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CASE REPORT | ENDOSCOPY

Gastrointestinal Amyloidosis as a Cause of Anemia: Rare and Rarely Considered

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ABSTRACT

Gastrointestinal involvement in amyloidosis is reported in 3% of cases, mostly associated with multiple myeloma. An elderly man with chronic kidney disease presented to the hospital after a large melenic bowel movement. The patient was tachycardic and anemic to 3.8 g/dL on admission and was transfused blood. Endoscopy and colonoscopy were unremarkable. Subsequently, the patient had 2 more admissions for severe anemia requiring blood transfusion. Repeat esophagoduodenoscopy with capsule endoscopy were unremarkable. The patient was diagnosed with monoclonal gammopathy of undetermined significance by hemoglobin electrophoresis, and endoscopy biopsy revealed intestinal amyloidosis in a duodenal specimen. The patient's recurrent anemia was attributed to bleeding from gastrointestinal amyloidosis, in the absence of other identifiable sources of anemia, and was managed with intravenous iron infusions.

KEYWORDS: amyloidosis; gastrointestinal bleeding; anemia; plasma cell dyscrasias; upper endoscopy; capsule endoscopy

INTRODUCTION

Amyloidosis is defined as the deposition of extracellular insoluble fibrils, which can cause a spectrum of clinical presentations based on the organs involved.[1] Common organs involved include the heart, kidney, and adrenal gland.[1] According to prior literature, gastrointestinal (GI) involvement in amyloidosis occurs in 3%, with 79% of these having an underlying systemic amyloidosis.[2] Secondary amyloidosis can occur in plasma cell dyscrasias such as multiple myeloma (MM), smoldering multiple myeloma (SMM), and monoclonal gammopathy of undetermined significance (MGUS). The risk of AA amyloidosis is higher in MM and SMM than in MGUS—78% in SMM as compared with MGUS. Therefore, symptomatic GI primary amyloidosis is a rare entity[3] and even more so in the background of MGUS. We present a case of recurrent anemia and GI bleeding in a chronic kidney disease (CKD) patient with small bowel amyloidosis in the background of MGUS.

CASE DETAILS

An 84-year-old man, with medical history of gastroesophageal reflux disease, coronary artery disease, hyperlipidemia, and CKD (of unknown duration and baseline and based on reduced glomerular filtration rate), presented to the hospital because of a large melenic bowel movement. The patient did not report any recent shortness of breath, chest pain, syncope, orthopnea, extremity numbness or tingling, weight loss, and change in pattern of bowel movements. Home medications included aspirin, amlodipine, atorvastatin, and mirtazapine. On presentation, the patient was tachycardic and normotensive. On examination, the patient was comfortable with a pale conjunctiva. The abdomen was soft and nontender, no hepatosplenomegaly was appreciated on examination, and lower extremity examination did not reveal edema. Digital rectal examination revealed brown stool. No peripheral neuropathy was noted on physical examination.

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Initial investigations revealed normocytic anemia with a hemoglobin of 3.8 g/dL (normal range 13–17 g/dL) and mean corpuscular volume 100 fL (normal range 80–100 fL). The white blood cell and platelet counts, liver function tests, lactate dehydrogenase and haptoglobin, urine protein, and B12 and folate levels were within normal limits.

Computed tomography angiography of the abdomen, pelvis, and chest did not reveal any active bleeding. The patient was transfused with 2 units of packed red blood cells with appropriate improvement of hemoglobin to 7 g/dL and was admitted for further evaluation. Upper endoscopy (EGD) revealed erosive gastroduodenitis as shown in Figure 1, and hence, relevant biopsies were obtained. However, no active bleeding or stigmata of recent bleeding were identified on endoscopy and colonoscopy. Colonoscopy revealed polyps in the descending and sigmoid colon and rectum, which were removed with biopsies revealing tubular adenoma, tubulovillous adenoma, and tubular adenoma, respectively. The patient was discharged with a hemoglobin of 8.8 g/dL after a hospital course of 12 days.

Subsequently, the patient had 2 more admissions (length of stay 6 days and 11 days, respectively) for severe anemia (second admission hemoglobin 5.7 g/dL, discharge hemoglobin 7.2 g/dL; third admission hemoglobin 4.5 g/dL, discharge hemoglobin 8.4 g/dL) requiring blood transfusion. During these admissions, repeat EGD and capsule endoscopy were performed with negative results for the source of active bleeding, although EGD biopsy results revealed intestinal amyloidosis in a duodenal specimen, confirmed by Congo red staining as shown in Figure 2. Stomach biopsy revealed chronic inactive gastritis. Hematology was also consulted for evaluation of anemia, and further workup revealed a reticulocyte percentage of 1.6, absolute reticulocyte count of 0.04 M/μL, and reticulocyte index of 0.9 indicating hypoproliferative marrow response. Peripheral smear was unremarkable. Moreover, serum protein electrophoresis showed 2 low-level monoclonal proteins consistent with MGUS. As per hematology evaluation, the intestinal amyloidosis was AA amyloidosis. Furthermore, as per nephrology evaluation, the progressive CKD was secondary to longstanding diabetes and hypertension. However, the patient did not yet require dialysis.

