INTRODUCTION

Amyloidosis is a rare disease with a prevalence of 5.8 of 100,000 in the United States.\(^1\) It results from extracellular depositions of misfolded proteins throughout organs. Amyloidosis of the gastrointestinal (GI) tract in specific is rarer, with only 3% of usual patients with amyloidosis having GI tract involvement.\(^2\) Common presentations of GI amyloidosis are nonspecific and include abdominal pain, bleeding, pseudo-obstructions, and diarrhea. Laboratory and radiological investigations are often nondiagnostic, and definitive diagnosis requires histological examination.\(^3\)

Cytomegalovirus (CMV) colitis, on the other hand, is generally diagnosed in immunosuppressed patients and is rare in immunocompetent patients. Particularly, it has a high incidence in patients with inflammatory bowel disease.\(^4\) The symptoms of CMV colitis are similarly nonspecific and include diarrhea, abdominal pain, and bleeding. Diagnosis is primarily made through colonoscopy and histology to visualize inclusion bodies.

Prior associations with CMV colitis and multiple myeloma (MM) or amyloidosis are only described in immunocompromised patients undergoing treatments such as transplantation, monoclonal antibodies, or chemotherapy.\(^5\) We describe a unique case of CMV colitis in a 67-year-old patient with GI amyloidosis as part of the initial presentation of MM.

CASE REPORT

A 67-year-old Venezuelan man with a history of hypertension and benign prostatic hyperplasia was admitted to the hospital with bilateral lower extremity deep vein thromboses after transurethral resection of prostate 8 days before. He was started on therapeutic anticoagulation, but because of complications of gross hematuria, an inferior vena cava filter was placed. The hospital course was further complicated by arrhythmia, pericardial effusion, and type II non-ST-elevation myocardial infarction. Owing to bright red blood per rectum with diarrhea, gastroenterology consultation was sought. The patient denied pain, nausea, vomiting, or fevers and reported no prior episodes of rectal bleeding or diarrhea.

On physical examination, the patient had temperature 37.2°C, pulse rate 82, and blood pressure 118/71 with oxygen saturation 99% on room air. The abdomen was nondistended and nontender. Digital rectal examination showed brown stool. Initial laboratory examination showed a leukocyte count of 7.6 \(\times\) 10\(^3\)/\(\mu\)L, hemoglobin 11.3 g/dL, platelet count 372 \(\times\) 10\(^3\)/\(\mu\)L, blood urea nitrogen 13 mg/dL, serum creatinine 0.8 mg/dL, protein 3.7 g/dL, and calcium 7.3 mg/dL. An infectious stool panel was negative; \textit{Clostridium difficile} testing showed negative glutamate dehydrogenase and toxin, but positive polymerase chain reaction.

Abdominal and pelvic computed tomography (CT) revealed signs of acute colitis with diffuse colonic wall thickening. Colonoscopy displayed discontinuous areas of ulcerated, erythematous, easily friable mucosa with loss of the vascular pattern through the entire colon (Figure 1). A histologic examination showed terminal ileal mucosa with reactive epithelial changes and lymphoid aggregates. It further revealed positive Congo red stain with apple green birefringence in the terminal ileum and colon and CMV inclusions in the colon (Figure 2).

Subsequent testing demonstrated a serum albumin fraction of 1.46 g/dL, free kappa light chain 2.08 mg/dL, and free lambda light chain 111.65 mg/dL with a free kappa-to-lambda ratio of 0.019. No monoclonal spike was found on electrophoresis. Bone marrow...
biopsy showed lambda light chain restriction and CD138-positive plasma cells that composed 20% of the marrow biopsy, which was suggestive of amyloid light chain (AL) amyloidosis and MM. Echo demonstrated a segmental longitudinal strain pattern indicative of apical sparing, which can be seen in cardiac amyloid. However, the technetium pyrophosphate scan was negative. Further imaging and laboratory test results did not indicate amyloidosis in other organs.

The patient was started on valganciclovir, but no specific amyloidosis treatment, and showed no improvement in GI symptoms. Repeat abdominal CT demonstrated worsening subcutaneous soft-tissue edema, but improved mural thickening of the colon. During this time, the patient’s clinical status continued to worsen, and he ultimately died 40 days after admission of cardiac causes, possibly because of cardiac amyloidosis.

DISCUSSION

We present a unique case of CMV colitis and GI amyloidosis occurring concurrently. The patient presented with nonspecific GI symptoms, and the diagnosis was confirmed by histologic examination of the colon. A bone marrow biopsy confirmed a

Figure 1. (A) Sigmoid colon; (B) terminal ileum. Colonoscopy images showing skipped areas of ulcerated, erythematous, friable, and congested mucosa.

Figure 2. Photomicrographs (original magnification 1×). (A) Hematoxylin and eosin stain of the colonic epithelium with CMV colitis. (B) Immunohistochemistry for CMV highlights viral inclusions. (C) Colonic epithelium with amyloidosis. (D) Congo red stain showing salmon pink amyloid deposits. CMV, cytomegalovirus.
diagnosis of MM. We suggest that GI amyloidosis should be considered on differential diagnosis in patients presenting with nonspecific GI symptoms, particularly in the setting of diffuse symptoms in other organs.

