



A Case of Multiple Myeloma with Extremely Rare Manifestation

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Abstract

Introduction: Multiple myeloma (MM) is a neoplastic proliferation of immunoglobulin-producing plasma cells that have multiple presentations due to the infiltration of plasma cells in the bone marrow and other organs. Common manifestations include anemia, bone pain, fatigue, and hypercalcemia. MM presented with rectorrhagia is very rare.

Case Presentation: A 74-year-old woman with a history of rectorrhagia episodes from about nine months ago presented with severe anemia, weakness, and lethargy. The findings of endoscopy and colonoscopy did not justify the patient's manifestation, and finally, due to thrombocytopenia and anemia, a bone marrow biopsy was performed, and multiple myeloma was diagnosed.

Conclusions: Although GI bleeding in Multiple myeloma is a very rare manifestation, this diagnosis must be considered in the differential diagnosis of patients with unexplained and refractory GI bleeding.

Keywords: Plasmacytoma, Multiple Myeloma, Rectorrhagia, Gastrointestinal

1. Introduction

Multiple myeloma is a neoplastic proliferation of immunoglobulin-producing plasma cells. Anemia, renal failure, skeletal destruction, recurrent infections, and hypercalcemia are the most common features of the disease. Clinicopathological studies demonstrated that clinically apparent extraosseous manifestations were present in less than 5% of patients with MM. The liver, spleen, and lymph nodes were the most frequent sites of occurrence in approximately two-thirds of these patients, while the central nervous system, kidney, skin, pleura, lung, testes, pancreas, thyroid, adrenal glands, and omental involvement also had been revealed (1). Involvement of the GI system, particularly demonstrated with GI hemorrhage, in the course of MM is extremely rare (2).

Gastrointestinal (GI) bleeding usually originates from peptic ulcers, acute gastric mucosal lesions, esophageal varices second to hepatic cirrhosis, and primary digestive system neoplasms. However, some potent asymptomatic diseases of the blood system manifesting as GI hemorrhage may be clinically ignored. The incidence of gastrointestinal bleeding has been reported in 10–30% of patients with neoplastic diseases of the hematopoietic organ (3). The pathogenesis of gastrointestinal bleeding in these diseases is usually multifactorial and may be caused by direct malignant hematopoietic cell infiltrations, mucosal

changes ensuing from bone marrow suppression, immunodeficiency states, infections due to various organisms, or preceding peptic ulcers (4-6).

In the present study, we report a 74-year-old female who initially demonstrated GI bleeding and was finally diagnosed with MM. Further laboratory examinations supported this diagnosis, including analysis of globulin in the blood and 73% of plasmacytosis in the bone marrow. This case may promote the possible involvement of plasma cell myeloma in the differential diagnosis of patients with unexplained and refractory GI bleeding.

The presented case is important in terms of two aspects. Once, no lesions were detected in the examination of the patient's femoral head, hip, and humerus, while the bone marrow analysis showed a high plasma cell percentage. Second, we describe a case that was finally diagnosed with MM but was initially manifested as gastrointestinal hemorrhage.

According to our data, this clinical manifestation is the first MM case regarding sex and the highest percentage of plasmacytosis and GI bleeding worldwide.

2. Case Presentation

A 74-year-old woman with a history of hypertension and Bell's palsy since near a month ago, and several rec-

torrhagia events since about nine months ago, the latest of which occurred about a month ago, presented with severe anemia, weakness, and lethargy. Due to the non-improvement of rectorage and worsening of anemia despite receiving packed cells on an outpatient basis and not going to the doctor for further examination, she was hospitalized with severe weakness and lethargy.

The patient's weakness and lethargy started about two weeks ago and increased progressively. Vital signs were stable at admission; pale conjunctiva, facial asymmetry due to Bell's palsy, and a soft abdomen without tenderness, rebound, or guarding were detected in the patient's examination.

During these nine months, the patient underwent several packed cell transfusions as well as colonoscopy and upper GI endoscopy, with the latter showing only some evidence of hiatal hernia and the former, small internal hemorrhoid, two polypoid lesions and patchy mucosal erythema that were biopsied. The specimen showed a chronic inflammation pattern with no ulcer, cryptic abscess, cryptitis, dysplasia, or granuloma. Given the patient's clinical condition, mesalazine suppository and folic acid were prescribed daily for a short period, and she was recommended to return one month later. Unfortunately, the patient obstinately extended the medication and avoided returning to the GI clinic.

