

Diagnostic Challenges in Multiple Myeloma: A Case of Recurrent Acute Kidney Injury, Hypercalcemia, and Anemia

Klejda ÇOLLAKU

CORRESPONDING AUTHOR

Email: Klejda.collaku@yahoo.com

NEPHROLOGIST, KAMËZ COMMUNITY HEALTH
AND SOCIAL CARE CENTER, ALBANIA

Erjola LIKAJ

DEPARTMENT OF NEPHROLOGY, DIALYSIS AND TRANSPLANTATION
UNIVERSITY HOSPITAL CENTER "MOTHER TERESA", TIRANA, ALBANIA

Polikron PULLUQI

DEPARTMENT OF HEMATOLOGY,
UNIVERSITY HOSPITAL CENTER "MOTHER TERESA", TIRANA, ALBANIA

Adela PEROLLA

DEPARTMENT OF HEMATOLOGY
UNIVERSITY HOSPITAL CENTER "MOTHER TERESA", TIRANA, ALBANIA

Abstract

Multiple myeloma (MM) is a hematologic malignancy with heterogeneous clinical presentations, often delaying diagnosis [1,3,4]. Renal impairment is one of its most frequent and severe complications, primarily due to light-chain cast nephropathy,

hypercalcemia-induced nephropathy, or nephrotoxic exposures [2,5,10]. We present a case of recurrent acute kidney injury (AKI), episodic hypercalcemia, progressive anemia, and disproportionately elevated inflammatory markers, including hyperferritinemia and markedly elevated D-dimer (>10,000 ng/mL), which initially suggested alternative etiologies such as infection, thromboinflammation, or macrophage activation, but may also reflect tumor activity [9,11]. Serial clinical deterioration ultimately led to a bone marrow aspirate confirming MM [8,13]. This case underscores the diagnostic challenges of MM when renal involvement and inflammatory dysregulation dominate the early clinical picture [6,12]. It highlights the importance of timely hematologic evaluation, repeated assessment of monoclonal components, and early suspicion of myeloma kidney in patients with unexplained recurrent renal dysfunction [2,5,10].

Introduction

Multiple myeloma represents approximately 10% of hematologic malignancies and is characterized by clonal proliferation of plasma cells producing monoclonal immunoglobulin or free light chains [1,3,4]. Classical CRAB criteria—hyperCalcemia, Renal failure, Anemia, and Bone lesions—remain central to diagnosis; however, these features may evolve progressively, sometimes over months or years [1,3,4,15]. Delayed diagnosis is particularly likely when renal involvement presents before overt hematologic abnormalities, or when inflammatory markers mimic infectious or autoimmune disease [2,9,11].

Renal impairment occurs in 20–50% of MM patients at presentation and is an independent predictor of mortality [2,5,10]. Cast nephropathy is the most characteristic renal lesion, resulting from intratubular precipitation of monoclonal free light chains with Tamm-Horsfall proteins [5,10]. However, the clinical picture is often confounded by dehydration, medications (NSAIDs, ACE inhibitors, contrast), infections, and metabolic abnormalities [2,9].

This case report describes a patient with recurrent AKI, hypercalcemia, severe fluctuations in inflammatory markers—including ferritin >1000 ng/mL and D-dimer values persistently above 10,000 ng/mL—with delayed diagnosis of a hematologic malignancy [9,11]. The case illustrates how atypical laboratory patterns may overshadow the classical MM presentation and emphasizes the need for a high index of suspicion [6,12,13].

Case Presentation

Clinical Course Overview

Between July 2024 and June 2025, the patient experienced multiple distinct episodes of AKI, with creatinine peaks ranging 1.14–6.21 mg/dL and urea ranging 33.4–115.1 mg/dL. Renal function frequently improved after hydration and empiric therapy, only to deteriorate again within weeks. Early episodes were attributed to dehydration, infection, or subclinical sepsis due to elevated inflammatory markers.

The patient also developed progressive normocytic anemia, intermittent hypercalcemia, and constitutional symptoms including severe headache, hypotension, nausea, fatigue, anorexia, and mild bone discomfort, which were initially non-specific.

Patient History

A 65-year-old woman with type 2 diabetes mellitus (on insulin glargine), hypertension (lercanidipine, carvedilol, furosemide), and dyslipidemia (atorvastatin) presented in July 2024 with severe headache, hypotension, oliguria, nausea, and vomiting. She had no prior chronic kidney disease and was not on calcium or vitamin D supplementation.

Initial Hospitalization (20–30 July 2024)

Initial laboratory evaluation revealed severe acute kidney injury (AKI) with creatinine 6.21 mg/dL and urea 115.1 mg/dL, accompanied by anemia (Hgb 7.6 g/dL; RBC $2.23 \times 10^6/\mu\text{L}$). Supportive management with intravenous fluids and blood transfusion resulted in substantial renal recovery at discharge (creatinine 1.14 mg/dL; urea 33.4 mg/dL).