The most common subtype of amyloid in GI amyloidosis is AL amyloid. The small intestine, particularly the duodenum, is the most common site of deposition, followed by the stomach and colorectum. Clinical presentation of GI amyloidosis is variable depending on the location of involvement and severity of infiltration. AL amyloid deposition usually occurs in muscularis mucosa, submucosa, and muscularis propria. It can also involve the vasculature to cause bowel infarction; the most common colonic imaging findings include hemorrhagic bullous colitis and mucosal friability. CT findings usually display colonic wall thickening or luminal narrowing. Diagnoses are made through histology.

It is noteworthy that CMV colitis occurred concurrently with amyloidosis in our patient. Although it is established that immune dysfunction and hypogammaglobulinemia in amyloidosis lead to susceptibility to infection, the infecting organisms in early disease usually include Haemophilus influenzae, Streptococcus pneumoniae, and Escherichia coli. Immunosuppressing therapies such as transplantation or chemotherapy increase the likelihood of opportunistic infections. Despite this, CMV has rarely been reported in patients with amyloidosis. The rare cases reported in the literature exclusively occurred in advanced-stage MM coupled with immunomodulators (daratumumab or thalidomide) or autologous stem cell transplantations.

The management of CMV colitis usually involves medical management with ganciclovir or valganciclovir. However, foscarnet may be used as an alternative if resistance or intolerance occurs, and surgery is reserved for a failure of medical therapy. Our patient was managed with valganciclovir. However, our case highlights the difficulty in assessing the effectiveness of antiviral treatment for CMV in GI amyloidosis because of symptom overlap between both conditions. The patient continued with diarrhea and rectal bleeding and deteriorated quickly even after antiviral treatment. Unfortunately, no specific treatment exists for GI amyloidosis, and treatment is specific to the underlying cause. Because patients with GI tract involvement have worse prognosis, treatments for GI amyloidosis should be explored.

This is the first case report of concurrent CMV colitis and GI amyloidosis in patients not undergoing immunosuppressive treatments. We suggest that amyloidosis should be on the differential for hospitalized patients with acute multiorgan dysfunction and nonspecific GI symptoms.

DISCLOSURES

Author contributions: P. Atuluru was responsible for project conception/design, literature review, data gathering, and manuscript drafting/revisions and is the article guarantor. C. Jiang was responsible for project conception/design, literature review, data gathering, and manuscript drafting/revisions. T. Alkathery was responsible for project conception/design and data gathering. E. Manten was responsible for project conception/design and data gathering. S. Kumar was responsible for project conception/design, data gathering, and manuscript drafting/revisions.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Received April 12, 2022; Accepted August 24, 2022

REFERENCES

1. Duhamel S, Mohty D, Magne J, et al. Incidence and prevalence of light chain amyloidosis: A population-based study. Blood. 2017;130(Suppl 1):5577.
2. Cowan AJ, Skinner M, Seldin DC, et al. Amyloidosis of the gastrointestinal tract: A 13-year, single-center, referral experience. Haematologica. 2013; 98(1):141–6.
3. Dahiya DS, Khichoo A, Singh J, Albosta M, Wani F. Gastrointestinal amyloidosis: A focused review. World J Gastrointest Endosc. 2021;13(1):1–12.
4. Hiisong E, Chen Z, Yantiss RK. Cytomegalovirus reactivation in inflammatory bowel disease: An uncommon occurrence related to corticosteroid dependence. Mod Pathol. 2019;32(8):1210–6.
5. Sameh S, Sawsen B, Imen B, et al. Neuro-meningeal cryptococcal infection revealing a multiple myeloma. Pan Afr Med J. 2020;36:632.
6. Syed U, Ching Companioni RA, Alkhawam WA, Walfish A. Amyloidosis of the gastrointestinal tract and the liver: Clinical context, diagnosis and management. Eur J Gastroenterol Hepatol. 2016;28(10):1109–21.
7. Tada S, Iida M, Iwashita A, et al. Endoscopic and biopsy findings of the upper digestive tract in patients with amyloidosis. Gastrointest Endosc. 1990;36(5):10–4.
8. Lee BS, Chudasama Y, Chen AI, Lim BS, Taira MT. Colonoscopy leading to the diagnosis of AL amyloidosis in the gastrointestinal tract mimicking an acute ulcerative colitis flare. ACG Case Rep J. 2019;6(1):e00289.
9. Tete SM, Bilj M, Sahota SS, Bos NA. Immune defects in the risk of infection and response to vaccination in monoclonal gammopathy of undetermined significance and multiple myeloma. Front Immunol. 2014;5:257.
10. Lavi N, Okasha D, Sabo E, Oren I, Benyamini N, Bar-Yoseph H. Severe cytomegalovirus enterocolitis developing following daratumumab exposure in three patients with multiple myeloma. Eur J Haematol. 2018;101(5):699–702.

11. Yerushalmi-Feler A, Padlipsky J, Cohen S. Diagnosis and management of CMV colitis. Curr Infect Dis Rep. 2019;21(2):5.
12. Wetwittayakhlang P, Sripongpun P, Jandee S. Primary gastrointestinal amyloidosis: An unusual cause of acute intestinal pseudo-obstruction. Case Rep Gastroenterol. 2019;13(3):462–7.