The laboratory results were as follows: pancytopenia with Hb, 2.5 g/dL (12 - 16 g/dL); Hct:8.4 (37 - 47%); Mcv:89.4 (80 - 95); RBC, $0.94 \times 10^6/\text{mm}^3$

($4 - 5.5 \times 10^6/\text{mm}^3$); WBC = $3.5 \times 10^3/\text{mm}^3$ ($4 - 11 \times 10^3/\text{mm}^3$); platelet (plt), $72 \times 10^3/\text{mm}^3$ ($150 - 350 \times 10^3/\text{mm}^3$); erythrocyte sedimentation rate (ESR) (118 mm/h (10 - 20 mm/h)); and serum total protein, 11 gr/dL (6.6 - 8.7 gr/dL), albumin, 2.1 g/dL (3.5 - 5.4 g/dL); globulin, 8.8 g/dL (2 - 4 g/dL); lactate dehydrogenase (LDH), electrolytes, glucose, fat and renal function tests were all normal. Prothrombin Time (PT), 17 sec (12-15 sec); international normalized ratio (INR), 1.6 (0.9 - 1.1); partial thromboplastin time (PTT), 43 sec (35 - 45 sec). The patient's peripheral blood smear also confirmed CBC disorder (pancytopenia). According to the hematology consultation, BMB & BMA were recommended, and she was transferred to the hematology ward. In the bone marrow aspirate, 73% of plasma cells were identified.

In the hematology ward, X-rays of the skull, hip, femur, humerus, and chest revealed no clear lytic or sclerotic lesions. The patient was recommended to take MRI, a radionuclide scan, and a bone scan and do serum protein electrophoresis and serum Beta 2 microglobulin. Still, unfortunately, she did not perform these tests.

Thalidomide tablets were prescribed daily for the treatment of the patient. Besides, six units of packed cells were

transfused. She was discharged with an improvement in her general condition. No recurrence of GI bleeding was reported. A recommendation for monthly visits to the hematology clinic was done, and daily thalidomide tablets were prescribed.

At the patient's follow-up after discharge, hemoglobin and platelets reached 9.1 gr/dL and $157,000/\text{mm}^3$, respectively. No recurrence of GI bleeding was detected, the patient did not report weakness and lethargy, and her clinical findings indicated a good response to treatment.

3. Discussion

MM is the second most prevalent hematologic malignancy and accounts for about 2% of cancer-related mortality (7). Although it usually involves BM, extramedullary involvement of the disease can occur in about 20% of cases. The upper respiratory tract, including the oropharynx, nasopharynx, nose cavities, sinuses, and larynx, is the most common site of extramedullary involvement (7, 8). MM cases with GI manifestations are rare. Some symptoms include nausea, vomiting, and colic, which totally occur in 20% of cases; bleeding from the gums or nose is rare.

Gastrointestinal bleeding (GIB) has been detected in 10 - 30% of patients with hematologic neoplastic diseases, one of which is MM (2, 9).

MM causes GI bleeding through several pathways: direct plasma cell infiltrations in the form of plasmacytomas, amyloid infiltration of the gut wall resulting in increased capillary fragility, platelet or coagulation abnormalities, and preceding peptic ulcers may sometimes be secondary to treatment with anti-inflammatory medications and corticosteroids (2).

Abnormal hemostasis, specifically the imbalance in the function of all major components of the coagulation cascade, may increase the risk of bleeding in patients with MM. DiMinno et al. (4) suggest that bleeding occurring in dysproteinemia may result from a specific interaction of monoclonal paraproteins with platelets. Saif et al. (5) consider that patients with MM may develop bleeding diathesis secondary to various mechanisms. One such mechanism is the direct inhibition of fibrin monomer aggregation due to the paraprotein, prolonging the thrombin and reptilase time.

The likely mechanism of rectorrhagia in our patient was colitis and coagulopathy caused by the M component and failure of antibody-coated platelets function.

Daram et al. (10) reported a case of a 53-year-old woman who presented with acute GIB as hematemesis and underwent treatment with stem cell transplantation. Chang et al. (11) introduced a MM case presented with nausea, vomiting, and massive hematochezia. Maza et al. reported a

rare case of rectal bleeding and anemia with polypoid and ulcerative colonic lesions (12). In the case presented here, the patient presented with the initial manifestations of recurrent rectorrhagia and anemia, and MM treatment was done. According to histological and laboratory findings, she was treated with thalidomide and responded well to treatment.

The disease often occurs in 50 - 80 years of age and is more common in men than women. Plasmacytosis > 30%, which is one of the main criteria for MM diagnosis, was more than 70% in our case, which was an elderly woman.

