

# Systemic Immunoglobulin Light Chain Amyloidosis Involving the Large Intestine

Renugadevi Swaminathan, MD, MPH<sup>1</sup>, Samuel Igbiniedion, MD<sup>2</sup>, and Sudha Pandit, MD<sup>2</sup>

<sup>1</sup>Department of Internal Medicine, Louisiana State University Health, Shreveport, LA

<sup>2</sup>Department of Medicine, Section of Gastroenterology and Hepatology, Louisiana State University Health, Shreveport, LA

## ABSTRACT

Amyloidosis is characterized by extracellular tissue deposition of fibrils resulting in disruption of tissue structure and function. Gastrointestinal amyloidosis commonly results from chronic inflammatory disorders (amyloid A amyloidosis) and is less commonly seen in immunoglobulin light chain amyloidosis. We present a rare case of a 50-year-old man with a history of immunoglobulin light chain amyloidosis who presented with abdominal pain, blood in stool, diarrhea, and weight loss. Colonoscopy and biopsies revealed amyloid deposits in the colon. The patient subsequently was referred to colorectal surgery for evaluation of total colectomy with further plans for chemotherapy and subsequent hematopoietic cell transplantation.

## INTRODUCTION

Amyloidosis is characterized by extracellular tissue deposition of fibrils resulting in disruption of tissue structure and function.<sup>1</sup> Gastrointestinal (GI) amyloidosis commonly results from chronic inflammatory disorders such as rheumatoid arthritis and inflammatory bowel disease (amyloid A [AA] amyloidosis), plasma cell dyscrasia (immunoglobulin light chain [AL] amyloidosis), and end-stage renal disease ( $\beta$ -2 amyloidosis).<sup>2</sup> Although AL amyloidosis is the most common type of systemic amyloidosis, GI involvement is more common with AA amyloidosis as compared to AL amyloidosis.<sup>3,4</sup> GI manifestation in amyloidosis results from mucosal infiltration or neuromuscular infiltration, and patients may present with abdominal pain, esophageal reflux, altered bowel habit, GI bleeding, malabsorption, and weight loss.<sup>5</sup> The clinical presentation could vary based on the patterns of amyloid deposition.<sup>1,6,7</sup> AA amyloidosis usually presents with diarrhea and malabsorption because granular amyloid deposition occurs mainly in the mucosa leading to erosions. The AL amyloidosis presents with constipation and intestinal obstruction because amyloid deposition occurs in the muscularis mucosae, submucosa, and muscularis propria leading to thickening of the valvulae conniventes and polypoid protrusions.<sup>8</sup> GI amyloidosis can be diagnosed with a tissue biopsy. The amyloid deposits are Congo red positive and demonstrate apple-green birefringence under polarized light and exhibit linear nonbranching fibrils on the electron microscopy.<sup>9</sup> The GI involvement of AL amyloidosis is considered as biopsy evidence of GI tract infiltration along with GI symptoms. Biopsy-confirmed symptomatic GI amyloidosis is rare.<sup>1,10</sup> Here, we report a rare case of biopsy-proven symptomatic AL amyloidosis involving the large intestine.

## CASE REPORT

A 50-year-old white man with a medical history significant for end-stage renal disease secondary to AL amyloidosis on hemodialysis presented to the emergency department with complaints of diffuse abdominal pain, diarrhea, and bright red blood per rectum over the past 2 weeks. The patient also reported decreased appetite and weight loss of 25 pounds in 3 months and denied fever, chills, nausea, vomiting, bloating, obstipation, dysphagia, odynophagia, hematemesis, or dark black stool on presentation. He denied any previous episodes of GI bleeding. On arrival, his blood pressure and pulse rate were 114/68 mm Hg and 111 beats/min, respectively. His temperature was 98.4°F (36.9°C), and the respiratory rate was 16/min. Physical examination was significant for pallor and diffuse abdominal tenderness with voluntary guarding. Laboratory findings on admission were white blood cell 13 K/ $\mu$ L, hemoglobin 5.8 g/dL, platelet 288 K/ $\mu$ L, BUN 34 mg/dL, creatinine 9.84 mg/dL, and albumin 1.9 g/dL. C-reactive protein and fecal calprotectin were elevated to 4.9 mg/dL and 2,809  $\mu$ g/g, respectively. The patient was resuscitated with 2 units of packed red blood cells with subsequent improvement in



**Figure 1.** Axial view of abdominal computed tomography demonstrating colonic mural thickening with pericolic fat stranding.

