Multiple Myeloma Presenting as Chronic Diarrhea

Arouj Bajwa, MD1, Judy Trieu, MD, MPH2, Kamran Mirza, MD, PhD3, Xianzhong Ding, MD3, and Brian Liem, DO2

1Department of Internal Medicine, Loyola University Medical Center, Maywood, IL
2Division of Gastroenterology and Nutrition, Loyola University Medical Center, Maywood, IL
3Department of Pathology, Loyola University Medical Center, Maywood, IL

ABSTRACT

Extramedullary gastrointestinal tract involvement in plasma cell dyscrasias is rare and represents a diagnostic challenge. We present a 66-year-old man with an unusual presentation of multiple myeloma. He presented with chronic diarrhea, and extensive biopsies in the jejunum allowed for the presumptive diagnosis of multiple myeloma to be made and the weighted decision to treat without a definitive diagnosis. Plasma cell dyscrasias can have highly varied presentations, unclear differentiation, and require a multidisciplinary approach for diagnosis and management. Adequate tissue sampling of the small bowel is critical in assessing patients with chronic diarrhea.

INTRODUCTION

Multiple myeloma (MM) is a neoplastic plasma cell disorder that represents approximately 10% of all hematological malignancies. It is characterized by uncontrolled clonal proliferation of malignant plasma cells in the bone marrow. Common presentations include anemia, renal failure, hypercalcemia, increased susceptibility to infection, and bone pain. Gastrointestinal (GI) tract involvement in MM is rare and may represent a diagnostic challenge. The most commonly reported sites in the GI tract are the small intestine, stomach, and colon. Reported cases of GI manifestations include GI bleeding, abdominal pain, diarrhea, or bowel obstruction. These are usually a result of deposition of clonal plasma cells or accumulation of monoclonal immunoglobulins or its fragments causing mucosal injury. In this report, we discuss a case of MM initially presenting as chronic diarrhea and diagnosed with endoscopic small intestinal biopsies.

CASE REPORT

A 66-year-old man presented with chronic diarrhea for 6 months. Despite having a good appetite, he lost 60 pounds of weight. He endorsed night sweats and low-grade fevers. Six months ago, he was diagnosed with Clostridium difficile infection, received multiple antibiotic treatments for refractory infection, and underwent fecal microbiota transplant. He continued to have diarrhea despite repeat testing being negative for an infectious etiology. He had a medical history of stroke and migraines. Home medication included aspirin.

During his initial visit with a gastroenterologist, vital signs were within normal limits and physical examination was unremarkable. Laboratory investigation revealed normocytic anemia with hemoglobin 11.9 g/dL, white blood cell count 4.1 K/μL, platelets 236 K/μL, creatinine 0.8 mg/dL, serum total protein 6.1 g/dL, albumin 2.3 g/dL, and calcium 7.9 mg/dL. Viral stool panel and C. difficile toxin were both negative. An abdominal and pelvic contrast-enhanced computed tomography scan showed diffuse thickening of the small bowel, most prominent in the jejunum. Initial esophagogastroduodenoscopy performed at an outside institution described localized hypertrophic villi in the duodenal bulb and duodenum; the colon was normal (Figure 1). Duodenal biopsy showed diffuse lymphangiectasia-containing eosinophilic material with positive periodic acid–Schiff stain, negative Congo red stain, and foamy macrophages in the lamina propria, suggesting Waldenstrom macroglobulinemia (WM).
He established with our institution for further evaluation. He underwent an extensive hematologic workup, revealing high serum immunoglobulin M (IgM) (1,740 mg/dL), IgM kappa monoclonal paraproteinemia on serum protein electrophoresis and immunofixation, and increased serum-free light chains, with an elevated kappa to lambda ratio of 3:19. Bone marrow biopsy was remarkable for 35% plasma cells, with immunohistochemistry revealing it to be kappa light chain–restricted (Figure 2). A workup for amyloid including Congo red stains of bone marrow smear, fat pad biopsy, and small and large intestine biopsies was negative. MYD88 mutation was not identified, and the initial concern for WM was ruled out. A bone survey was performed and was negative for malignant skeletal involvement.

Although the patient had 35% bone marrow monoclonal plasma cells, suggesting MM, he lacked end-organ damage commonly seen with MM, such as hypercalcemia, renal insufficiency, significant anemia, or bony lesions. To evaluate whether MM was primarily manifesting only in the GI tract, he underwent an enteroscopy and colonoscopy with ileoscopy; extensive biopsies were collected. The visualized duodenal, jejunal, and ileal mucosa were diffusely and severely congested, flattened, and inflamed. The colonoscopy and associated biopsies were normal. Only the jejunal biopsies revealed macroimmunoglobulin deposition and polytypic kappa and lambda light chains by staining (Figure 3). Additional testing, including B-cell clonality analysis by polymerase chain reaction, did not detect any clonal B-cell population.