A non-contrast CT scan demonstrated preserved renal morphology, mild bilateral pleural and pericardial effusions, hepatic steatosis, and mild ascites.

Second Major Hospitalization (5–20 Nov 2024)

The patient was rehospitalized for dyspnea and CT-confirmed basal pleuropneumonia. She exhibited severe anemia requiring transfusion, markedly elevated inflammatory markers (including D-dimer $>10,000$ ng/mL), and progressive renal impairment. Imaging demonstrated osteolytic bone involvement, including

a compression fracture at T12 and lucent lesions at L1. During this interval, she developed hypercalcemia and significant proteinuria (3424 mg/24h) with Bence Jones protein positivity and the first appearance of a monoclonal spike, accompanied by worsening renal indices (creatinine 4.33 mg/dL, urea 96.9 mg/dL). Although supportive management led to partial renal improvement, the post-discharge period remained marked by clinical instability, characterized by recurrent episodes of acute kidney injury, persistent anemia, intermittent hypercalcemia, and progressive biochemical abnormalities.

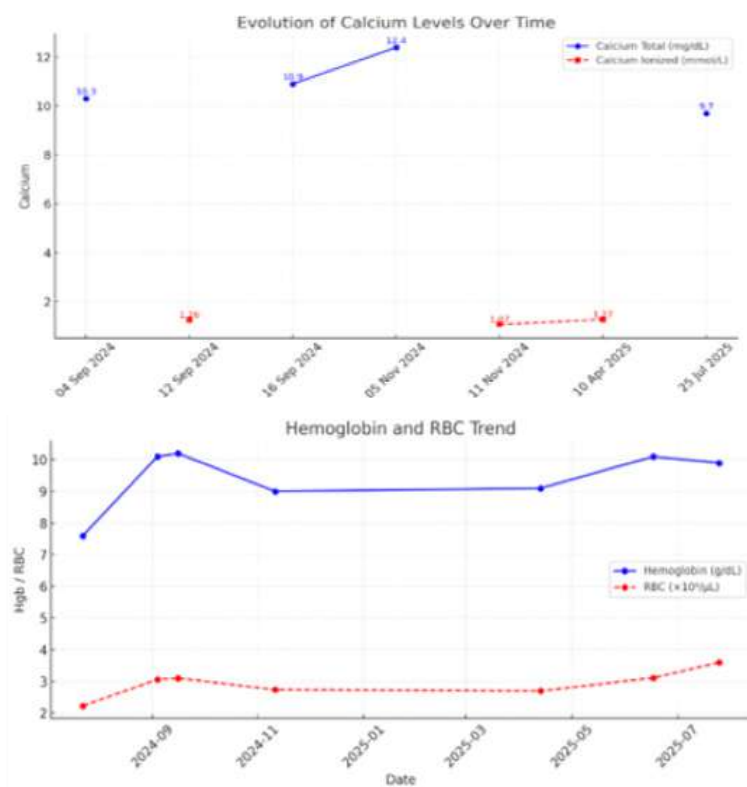
Definitive Diagnosis (May 2025)

Delayed hematologic evaluation revealed early multiple myeloma. Bone marrow aspiration demonstrated 17% plasma cells, elevated monoclonal components (MC, MM, S, M, MBP), and dyspoiesis. MRI confirmed marrow involvement consistent with monoclonal gammopathy.

Key Laboratory Data

FIGURE 1. Laboratory trends over time in a patient with suspected multiple myeloma.





(A) Serum creatinine levels demonstrating recurrent episodes of acute kidney injury (AKI). (B) Serum urea levels illustrating the same recurrent AKI episodes. (C) Total and ionized calcium levels over time, highlighting episodes of hypercalcemia coinciding with AKI recurrence. (D) Hemoglobin and red blood cell (RBC) counts showing trends of anemia across multiple hospitalizations and follow-up.

TABLE 1. Trends of Inflammatory and Coagulation Markers During the Clinical Course.

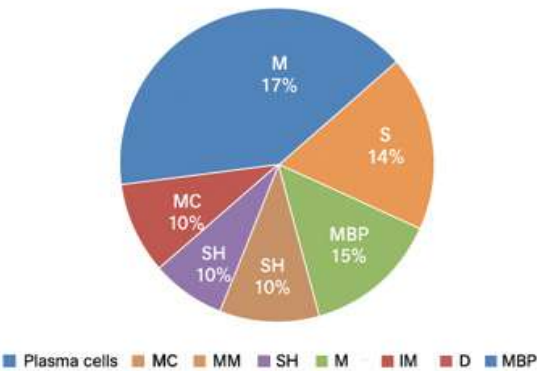
Date	Ferritin (ng/mL)	D-dimer (ng/mL)	Interpretation
13 sept 2024	870.97	9407.0	AKI
8 Nov 2024	1076.9	2500.2	Hyperferritinemia
11 Nov 2024	923	>10,000	AKI recurrence
3 May 2025	3000	3759.7	Hyperferritinemia,AKI
17 Jun 2025	786	>10,000	New AKI episode

