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From Macrocytic Anemia to Fulminant Multiple Myeloma: A Case of Rapid Progression with Cast Nephropathy and Septic Shock

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Abstract: ***Multiple myeloma can be difficult to recognize early because patients may initially present with vague symptoms and nonspecific laboratory abnormalities. We present the case of a 61-year-old male who was initially evaluated for progressive fatigue and macrocytic anemia despite normal iron, vitamin B12, and folate levels, along with an unrevealing gastrointestinal workup. Over the following months, he developed persistent anemia, rising total protein and globulin levels, and worsening weakness. Further evaluation revealed acute kidney injury, marked hyperproteinemia, rouleaux formation, and monoclonal protein, leading to the diagnosis of IgG lambda multiple myeloma with cast nephropathy. Despite transfer to a tertiary care center, initiation of dialysis, and treatment with bortezomib and dexamethasone, his course was complicated by pneumonia, septic shock, respiratory failure, and ultimately death. This case emphasizes the importance of maintaining clinical suspicion for plasma cell dyscrasia in patients with unexplained anemia and elevated serum protein levels. Earlier recognition and diagnostic testing may allow for timely intervention before progression to renal failure and other life-threatening complications.***

Keywords: multiple myeloma, cast nephropathy, acute kidney injury, monoclonal gammopathy, serum protein electrophoresis, anemia, delayed diagnosis

1. Introduction

Multiple myeloma is a plasma cell malignancy characterized by clonal proliferation of monoclonal immunoglobulin-producing cells in the bone marrow [1,2]. It commonly presents with the classic CRAB features of hypercalcemia, renal dysfunction, anemia, and bone lesions [1,3]. While the disease is often described as slow-growing, its initial manifestations are frequently subtle and nonspecific, which can contribute to delayed diagnosis [1,4].

Initial laboratory abnormalities, such as unexplained anemia or elevated total serum protein, may represent the earliest findings of multiple myeloma but are often overlooked [4,5]. Because these abnormalities may be nonspecific, diagnosis can be delayed until more advanced manifestations occur, including renal failure due to light chain cast nephropathy [6].

We present a case of IgG lambda multiple myeloma in which unexplained macrocytic anemia with normal vitamin B12 and folate levels, along with persistent hyperproteinemia and hyperglobulinemia, preceded rapid progression to cast nephropathy. The patient ultimately developed dialysis-dependent renal failure and fatal infectious complications. This case highlights the importance of recognizing these early laboratory abnormalities as potential clues to plasma cell dyscrasia and obtaining timely diagnostic testing, including SPEP, UPEP, and serum free light chains.

2. Case Presentation

A 61-year-old male presented with progressive fatigue and anemia. His past medical history was significant for Becker muscular dystrophy, dilated cardiomyopathy status post pacemaker placement, prior saddle pulmonary embolism on chronic anticoagulation with apixaban, and chronic prednisone use.

In April 2025, the patient was found to have a new-onset macrocytic anemia with a hemoglobin (Hgb) of 10.7 g/dL (decreased from 13 g/dL the prior year) and a mean corpuscular volume (MCV) of 102.8 fL. He denied significant gastrointestinal bleeding, though he reported occasional minimal bright red blood per rectum. Initial evaluation included iron studies, vitamin B12, and folate levels, which were all within normal limits. Esophagogastroduodenoscopy and colonoscopy were unremarkable.

Over the following months, the patient continued to experience persistent fatigue and progressive weakness. Laboratory abnormalities persisted, including elevated total serum protein (10.2–10.5 g/dL) with increased globulin levels (up to 7.2 g/dL). In September 2025, he developed worsening dizziness, tremor, and generalized weakness. This prompted further outpatient evaluation. Given the constellation of anemia and elevated protein levels, serum protein electrophoresis (SPEP) was ordered. Laboratory studies obtained in the outpatient setting demonstrated a significant decline in kidney function, with an estimated GFR of 33 from a prior baseline of 111 earlier that year. Additionally, the patient reported a persistent metallic taste in his mouth, which may be attributable to uremia in the setting of renal dysfunction (BUN increased to 55 mg/dL from a baseline of 14). Given this acute change, the patient was contacted and advised to present to the local emergency department for further evaluation and management.

