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Case Report

Unconventional Presentation of Multiple Myeloma: A Case Study

Anum Abbas, Urwa Rasool

Bahawal Victoria Hospital Bahawalpur

Abstract

Multiple myeloma (MM) is a hematologic malignancy characterized by the clonal proliferation of plasma cells within the bone marrow, often presenting with classic symptoms such as bone pain, anemia, hypercalcemia, renal dysfunction, and recurrent infections. As the second most common blood cancer, it represents about 1% of all cancer cases, contributes to 2% of cancer-related deaths, and comprises 12–15% of oncological and hematological disorders. . Renal failure is a significant concern for multiple myeloma patients, often stemming from tubulointerstitial pathology caused by high levels of circulating monoclonal immunoglobulin free light chains. These proteins can induce kidney problems including proximal tubule cell toxicity, tubulointerstitial nephritis, and myeloma kidney (cast nephropathy). Less frequently, elevated free light chains may lead to conditions like immunoglobulin light chain amyloidosis and light chain deposition disease, which typically exhibit a slow progression of renal failure rather than acute injury. early diagnosis and appropriate treatment is crucial. This case presents an unusual presentation of multiple myeloma, resulting in a delay in both diagnosis and treatment initiation. It is crucial for clinicians to persist in reporting unusual presentations of multiple myeloma and to view it as a potential diagnosis in patients exhibiting serious and uncommon symptoms.

Keywords: multiple myeloma, myeloma cast nephropathy, immunoglobulin light chains, hypercalcemia, smoldering multiple myeloma

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Corresponding Author: Dr. Anum Abbas, **Email:** anumabbas687@gmail.com

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Introduction

Multiple myeloma (MM) is a blood cancer characterized by the abnormal proliferation of plasma cells in the bone marrow. It is impacted by gender, race/ethnicity, and age, showing a higher occurrence among older individuals.[1,2] The disease is more prevalent in men compared to women.[3] As the second most common blood cancer, it represents about 1% of all cancer cases, contributes to 2% of cancer-related deaths, and comprises 12–15% of oncological and hematological disorders[2]. A retrospective analysis of 1027 patients diagnosed with MM at a single institution revealed the following symptoms and signs at presentation: anemia (73%), bone pain (58%), elevated creatinine (48%), fatigue/general weakness (32%), hypercalcemia (28%), and weight loss (24%, with half of them losing ≥9 kg). Symptoms and signs present in 5% or fewer of patients included paresthesias (5%), hepatomegaly (4%), splenomegaly (1%), lymphadenopathy (1%), and fever (0.7%).[4] In a significant French study involving 1038 patients with MM, approximately 25% met the renal impairment criterion set by the 2014 International Myeloma Working Group (IMWG), defined as serum creatinine >2 mg/dL or estimated glomerular filtration rate (eGFR) <40 mL/min/1.73 m^2. Among these patients, 12.9% required dialysis. Other studies have reported dialysis dependence in 6–8% of MM patients throughout the clinical course of the disease.[5]

The revised IMWG criteria delineate three myeloma-defining events (MDEs): (1) clonal bone marrow plasma cells ≥60%, (2) abnormal serum free light chain (sFLC) ratio ≥100 (involved kappa) or <0.01 (involved lambda), and (3) one or more focal lesions >5 mm on MRI scans. The presence of any one of these markers is sufficient for a diagnosis of MM, regardless of symptoms or CRAB features[6]. Serum free light chain (FLC) concentrations are indicative of the likelihood of developing acute kidney injury (AKI) and its subsequent recovery. AKI is uncommon when serum FLC concentration is below 50 mg/dL but becomes significantly more likely when the concentration exceeds 80–200 mg/dL[5]. Kidney biopsy is the gold standard for distinguishing between

light chain cast nephropathy (LCCN), monoclonal gammopathy of renal significance (MGRS) lesions, and other unrelated causes of acute kidney injury (AKI).[7]

Multiple myeloma is a complex disease with diverse clinical presentations. Smoldering multiple myeloma (SMM) is characterized by the existence of a serum monoclonal (M) protein level equal to or exceeding 3 g/dL and/or clonal bone marrow plasma cells (BMPCs) ranging from 10% to 60%, without any indication of end-organ damage (referred to as CRAB criteria) or other manifestations of multiple myeloma-related disorders.[8] The American National Cancer Data Base (NCDB) study shed light on the incidence of SMM, estimating it to be 0.9 cases per 100,000 individuals, a figure similar to that reported by a European study, which stated 0.4 cases per 100,000 persons,[9] whereas multiple myeloma affects 7 out of every 100,000 people.[9]

Case Report

A 52-year-old female, a housewife with a history of hypertension for the past 5 years (with poor compliance), presented to us in October 2023 with complaints of fever, nausea, vomiting, decrease urine output, and generalized body weakness over the last 3 months. Additionally, she reported joint pains in the small joints of her hands ,wrist and feet for the past 2 years, for which she frequently took NSAIDs. There were no other systemic symptoms reported. On examination, her blood pressure was 120/90 mmHg, pulse rate was 68 beats per minute, temperature was normal, and respiratory rate was 16 breaths per minute, rest of systemic examination was normal. On investigation her hemoglobin level was 5.5 g/dl, TLC 5900/microliters, platelet 138k, sr calcium 8.9mg/dl(corrected), serum phosphorous level 5.4mg/dl,serum albumin 3.0g/dl, sr creatinine 14.4 mg/dl, urea 219 mg/dl, urine complete examination showed protein 3+, RBC nill, pus cell 8-10, anti HCV negative, HbsAg negative ,HIV negative, 24 hour urinary protien 7.28g, ultrasound showed bilateral normal size kidneys with intact corticomedullary differentiation.