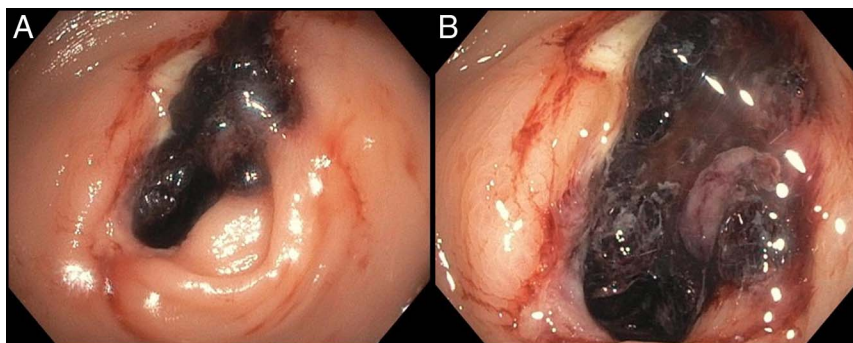
hemoglobin. Infectious workup, including the stool studies, was negative. Abdominal computed tomography showed a long segment of colonic mural thickening involving the ascending and transverse portions with submucosal edema, pericolic fat stranding, and vascular congestion. The imaging did not show any evidence of mechanical bowel obstruction, pneumatosis, or bowel perforation, and the findings were consistent with colitis (Figure 1).

Later, the patient underwent lower GI endoscopy for further evaluation. The scope was unable to be advanced beyond the proximal descending colon as a large amount of adherent blood clots was covering the colon (Figure 2). No further attempts were made to remove the blood clots through snare, given the risk of perforation. Repeat colonoscopy a few days later revealed patchy areas of erythema with ulceration from the sigmoid colon to transverse colon, with a stricture in the transverse colon, and the findings were consistent with chronic ischemia (Figure 3). Tissue biopsies were obtained from the ischemic appearing colon. Histological examination of the colon biopsy revealed ulceration and inflammation (Figure 4). Congo red and thioflavin T stains were performed on the colon biopsy, which was positive for amyloid (Figure 4). CD138-positive plasma cells highlighted in the mucosa were polyclonal on in situ hybridization stains for  $\kappa$  and  $\lambda$ .

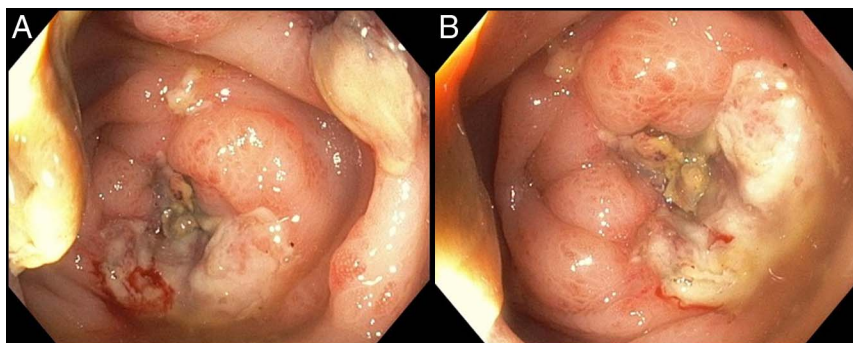
The patient had a renal biopsy and bone marrow biopsy 2 months before the current hospitalization. Renal biopsy showed extensive amyloid deposition in the kidney, and findings were consistent with lambda light chain deposition disease. Bone marrow biopsy showed atypical plasmacytosis with lambda light chain predominance and vascular changes compatible with amyloid. The patient was referred to hematology-oncology for outpatient follow-up; however, he missed the clinic appointment and never received any treatment and presented to the emergency department 2 months later with GI symptoms. Colon biopsy during the hospitalization confirmed GI involvement of amyloidosis. Hereafter, colon resection is planned for this patient since amyloid protein accumulation in the organs is generally an irreversible phenomenon. After the surgical resection, the patient is planned for chemotherapy and will be evaluated for hematopoietic cell transplantation.