Shortly thereafter, the patient presented to the emergency department on September 24, 2025, for worsening weakness and was found to have acute kidney injury (creatinine 2.7 mg/dL from a baseline of 0.5–0.6 mg/dL and GFR 26 from a baseline 111), worsening anemia (Hgb 7.5 g/dL), and marked hyperproteinemia (total protein 12.1 g/dL, globulin 9 g/dL). He was admitted for further evaluation. Workup included SPEP, urine protein electrophoresis (UPEP), serum free light chains, and peripheral smear, which demonstrated rouleaux formation, raising concern for plasma cell dyscrasia.

Hematology consultation was obtained, and there was high suspicion for multiple myeloma, given the combination of anemia, renal dysfunction, and hyperproteinemia. The patient's clinical course worsened during hospitalization with declining Hgb (nadir 6.7 g/dL) requiring transfusion and persistent renal dysfunction.

Due to the need for specialized care, the patient was transferred to a tertiary care center, where further evaluation confirmed a diagnosis of IgG lambda multiple myeloma, International Staging System (ISS) stage III, with cast nephropathy. Bone marrow biopsy demonstrated 72% monoclonal plasma cells. The patient required initiation of dialysis for renal failure. He was initiated on treatment with bortezomib and dexamethasone, with plans for multi-agent therapy including daratumumab and lenalidomide.

On October 6, 2025, the patient presented to the emergency department with rib pain, cough, and weakness. Imaging demonstrated right lower lobe pneumonia (Figure 1). Laboratory evaluation showed stable anemia (Hgb 8.9 g/dL) and persistent renal dysfunction. He was discharged with outpatient antibiotic therapy. The following day, he returned with worsening shortness of breath, hypotension, and signs of sepsis. Laboratory evaluation revealed markedly elevated procalcitonin (109 ng/mL) and rising lactate levels. He was admitted to the intensive care unit for septic shock requiring vasopressor support. His condition rapidly deteriorated, with worsening metabolic acidosis (pH 7.18) and respiratory failure requiring intubation. Shortly after intubation, he developed pulseless electrical activity arrest. Despite aggressive resuscitative efforts, including multiple rounds of advanced cardiac life support, the patient expired on October 7, 2025.

Table 1: Clinical Timeline and Diagnostic Progression of IgG Lambda Multiple Myeloma

Date	Symptoms	Labs	Diagnostics	Clinical Actions
Pre-2025	Baseline Becker MD, cardiomyopathy, PE	Hgb: 14.9, 15.3, low Cr (0.5-0.6) Total protein: 9.3 (10/2024) Globulin: 5 (10/2024)	–	On prednisone, apixaban
April 2025	Fatigue, anemia	Hgb 10.7 (from 13), MCV 102.8 Total Protein: 10.5 Globulin: 7.2 Calcium: 9.4 GFR: 114	–	GI workup ordered
Mid-2025	Persistent anemia	B12/folate normal, iron normal	EGD/colonoscopy negative	No clear cause identified
July 2025	Ongoing fatigue	Anemia persists Cr: 0.6 Hgb: 10.8 Total Protein: 10.2	–	Monitoring
Sept 2025 (clinic)	Dizziness, tremor, fatigue	Increased total protein Calcium: 9.3 GFR: 33	–	SPEP ordered
Sept 24, 2025	Weakness, AKI	Hgb: 7.5, Cr: 2.7, Total Protein: 12.1, Globulin: 9, Gamma globulin: 5 Calcium: 9.6 GFR: 26	SPEP/UPEP, demonstrating monoclonal protein; peripheral smear with rouleaux formation	Admitted
Sept 25, 2025	Worsening anemia	Decreased Hgb (6.7) → transfused (recheck Hgb = 8) Cr: 2.3 Total Protein: 11.3 Globulin: 8.2 Calcium: 9.2 GFR: 32	Light chains pending	Hematology consult
Late Sept 2025	Renal failure	Hgb: 8.1; Cr elevated; persistent hyperproteinemia; IgG: 6846; Beta-2-microglobulin >41; albumin 3.0	SPEP: M-spike (gamma region); UPEP: monoclonal protein; FLC: lambda 7493 mg/L, K/L <0/.01; Bone marrow biopsy: 72% monoclonal lambda plasma cells	Diagnosis: IgG lambda multiple myeloma (ISS III); transfer to tertiary center; initiated chemotherapy (bortezomib + dexamethasone)
Oct 6, 2025	Rib pain, cough	Cr: 2.3 Total Protein: 9.2 Globulin: 6.3 Hgb: 8.9 Calcium: 8.0 GFR: 57	CT: pneumonia	Discharged on antibiotics
Oct 7, 2025	SOB, hypotension	Increased lactate; Procalcitonin: 109, Cr: 2.7 Total Protein: 7.8 Hgb: 9.3 Calcium: 6.7	–	ICU admission

