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CASE REPORT | COLON

Colonoscopy Leading to the Diagnosis of AL Amyloidosis in the Gastrointestinal Tract Mimicking an Acute Ulcerative Colitis Flare

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ABSTRACT

The 2 most common types of amyloidosis are light chain (AL) and reactive (AA). AL is associated with plasma cell dyscrasias; reactive (AA) is associated with chronic inflammatory conditions. A few cases have described AL amyloidosis mimicking colitis. However, endoscopic findings leading to the diagnosis of AL amyloidosis are rare. We report a 77-year-old woman with a medical history of ulcerative colitis who presented with recurrent nonbloody watery diarrhea. Colonoscopy revealed features suspicious for amyloidosis. Bone marrow biopsy showed multiple myeloma and AL amyloidosis. This case demonstrates the importance of generating a broad differential and the pivotal role of endoscopic findings in diagnosing uncommon diseases.

INTRODUCTION

Amyloidosis is a rare disorder that is caused by the extracellular deposition of abnormal protein fibrils in various organs and tissues. There are 6 types of amyloidosis: primary, secondary, hemodialysis-related, hereditary, senile, and localized.[1] The 2 most common forms of amyloidosis are light chain (AL) amyloidosis and reactive (AA) amyloidosis.[2] AL amyloidosis refers to immunoglobulin light chain deposition commonly associated with plasma cell dyscrasias such as multiple myeloma. AA amyloidosis is associated with amyloid A, an acute phase reactant that deposits in the setting chronic inflammatory states such as rheumatoid arthritis, inflammatory bowel disease (IBD), and chronic infections.[3] A few cases have described AL amyloidosis mimicking an ulcerative colitis (UC) flare-up.[4–6] However, these patients not only had symptoms of UC flare-up but also had symptoms of systemic amyloidosis. Our case is unique in that the patient only had gastrointestinal (GI) symptoms and that colonoscopic findings led to the diagnosis.

CASE REPORT

A 77-year-old white woman with a medical history of UC on adalimumab, azathioprine, mesalamine rectal suspension enema, and prednisone came to the emergency department with a chief complaint of 10–20 episodes of nonbloody watery diarrhea daily for a week. Abdominal and pelvic computed tomography showed colitis of the transverse and descending colon with infectious workup being negative. The intravenous steroid was started with a presumptive diagnosis of acute exacerbation of UC. Her symptoms improved, and she was discharged home with an oral steroid taper regimen.

The patient, however, came back a day later with 14 new episodes of nonbloody diarrhea, abdominal cramping, and nausea. Laboratory tests showed leukocytosis of 15,900/mL and chronic anemia of 9.4 g/dL, but no hypercalcemia and no renal dysfunction were present. Abdominal and pelvic computed tomography with no contrast showed colitis with unchanged multiple thoracolumbar spine compression fracture deformities that were attributed to chronic steroid usage in the past. Colonoscopy was performed to

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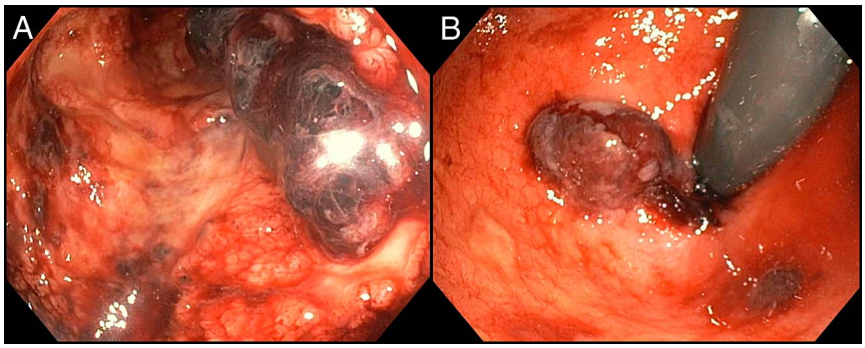

Figure 1. Colonoscopy showing (A) extensive submucosal hemorrhage and (B) purplish blebs in the sigmoid colon.

assess the severity of the disease and exclude infectious etiologies such as *Cytomegalovirus* and *Clostridioides difficile*. A few areas of superficial erosions were found in the terminal ileum. Mild inflammation was found in the transverse colon, descending colon, and rectum. Multiple biopsies were taken from these sites. On withdrawal of the scope, friable mucosa with submucosal hemorrhage and purplish blebs were noted in the distal transverse colon to the rectum (Figure 1). These findings were suspicious for amyloidosis, and further workup was initiated. Serum protein electrophoresis showed total protein of 5.6 g/dL, albumin of 4.08 g/dL, α-1-globulin electrophoresis of 0.20 g/dL, α-2-globulin electrophoresis of 0.45 g/dL, β-globulin electrophoresis of 0.24 g/dL, γ-globulin electrophoresis of 0.62 g/dL, and M-protein serum level of 0.55 g/dL. Immunofixation showed IgG-λ monoclonal gammopathy. The free lambda light chain level was 508 mg/L with κ/λ ratio of $<$0.33. Immunoglobulin levels were IgG of 688 mg/dL, IgA of $<$7 mg/dL, and IgM of $<$19 mg/dL. Biopsies from colonoscopy were positive for amyloidosis (Figure 2). Hematology/oncology was consulted and proceeded with bone marrow biopsy that showed multiple myeloma and AL amyloidosis (Figure 3). Bone marrow showed 30%–40% plasma cells and focal amyloid deposition. Fluorescence in situ hybridization showed *t*(4,14) in 5% of cells. The Durie-Salmon score was IIIa, indicating high cell mass, but without renal involvement. Adalimumab and azathioprine were stopped, and the patient was started on chemotherapy. Once her GI symptoms improved, she was discharged from the hospital. Despite continuing with chemotherapy, the patient continued to have episodes of severe diarrhea and hematochezia that required repeated hospitalizations. Given her poor prognosis, she elected to go on hospice and died approximately 10 months after the diagnosis of AL amyloidosis.

