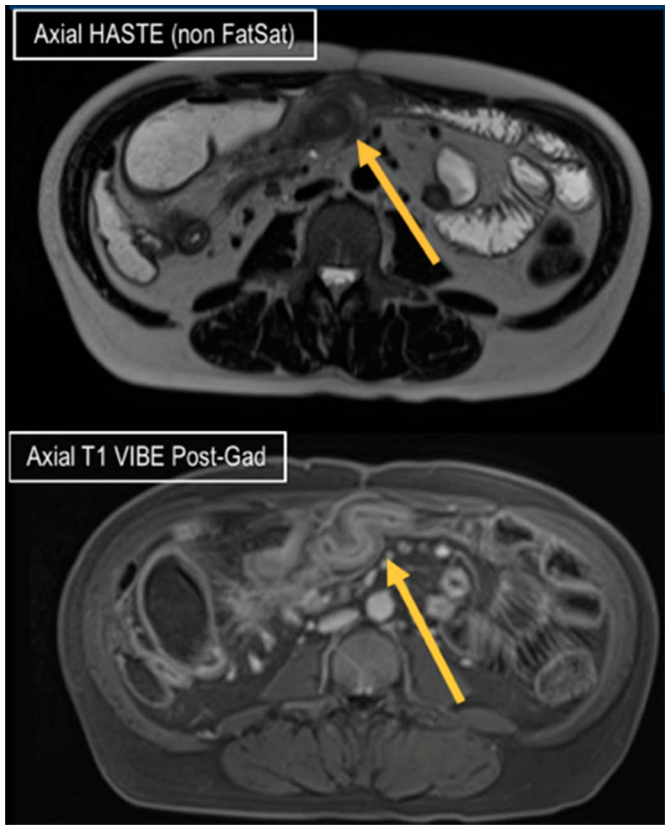

Figure 4. Gadolinium-enhanced magnetic resonance (MR) enterography. Axial HASTE and T1 VIBE post-contrast image showing segmental small bowel narrowing with mural thickening and edema (yellow arrows).

DISCLOSURES

Author contributions: K. Hathorn and T. Qazi gathered data and drafted the manuscript. MT Caton gathered data. JR Allegretti critically revised the manuscript and is the article guarantor.

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Informed consent was obtained for this case report.

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