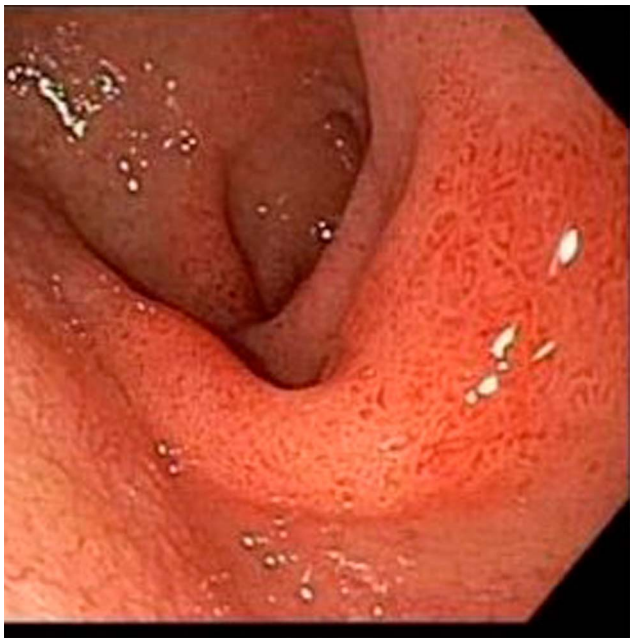

Figure 1. Duodenitis of the D1-D2 junction.

The patient's recurrent severe anemia was attributed to bleeding from GI amyloidosis, in the absence of other identifiable sources of bleeding and was managed with intravenous iron infusions and erythropoietin. Because the patient had frequent hospitalizations for anemia, erythropoietin was used to prevent the contribution of anemia of chronic disease due to CKD.

As per hematology recommendations, the patient needed further outpatient workup to identify the cause of AA amyloidosis. However, the patient has not followed up in clinic since this past admission which was 1 year ago.

DISCUSSION

Amyloidosis can be classified as primary and secondary AL amyloidosis.[4] Primary amyloidosis is attributed to the deposition of immunoglobulin light chains or their components due to plasma cell dyscrasias such as multiple myeloma.[4] Secondary amyloidosis is related to acute-phase reactant serum amyloid A protein, and its etiologic basis includes infection, inflammation, neoplasia, and renal dysfunction.[1] Other forms of amyloidosis include familial amyloidosis secondary to ATTR and hemodialysis-associated amyloidosis secondary to AB2 amyloid.[1]

Amyloid deposition in the bowel and extraintestinal locations, such as the liver, can manifest in various ways—from mild presentations such as altered bowel movement, malabsorption, abdominal discomfort, nausea, early satiety, vomiting and pain, to more severe presentations like GI bleeding.[2–4] Weight loss is noted to be the most frequent presentation of amyloidosis, followed by GI bleeding, which may be overt or obscure.[2] In a case series of 37 cases of GI amyloidosis, the relative frequency of amyloid deposition was 100% in the duodenum, 95% in the stomach, and 91% in the colorectum.[2] Compatible with the above-discussed findings, our patient presented with melena and severe anemia. Interestingly, there were no other, seemingly mild, manifestations of amyloidosis in our patient such as malabsorption or gastric dysmotility, making this case particularly challenging and interesting.

The pathophysiologic mechanisms of GI bleeding from amyloidosis includes small-vessel vulnerability due to amyloid infiltration and dysfunctional hemostasis due to factor X deficiency.[3] The resultant mucosal ischemia and injury lead to a spectrum of endoscopic findings, such as erosions,