DISCUSSION

Amyloidosis is a rare disorder. One epidemiologic study reported incidence densities of 6.13 per million person-years for AL amyloidosis and 1.21 per million person-years for AA amyloidosis.[7] Depending on the type of amyloidosis, GI tract involvement varies. The GI tract is affected in approximately 60% of patients with AA amyloidosis, but less common in patients with AL amyloidosis, with only 8% of patients.[8,9] AA amyloidosis is typically associated with chronic inflammatory states such as IBD. Among patients with IBD, patients who have Crohn's disease are more predisposed than those who have UC. The incidence of AA amyloidosis in Crohn's disease is approximately 0.9% and 0.07% with UC.[10]

There have been a couple of case reports that describe AL amyloidosis mimicking an UC flare-up. Casad and Bocian described a patient with a medical history of chronic lung fibrosis in the setting of possible UC flare.[4] While attempting to find the etiology of his chronic lung fibrosis, the clinicians were able to diagnose AL amyloidosis. Rahman et al presented a case in which heart failure symptoms led to the discovery of AL amyloidosis in the setting of suspected UC flare.[5] Janczewska et al published a case about a patient with UC

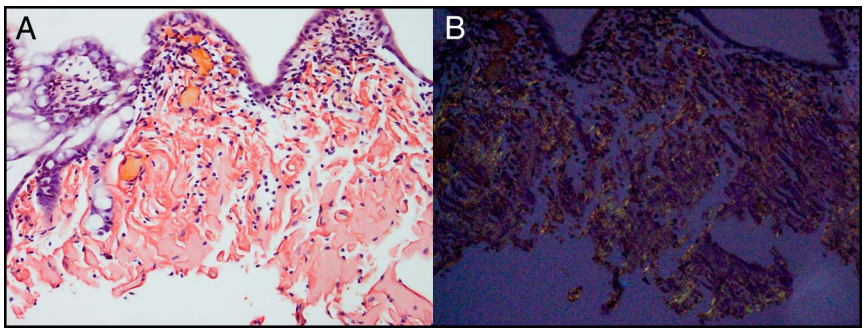

Figure 2. Biopsy of the colon specimen showing (A) amyloid deposits without polarization and (B) apple-green birefringence of amyloid deposits after Congo red staining.

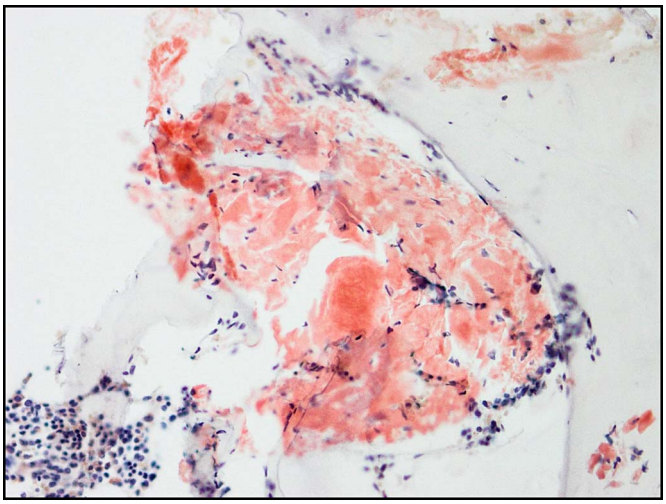

Figure 3. Biopsy of the bone marrow showing amyloid deposits after Congo red staining.

with a history of chest pain and liver function test abnormalities.[6] These symptoms and laboratory anomalies led to an extensive workup, and AL amyloidosis was identified. All of these cases describe patients who had other organ abnormalities that provided clues for the diagnosis of amyloidosis. Our case is unique in that the patient only had GI symptoms and that endoscopic findings played a crucial role in aiding this diagnosis.

For AL amyloidosis, amyloid mainly deposits in the submucosal layer and muscular layer.[11,12] On the other hand, AA amyloidosis deposits more frequently in the lamina propria mucosa and submucosal layer.[11,12] Because of these differences, polypoid protrusions and thickening of valvulae conniventes are more common in AL amyloidosis, whereas fine granular appearance, mucosal friability, and erosions are more common in AA amyloidosis.[12,13] Other colonoscopy findings for AL amyloidosis have been described such as multiple bullous hemorrhagic lesions, submucosal hematomas, and submucosal hemorrhages.[3,14,15] Our patient had friable mucosa with submucosal hemorrhage and purplish blebs. These findings led to the suspicion that the patient may have amyloidosis, and thus, extensive workup was initiated. Although these associations have been reported, the gold standard for diagnosis is tissue biopsy with Congo red stain showing green birefringence under polarized light.

In conclusion, this case emphasizes that endoscopic findings play a vital role in diagnosing rare diseases. Our patient had AL amyloidosis rather than AA amyloidosis, as most would expect, in the setting of UC. Her diagnosis of multiple myeloma was made in an unusual fashion because suspicious findings on colonoscopy prompted a further workup revealing this diagnosis.

DISCLOSURES

Author contributions: BS Lee wrote and revised the manuscript. Y. Chudasama revised the manuscript and is the article guarantor. AI Chen revised the manuscript. BS Lim revised the manuscript and provided the colonoscopy images. MT Taira provided the pathology images.

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Informed consent could not be obtained from the family of the deceased. All identifying information has been removed from this case report to protect patient privacy.

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