## DISCUSSION

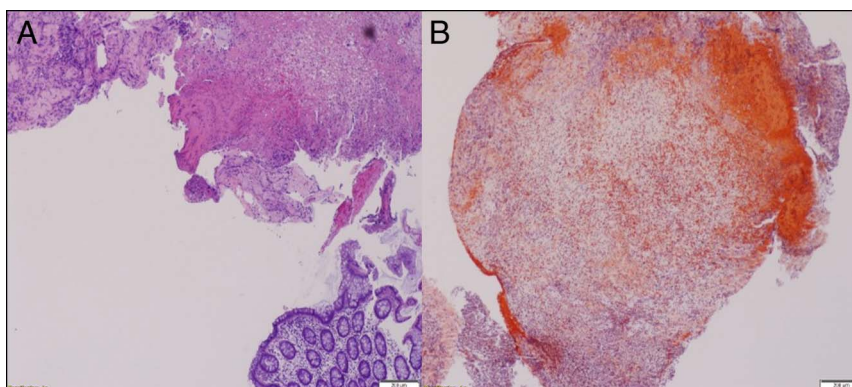
In GI amyloidosis, GI-related symptoms are reported to be variable. In primary (AL) amyloidosis, the range is between 8% and 60%, and in secondary (AA) amyloidosis, it is 10%–70%.<sup>11</sup> Amyloid deposition into the blood vessel walls can lead to bowel ischemia and muscle atrophy, which can result in mucosal ulceration.<sup>12</sup> Management includes treatment of the underlying disease that contributes to amyloidosis and symptom control.<sup>13,14</sup> Chemotherapy for amyloidosis is aimed at inhibiting the production of amyloid protein.<sup>3</sup> Although the accumulation of amyloid protein in the organs is generally an irreversible phenomenon, studies show that accumulation is reversible at an early stage; hence, it is vital to attempt early detection.<sup>3,4</sup> The advent of high-dose melphalan with autologous stem cell transplantation has improved the outcome in patients with AL amyloidosis. Reports show 25%–45% of patients treated with this modality have shown reversal of organ dysfunction and a median overall survival of approximately 5 years.<sup>4</sup> However, the major concern is complications associated with the treatment and treatment-related mortality. Appropriate patient selection can decrease the treatment-related adverse events, and ideal candidates are reported to be relatively young patients without renal dysfunction or cardiac dysfunction.<sup>4,15</sup>



**Figure 2.** (A and B) Colonoscopy demonstrating a large amount of adherent blood clots in the descending colon.



**Figure 3.** (A and B) Colonoscopy demonstrating the stricture and ulceration in the transverse colon.



**Figure 4.** (A) Histopathological examination colonic mucosae with ulceration, necrosis, granulation tissue, and fibrinopurulent exudate. (B) Congo red stain of the colon biopsy revealing salmon pink staining in the areas with amyloid deposition.

The prognosis depends on the underlying etiology of amyloid deposition and is usually good for patients with focal amyloidosis, whereas it is poor for patients with systemic disease. AL amyloidosis with GI involvement is typically associated with poor prognosis. A prospective study of 137 patients with AL amyloidosis by Lim et al showed a median survival time of 7.95 months for patients with GI involvement and 15.84 months for those without GI involvement.<sup>16</sup> Patient who presents with GI bleeding, abdominal pain, and diarrhea in the setting of primary amyloidosis should be evaluated for GI involvement. It is crucial to attempt early detection because it is essential to avoid life-threatening amyloidosis-related GI complications such as ischemia or intestinal perforation.<sup>3</sup>

## DISCLOSURES

Author contributions: R. Swaminathan wrote the manuscript and is the article guarantor. S. Igbinedion and S. Pandit edited the manuscript and approved the final version.

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Informed consent was obtained for this case report.

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