This table illustrates the persistent and disproportionate elevation of ferritin and D-dimer levels, including marked hyperferritinemia and D-dimer values exceeding 10,000 ng/mL, which contributed to diagnostic uncertainty by suggesting alternative etiologies such as infection or thromboinflammatory states. These abnormalities were later recognized as part of the systemic inflammatory response associated with underlying multiple myeloma.

Bone Marrow Evaluation

A bone marrow aspirate performed in May 2025 revealed an increased plasma cell population (>10%) with monoclonal morphology, findings that were consistent with and supportive of a diagnosis of multiple myeloma.

FIGURE 2. Bone marrow composition (May 2, 2025).



Percentage distribution of marrow elements highlighting plasma cell predominance, supporting the diagnosis of multiple myeloma.

Imaging

CT Scan – July 2024

Preserved renal morphology without evidence of obstruction, with mild pleural effusion and small-volume ascites. Small lytic lesions were identified on this initial CT scan, indicative of early bone involvement.

Skull X-ray (Rogafi Crani) – November 2024

Small, well-defined rounded lucencies are observed in the cranial bones, suggestive of osteolytic lesions and consistent with early myeloma-related bone involvement.

Spine X-ray -November 2024

Imaging demonstrates a compression fracture at T12, with additional small lucencies at L1, suggestive of early osteolytic involvement related to multiple myeloma.

FIGURE 3. X-ray (November 2024)



(A) Skull X-ray showing small osteolytic lesions in the cranial bones. (B) Spine imaging demonstrating a compression fracture at T12 and small lucencies at L1.

Discussion

This case highlights the diagnostic challenges of MM presenting with recurrent AKI, episodic hypercalcemia, and evolving anemia [1,2,3,4]. The patient experienced multiple AKI episodes over 12 months, characterized by rapid rises in creatinine, partial recoveries, and recurrences without clear external triggers [2,5,9]. This pattern is typical of cast nephropathy, where free light chains intermittently overwhelm tubular reabsorption thresholds [5,10]. Minor insults, including volume shifts, infections, or NSAID exposure, may precipitate acute declines [2,9]. Early testing for serum free light chains could have facilitated a timelier diagnosis [8,15].

Extremely elevated inflammatory markers, including ferritin (>1000 ng/mL) and D-dimer ($>10,000$ ng/mL), initially suggested sepsis, macrophage activation syndrome, or thromboinflammation [9,11]. In MM, these elevations can result from high tumor burden, cytokine overexpression, impaired renal clearance, or endothelial activation [10,15]. This emphasizes that atypical inflammatory patterns do not exclude MM and may contribute to diagnostic delays [2,9,11].

Hypercalcemia and anemia emerged sequentially, with episodic hypercalcemia contributing to renal vasoconstriction and tubular injury, and anemia gradually fulfilling CRAB criteria [1,3,4,15]. Repeated negative infectious or inflammatory workups illustrate a common real-world pitfall, where hematologic disease is considered only after prolonged evaluation [6,12].

Bone marrow evaluation ultimately confirmed plasma cell dyscrasia [8,13]. Earlier hematology referral, particularly after the second or third AKI episode, might have mitigated renal decline [2,5,10]. Timely initiation of disease-specific therapy correlates with better renal recovery [2,5,10].

Conclusions

This case highlights that MM can present with a misleading pattern of recurrent AKI, episodic hypercalcemia, and anemia, even in the absence of classic skeletal lesions [1,2,3,4]. Disproportionate inflammatory markers, such as elevated ferritin or D-dimer, may further complicate the diagnostic pathway [9,11]. Clinicians should maintain a high index of suspicion for MM in patients with:

- Unexplained or recurrent AKI [2,5,10]
- Partial renal recovery followed by relapse [2,5,9]
- Anemia or hypercalcemia, even if initially mild [1,3,4,15]
- Disproportionate inflammatory marker elevations [9,11]

Early evaluation with serum free light chain analysis, SPEP/UPEP, and prompt hematology referral are essential [8,15]. Supportive care can temporarily maintain renal function, but definitive disease-specific treatment is required to control progression [2,5,10]. Addressing barriers to timely diagnostic evaluation, including patient reluctance, and providing counseling are critical to prevent irreversible organ damage [6,12,13].

Informed Consent

Written informed consent was obtained from the patient for the publication of this case report and any accompanying clinical data and images.

Conflict of Interest

The authors declare no conflict of interest.

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