Although he only technically met criteria for smoldering myeloma, owing to the severity of his symptoms and deposition of light chains and IgM, a multidisciplinary team of gastroenterology, hematology, and pathology specialists decided to treat him for MM because clinical suspicion for transformation without meeting strict criteria for MM was high. He was started on chemotherapy with lenalidomide and bortezomib. He completed 8 cycles with resolution of his diarrhea. Given his presumed diagnosis of symptomatic MM, he underwent successful autologous hematopoietic cell transplantation and continues to be asymptomatic.

DISCUSSION

GI involvement of MM is extremely rare and only reported in the literature as case reports. Mechanisms by which MM can affect the GI tract are direct infiltration, amyloidosis, plasmacytoma, or hypercalcemia (inducing pancreatitis). The organs most commonly involved are small bowel, followed by stomach, colon, and esophagus. On imaging, GI lesions related to MM can appear as a large mass or bowel wall thickening, as seen in our patient. Tissue biopsy is needed to confirm diagnosis because imaging findings are nonspecific and can resemble primary GI malignancies.

Direct infiltration of the GI tract by MM is rare. Talamo et al reported biopsy-proven monoclonal MM cells in the GI tract in only 24 of 2,584 patients (0.9%) with MM diagnosed at the Myeloma Institute for Research and Therapy. Although our patient’s jejunal biopsies did not show evidence of clonality of plasma cells, there was evidence of macroimmunoglobulin
chronic diarrhea and symptoms of malabsorption. Delay in accurate diagnosis may result in end-organ damage, complications, and increased mortality.

DISCLOSURES

Author contributions: A. Bajwa wrote the manuscript and is the article guarantor. J. Trieu and B. Liem edited the manuscript. K. Mirza and X. Ding provided the pathology slide images and expert opinion.

Financial disclosure: None to report.

Previous presentation: This case was presented at the American College of Gastroenterology Annual Scientific Meeting; October 23–28, 2020; Virtual.

Informed consent was obtained for this case report.

Received November 18, 2020; Accepted April 29, 2021

REFERENCES

1. Rajkumar SV. Multiple myeloma: Every year a new standard? Hematological Oncol. 2019;37(1):62–5.
2. Kwak HS, Jin GY, Lee JM. Radiologic findings of multiple myeloma with gastric involvement: A case report. Korean J Radiol. 2002;3(2):133–5.
3. Tathineni P, Cancarevic I, Malik BH. Uncommon presentations of multiple myeloma. Cureus. 2020;12(6):e8400.
4. Talamo G, Cavallo F, Zangari M, et al. Clinical and biological features of multiple myeloma involving the gastrointestinal system. Haematologica. 2006;91(7):964–7.
5. Harris M, Burton IE, Scarffe JH. Macroglobulinemia and intestinal lymphangiectasia.5,6 This diffuse intestinal lymphangiectasia has been associated with protein-losing enteropathy and malabsorption in several reports.5,6

In the presence of a known plasma cell neoplasm, unexplained GI symptoms could be a result of coexisting amyloidosis.7 Over 10% of patients with MM have concomitant amyloidosis.8 Any region of the GI tract can be involved with amyloid infiltration, resulting in diarrhea, malabsorption, bleeding, or obstruction.7,9 Another way MM can present is GI plasmacytoma, a tumor histologically identical to monoclonal plasma cells. Symptoms depend on the organ involved, but reports include obstruction, diarrhea, and abdominal pain.10,11 GI infections may also occur in patients with MM because of compromised immune systems, which may explain our patient’s initial recurrent C. difficile infection.12 Other plasma cell dyscrasias, such as WM, amyloid light-chain amyloidosis, light chain deposition disease, and heavy chain deposition disease, can also have GI involvement.

Plasma cell dyscrasias can have highly varied GI presentations, unclear differentiations, and require a multidisciplinary approach for diagnosis and management. Adequate tissue sampling of the small bowel was critical in assessing our patient with deposition, which likely contributed to his clinical presentation. Case reports have highlighted the role of macroglobulin deposition, typically seen with WM, in causing increased interstitial viscosity and thus the development of secondary lymphangiectasia.5,6

Figure 3. Hematoxylin and eosiin–stained section of jejunal biopsies with polypoid outpouching of pale, acellular, eosinophilic material (black stars). This material stained positive for both kappa and lambda by immunohistochemical stains. The underlying plasma cells were polytypic. The material stained positive for periodic acid–Schiff stain and was negative for amyloid (by Congo red staining).

Copyright: © 2021 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of The American College of Gastroenterology. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.