		GFR: 32		
Oct 7, 2025	Septic shock	Severe acidosis (pH 7.18)	CXR: bilateral airspace opacities consistent with ARDS	Intubation, vasopressors → expired

a) **Abbreviations:** Hgb, hemoglobin; Cr, creatinine; GFR, glomerular filtration rate; SPEP, serum protein electrophoresis; UPEP, urine protein electrophoresis; FLC, free light chains; K/L, kappa/lambda ratio; IgG, immunoglobulin G; ARDS, acute respiratory distress syndrome; ICU, intensive care unit.
b) **Reference ranges:** Hgb 12–16 g/dL; Cr 0.6–1.3 mg/dL; GFR > or = 60 mL/min/1.73 m^2; total protein 6.1–8.1 g/dL; globulin 2.0–3.5 g/dL; IgG 600–1540 mg/dL; K/L ratio 0.26–1.65.

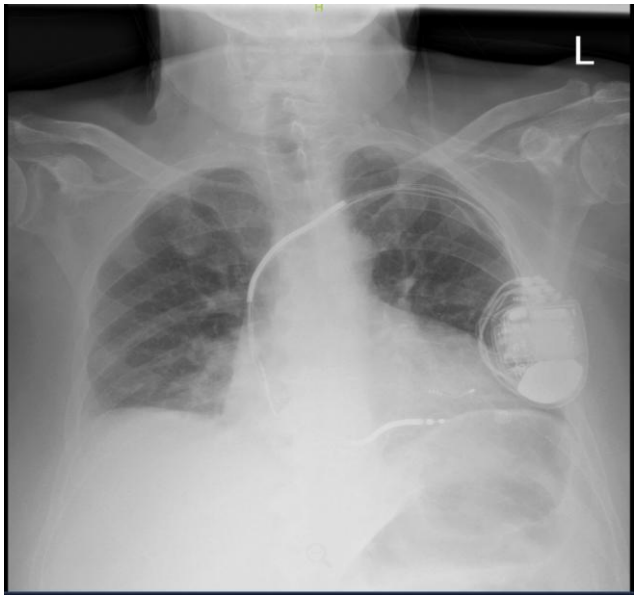

Figure 1: Chest Radiograph Demonstrating Bilateral Airspace Opacities. Portable AP chest radiograph demonstrating low lung volumes with bilateral, patchy airspace opacities in the mid-to-lower lung zones. A left-sided cardiac device with transvenous leads is present. Findings are suggestive of non-cardiogenic pulmonary edema in the appropriate clinical context.