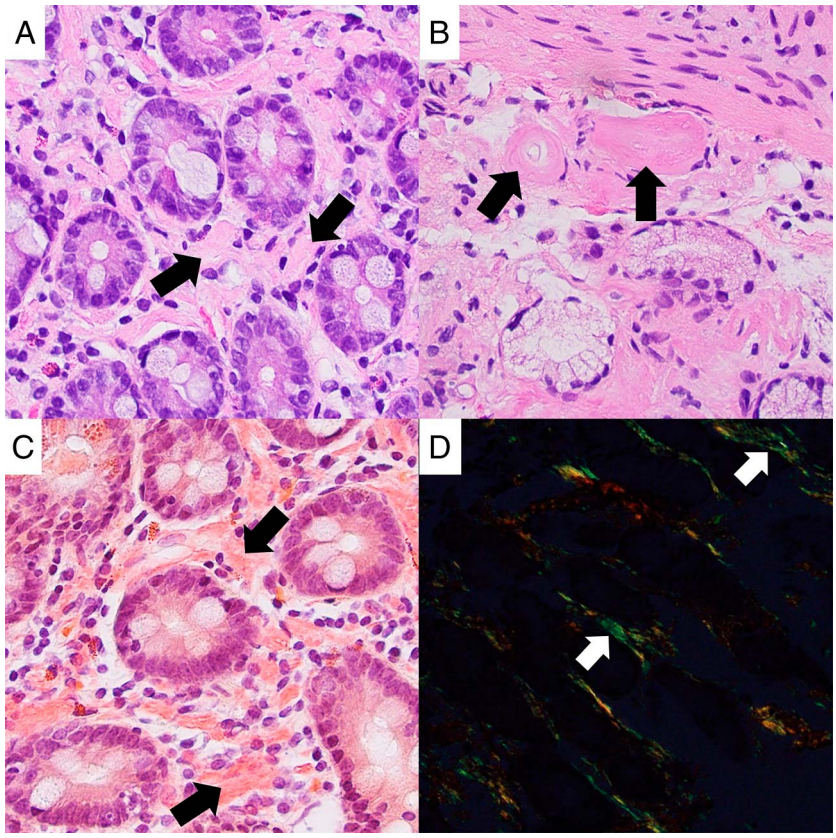

Figure 2. Duodenal biopsy shows glassy pink amorphous material infiltrating the lamina propria between crypts (A, black arrows) and submucosal arteriole walls (B, black arrows). A stain for Congo red highlights this material (C, black arrows), which becomes an apple green color using plane-polarized light (D, white arrows).

ulcerations, polyps, submucosal tumors, altered mucosal folds, plaque-like lesions, and hematomas—the latter seen frequently submucosally in patients presenting with GI bleeding.[2] Furthermore, in a prior study, duodenal biopsy was considered highly sensitive for diagnosing amyloidosis in patients with CKD and associates well with renal amyloidosis.[5] However, the gross endoscopic findings of our patient were unremarkable with no visible signs of bleeding or mass that may have been contributing to the melena on presentation.

Prior data do not outline a specific endoscopic therapy for GI bleeding secondary to amyloidosis and suggests the decision of endoscopic treatment modality be according to the discretion of the endoscopist based on the endoscopic findings and endoscopist's preference.[2] In this case described in the literature,[2] EGD revealed a nonbleeding ulcerated mass that was biopsied. By contrast, our case did not reveal any prominent mass, erosion, ulcer, or adherent clot in the upper GI tract, and the lower GI tract revealed polyps in the sigmoid colon, which were removed. In both cases, however, no hemostatic measures were performed endoscopically, and after the procedure, the patient was observed on an intravenous proton pump inhibitor.

It is important to note that prior research has suggested suspicion of GI amyloidosis in the presence of GI bleeding and visible masses, as well as in case of known plasma cell dyscrasias and obscure GI bleeding.[2] However, in our case, the patient had multiple episodes of melena and anemia without any endoscopic findings to explain the blood loss, and small intestinal source of GI blood loss was also ruled out on capsule endoscopy. It was the endoscopic finding of amyloid deposition in the duodenal biopsy that led to the workup for plasma cell dyscrasias and eventual diagnosis of MGUS. Furthermore, in MGUS, we do not expect the clinical findings seen in MM such as anemia, hypercalcemia, and renal dysfunction; however, our case did reveal anemia and CKD, which had multiple contributors.

Therefore, in patients with unexplained anemia and obscure GI bleeding, a high index of suspicion should be kept for GI amyloidosis despite the absence of classical endoscopic findings of masses, erosions, or ulcerations, as evident in our patient. While a major limitation was lack of further workup due to no post-discharge follow-up, our case exhibits several lessons. We also want to emphasize that clinicians should be aware of anchoring bias in patients with CKD presenting with anemia. While anemia of chronic disease and GI angioectasias are common causes of anemia in patients with CKD, the differential diagnosis should be broad in the beginning and workup for less common causes, including GI amyloidosis, should be undertaken after common causes are appropriately ruled out.

DISCLOSURES

Author contributions: N. Sharma and SM Baqir: study idea, data collection, manuscript writing and review. A. Basnet, K, Tiwari, and A. Sharma: manuscript writing and review. T. Chokshi and M. Pittman: data collection, manuscript review. B. Weindorf and S. Lapin: study idea, manuscript review. S. Lapin is the article guarantor.

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Ethical approval and consent to participate: We confirm that the protocol of the research has been approved by the Ethics Review Committee of the institution within which the work was undertaken, and it is in accordance with the relevant guidelines and regulations laid down by the Declaration of Helsinki. This article does not contain any studies with human participants performed by any of the authors. Approval was taken from the Ethics Review Committee prior to the study and was performed according to the standards laid out.

Previous presentation: This case was presented as a poster presentation at the NYACP Conference 2023; May 12, 2023; Albany, New York.

Informed consent was obtained for this case report.

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