Due to her symptoms, hemodialysis was initiated, and she received a transfusion of 4 units of blood. On further workup her iPTH was 81.5pg/ml(normal range:15-68), serum CK 127u/l(normal range:29-168), serum anti-CCP o.9u/ml(normal range:<5), ANA negative, ENA Quantrix negative .

She became anuric and dialysis dependant. Consequently, an ultrasound-guided renal biopsy was performed to determine the diagnosis. Surprisingly, the renal biopsy revealed tubulointerstitial nephritis with hard casts in the tubular lumina, suggestive of myeloma cast nephropathy.

She was prescribed prednisolone at a dosage of 1mg/kg/day. Additionally, whole-body X-rays, serum protein electrophoresis, serum lambda light chains, serum kappa light chains, and a bone marrow biopsy were conducted. The X-rays showed no lytic lesions, while the serum protein electrophoresis indicated hypoproteinemia and hypoalbuminemia, no monoclonal band is seen, gamma globulin are also reduced [total protein 5g/dl (normal range:6-8.5) ,albumin 3.2g/dl(normal range: 3.5-4.7), gamma globulins 0.4g/dl(normal range:0.7-1.5)], serum lambda light chain 18.29mg/dl(normal range:62-231), serum kappa light chain 76.76mg/dl (normal range:122-437). Bone marrow biopsy report was suggestive of multiple myeloma.

Chemotherapy was started promptly after the diagnosis with oral dexamethasone 40mg twice weekly, injection bortezomib 1.3mg/m*2 weekly which was changed to tab thalidomide(after each hemodialysis) after 5 doses due to side effects of bortezomib. Despite chemotherapy, she remained dependent on dialysis and exhibited no improvement in serum creatinine levels. Therefore, she was discharged on regular hemodialysis and referred to a hematologist for further management of multiple myeloma. However, she continues to undergo regular outpatient follow-up and is stable on hemodialysis.

Discussion

Multiple myeloma (MM) is a blood cancer characterized by the abnormal growth of plasma cells in the bone marrow, often accompanied by symptoms like bone pain, anemia, hypercalcemia, renal dysfunction, and recurrent infections.[10] In contrast, smoldering multiple myeloma (SMM) lacks these defining symptoms[10]. Diagnosis relies on clinical presentation and specific laboratory features.[10] Here, we present a case of a 48-year-old female with clinical and laboratory features resembling SMM, yet she developed acute renal failure, later diagnosed through renal histopathology as myeloma cast nephropathy. Despite chemotherapy, her renal function did not improve. On review of literature, we have found that the incidence of smoldering multiple myeloma is 0.9 out of every 100,000 individuals, whereas multiple myeloma affects 7 out of every 100,000 people.[9] A study was conducted at Mayo Clinic, Rochester, MN, between 2013 and 2022, using the 2018 Mayo 20/2/20 criteria for risk assessment, which included 406 SMM patients.[10] Median follow-up was 3.9 years. Among untreated high-risk patients (n=71), 51 progressed, showing bone lesions (37%), anemia (35%), hypercalcemia (8%), and renal failure (6%). Additionally, 24% met MM criteria based on marrow plasmacytosis (≥60%) and/or free light chain ratio (>100), while 45% had clinically significant manifestations (hypercalcemia, renal insufficiency, and/or bone lesions).[10] The lack of typical clinical history and laboratory features in our

patient, such as hypercalcemia, bony lytic lesions, and elevated serum free light chains, along with the unexpected diagnosis of myeloma cast nephropathy upon renal biopsy, accentuate the challenge leading to delayed diagnosis and treatment of MM, particularly when the disease is in an early phase and classical markers may appear within normal ranges.[10] This discussion highlights the difficulties encountered in diagnosing atypical manifestations of MM, emphasizes the significance of renal involvement as a presenting feature, and underscores the implications for management and prognosis.[10]

Conclusion

This case report emphasize the significance of adopting a comprehensive diagnostic approach and considering multiple myeloma (MM) in patients with atypical clinical features. This approach enables early detection and intervention. A thorough diagnostic assessment is crucial for confirming the diagnosis and guiding suitable treatment strategies. Identifying unusual presentations of MM is essential for enhancing diagnostic accuracy and ultimately enhancing patient outcomes through timely intervention. This case report raises questions: Why did renal failure manifest in an early stage of multiple myeloma, and why did chemotherapy not lead to improvement? Is the current treatment approach satisfactory for such cases?

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Authors' Contribution

AA: Conception.

AA, UR: Design of the work.

UR: Data acquisition, analysis, or interpretation.

AA: Draft the work.

AA, UR: Review critically for important intellectual content.

All authors approve the version to be published.

All authors agree to be accountable for all aspects of the work.

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