The symptoms mentioned so far for this disease are bone pain, hypercalcemia, weight loss, fatigue, diarrhea, anemia, etc., of which hypercalcemia, anemia, and weight loss were present in our case. Although bone pain is present in 68% of cases, this symptom was absent in our case. Despite the high prevalence of bone lesions in these patients, there were no such findings on the patient's CT and MRI of the head, humerus, and hip area. The absence of common features of MM further complicated the diagnosis. Rectorrhagia was the most important manifestation of the disease, and MM was suspected because of no bleeding lesions reported in upper GI endoscopy and colonoscopy, while severe pancytopenia and anemia were detected in labs. The BMA reported 73% plasma cell infiltration, which was a significant finding compared to 20 - 50% infiltration in previous studies (2).

3.1. Conclusions

MM is a systemic disease that may present rarely with lower GI bleeding. GI hemorrhage, especially when associated with pancytopenia, may be related to certain hematopoietic neoplasms, particularly myeloma, and these patients should be examined accordingly by bone marrow analysis and serum protein electrophoresis. Furthermore, early diagnosis of this disease has the advantages of improved life quality, decreased morbidity and cost of care of this disease, identifying preceding peptic ulcers and other lesions in the GI tract, as well as providing prophylactic steps to the GI mucosa, which is vulnerable to hemorrhage with further chemotherapy.

Footnotes

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References

- Kapadia SB. Multiple myeloma: a clinicopathologic study of 62 consecutively autopsied cases. *Medicine (Baltimore)*. 1980;59(5):380-92. [PubMed ID: 7432154].
- Lin M, Zhu J, Shen H, Huang J. Gastrointestinal bleeding as an initial manifestation in asymptomatic multiple myeloma: A case report and review of the literature. *Oncol Lett*. 2013;5(1):218-20. [PubMed ID: 23255923]. [PubMed Central ID: PMC3525485]. <https://doi.org/10.3892/ol.2012.945>.
- Kyle RA, Rajkumar SV. Multiple myeloma. *N Engl J Med*. 2004;351(18):1860-73. [PubMed ID: 15509819]. <https://doi.org/10.1056/NEJMra041875>.
- DiMinno G, Coraggio F, Cerbone AM, Capitanio AM, Manzo C, Spina M, et al. A myeloma paraprotein with specificity for platelet glycoprotein IIIa in a patient with a fatal bleeding disorder. *J Clin Invest*. 1986;77(1):157-64. [PubMed ID: 2935559]. [PubMed Central ID: PMC423321]. <https://doi.org/10.1172/JCI112270>.
- Saif MW, Allegra CJ, Greenberg B. Bleeding diathesis in multiple myeloma. *J Hematother Stem Cell Res*. 2001;10(5):657-60. [PubMed ID: 11672511]. <https://doi.org/10.1089/152581601753193869>.
- Pinto LS, Campagnoli EB, Leon JE, Lopes MA, Jorge J. Maxillary lesion presenting as a first sign of multiple myeloma: case report. *Med Oral Patol Oral Cir Bucal*. 2007;12(5):E344-7. [PubMed ID: 17767095].
- Cherpanath TG, Nieuwdorp M, Hazenberg MD, van Eeden S, van der Sluijs AF. Large nocturnal eyes causing gastrointestinal bleeding in asymptomatic multiple myeloma. CMV enterocolitis. *Neth J Med*. 2010;68(10):324-7. [PubMed ID: 21071781].
- Dolin S, Dewar JP. Extramedullary plasmacytoma. *Am J Pathol*. 1956;32(1):83-103. [PubMed ID: 13275567]. [PubMed Central ID: PMC1942586].
- Talamo G, Cavallo F, Zangari M, Barlogie B, Lee CK, Pineda-Roman M, et al. Clinical and biological features of multiple myeloma involving the gastrointestinal system. *Haematologica*. 2006;91(7):964-7. [PubMed ID: 16818286].
- Daram SR, Paine ER, Swingley AF. Upper gastrointestinal bleeding in a patient with multiple myeloma. *Gastroenterology*. 2012;142(2):e8-9. [PubMed ID: 22197163]. <https://doi.org/10.1053/j.gastro.2011.02.069>.
- Chang SS, Lu CL, Tsay SH, Chang FY, Lee SD. Amyloidosis-induced gastrointestinal bleeding in a patient with multiple myeloma. *J Clin Gastroenterol*. 2001;32(2):161-3. [PubMed ID: 11205655]. <https://doi.org/10.1097/00004836-200102000-00015>.
- Maza I, Vlodayky E, Eliakim RA. Rectal bleeding as a presenting symptom of AL amyloidosis and multiple myeloma. *World J Gastrointest Endosc*. 2010;2(1):44-6. [PubMed ID: 21160679]. [PubMed Central ID: PMC2999078]. <https://doi.org/10.4253/wjge.v2.i1.44>.