3. Discussion

Multiple myeloma is a plasma cell malignancy that often presents with nonspecific symptoms such as fatigue and anemia, which can delay diagnosis if early laboratory abnormalities are not recognized [1,3]. In this case, the patient initially demonstrated nonspecific but clinically significant findings, including macrocytic anemia without vitamin deficiency and elevated total serum protein. Both findings are recognized but frequently overlooked indicators of plasma cell dyscrasia. The educational value of this case lies in the combination of early, nonspecific abnormalities that were present before the development of renal failure, particularly macrocytic anemia without nutritional deficiency and persistent hyperglobulinemia.

Unexplained macrocytic anemia in the absence of vitamin B12 or folate deficiency should prompt further evaluation, as it may reflect underlying bone marrow pathology. Similarly, elevated total protein and globulin levels are important diagnostic clues warranting investigation for monoclonal gammopathy. Despite these findings, early abnormalities are often attributed to more common or benign etiologies, contributing to delays in diagnosis. Early use of serum protein electrophoresis (SPEP) is critical in such cases, as it allows for timely identification of monoclonal protein and earlier diagnosis of multiple myeloma [4,5].

As the disease progressed, this patient developed acute kidney injury secondary to light chain cast nephropathy, a well-recognized complication of multiple myeloma. Cast nephropathy results from the overproduction of monoclonal free light chains, which interact with the Tamm-Horsfall protein in the renal tubules, leading to tubular obstruction, inflammation, and rapid decline in renal function. This process can result in severe and sometimes irreversible renal failure if not promptly recognized and treated [6]. An additional notable feature in this case was the patient's report of a persistent metallic taste in his mouth. This likely represents an early manifestation of uremia in the setting of declining renal function. Uremic symptoms are known to include alterations in taste perception, likely related to the accumulation of metabolic toxins and changes in salivary composition seen in advanced kidney disease [7]. Although often underrecognized, this symptom may serve as a subtle clinical indicator of worsening renal impairment and should prompt further evaluation when presenting along with abnormal laboratory findings. According to the International Myeloma Working Group criteria, the presence of end-organ damage, such as renal failure, represents a myeloma-defining event and distinguishes active multiple myeloma from smoldering disease [3].

The patient's rapid clinical decline following diagnosis highlights the aggressive nature that multiple myeloma can exhibit, particularly in cases with high tumor burden. Bone marrow biopsy in this case demonstrated 72% monoclonal plasma cells, consistent with advanced disease and poor prognosis. Multiple myeloma is a heterogeneous disease, and patients with higher disease burden or advanced staging, such as International Staging System (ISS) stage III, are at increased risk for rapid progression and adverse outcomes [8].

In addition to disease burden, this patient had multiple risk factors for severe infection, including chronic corticosteroid use for the treatment of Becker muscular dystrophy and initiation of chemotherapy. Patients with multiple myeloma are inherently immunocompromised due to impaired humoral immunity, and treatment with corticosteroids and proteasome inhibitors further increases susceptibility to infection. Population-based studies demonstrate that patients with multiple myeloma have an approximately fivefold increased risk of infection compared to the general population, with the highest risk occurring within the first year after diagnosis [9]. Pneumonia and sepsis are among the most common infectious complications and represent major contributors to mortality in this population [9].

This case highlights how quickly clinical deterioration can occur when multiple high-risk features converge, including delayed diagnosis, high tumor burden, renal involvement, and

immunosuppression. Although multiple myeloma is often considered a chronic and progressive disease, some patients may present with, or rapidly develop, aggressive disease requiring urgent recognition and intervention.

Ultimately, this case highlights the importance of early recognition of subtle laboratory abnormalities. Unexplained macrocytic anemia and elevated serum protein levels should prompt evaluation for plasma cell dyscrasia, including early use of SPEP, to facilitate timely diagnosis and potentially prevent disease progression and associated complications.

4. Conclusion

Multiple myeloma may initially present with nonspecific symptoms and subtle laboratory abnormalities, including unexplained anemia and elevated serum protein or globulin levels. This case highlights the importance of maintaining clinical suspicion for plasma cell dyscrasia and obtaining timely diagnostic testing, such as SPEP, UPEP, and serum free light chains, before progression to renal failure and infectious complications.

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