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Multiple Myeloma with Light-Chain Amyloidosis Involving Heart, Kidneys, and Nerves: A Challenging Case Report

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Abstract: ***Introduction*:** Light-chain (AL) amyloidosis secondary to multiple myeloma (MM) is a rare but fatal condition requiring early diagnosis. We present a complex case of MM-associated AL amyloidosis with cardiac, renal, and gastrointestinal involvement, complicated by a history of medullary thyroid carcinoma. ***Case Presentation*:** A 60-year-old Bangladeshi male with hypothyroidism (post-thyroidectomy for medullary carcinoma) and peptic ulcer disease presented with bilateral leg edema, frothy urine, fatigue, and 8 kg weight loss over 2 months. Examination revealed moderate anemia, pitting edema, and hypoalbuminemia (3.15 g/dL) with nephrotic-range proteinuria (6.75 g/day). Laboratory studies showed monoclonal IgG lambda protein (kappa/lambda ratio: 0.22), elevated NT-proBNP (3900 pg/mL), and bone marrow plasmacytosis (25–30%). Renal biopsy confirmed amyloidosis with lambda-dominant deposits; echocardiography demonstrated restrictive cardiomyopathy. ***Diagnosis*:** Systemic AL amyloidosis with MM, involving the kidneys (nephrotic syndrome), heart (restrictive cardiomyopathy), and likely gastrointestinal tract (chronic constipation, weight loss). ***Interventions*:** Supportive care (diuretics, PPI, thyroxine) was initiated. Chemotherapy for MM/AL amyloidosis was planned but delayed due to the patient's deteriorating clinical status. *Outcomes*: The case highlights the rapid progression of multisystem amyloidosis, emphasizing the need for early suspicion in patients with nephrotic syndrome, monoclonal gammopathy, and cardiac dysfunction. ***Conclusion*:** This case underscores the diagnostic complexity of MM-associated AL amyloidosis, particularly with concurrent malignancies (medullary thyroid carcinoma). A high index of suspicion, timely organ biopsies, and multidisciplinary management are critical to improving outcomes.

Keywords: AL amyloidosis, Multiple myeloma, Medullary thyroid carcinoma, Nephrotic syndrome, Restrictive cardiomyopathy.

Case Report

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INTRODUCTION

Systemic amyloidosis is a group of disorders characterized by extracellular deposition of misfolded proteins as insoluble fibrils, leading to progressive organ dysfunction [1]. Immunoglobulin light-chain (AL) amyloidosis, the most common systemic form, occurs when clonal plasma cells produce amyloidogenic light chains (κ or λ) that aggregate in tissues [2, 3]. Approximately 10–15% of multiple myeloma (MM) patients develop AL amyloidosis, which confers a worse prognosis due to multi-organ involvement [4, 5]. The heart, kidneys, and peripheral nerves are frequently affected, with cardiac amyloidosis being the leading cause of mortality [6]. AL amyloidosis often presents diagnostic challenges due to its nonspecific early symptoms (e.g., fatigue, weight loss) and overlap with other conditions like chronic kidney disease or heart failure [7]. Renal involvement typically manifests as proteinuria or nephrotic syndrome, as seen in this case, while cardiac amyloidosis may present with restrictive cardiomyopathy or elevated biomarkers (NT-proBNP, troponin) without overt symptoms [8, 9]. Gastrointestinal deposition, though less common, can

cause chronic constipation, malabsorption, or bleeding [10]. The diagnosis hinges on histologic confirmation of amyloid deposits (Congo red staining with apple-green birefringence) coupled with evidence of monoclonal plasma cell dyscrasia [11]. The association between AL amyloidosis and MM is well-documented, with λ light chains (particularly IgG λ) constituting ~75% of cases [12]. Patients often exhibit elevated serum free light chains (FLC) and an abnormal κ/λ ratio (<0.26 or >1.65) [13]. Bone marrow biopsy may reveal plasmacytosis, though clonality can be patchy, necessitating repeat sampling [14]. Renal biopsy remains the gold standard for diagnosing amyloid nephropathy, with electron microscopy revealing fibrils of 9–12 nm diameter [15]. Cardiac involvement, present in 50–70% of AL amyloidosis cases, correlates with poor survival (median 6 months if untreated) [16]. Echocardiographic findings like increased ventricular wall thickness, granular sparkling, and apical sparing strain patterns are suggestive, but cardiac MRI or scintigraphy (e.g., 99mTc-DPD) may improve detection [17, 18]. Elevated NT-proBNP (>1,800 pg/mL) and troponin are prognostic markers incorporated into staging systems [19]. Concurrent malignancies in AL amyloidosis are rare but notable. Medullary thyroid carcinoma (MTC), as in this patient, shares a propensity for amyloid deposition due to calcitonin fibrils, though these are distinct from AL-type deposits [20]. The coexistence of MTC and MM-associated AL amyloidosis raises questions about shared pathogenic mechanisms, such as chronic inflammation or genetic predisposition [21]. Early diagnosis and intervention are critical. Treatment focuses on suppressing clonal plasma cells with chemotherapy (e.g., bortezomib, daratumumab) or stem cell transplantation, alongside organ-specific support [22]. However, outcomes remain poor in advanced disease, underscoring the need for heightened clinical suspicion in high-risk patients [23].

CASE PRESENTATION

Patient Information

A 60-year-old Bangladeshi male with a history of total thyroidectomy (June 2024) for medullary thyroid carcinoma (MTC), hypothyroidism (on thyroxine replacement), and peptic ulcer disease (PUD), presented to the nephrology department with:

- Bilateral lower extremity edema (2 months)
- Frothy, straw-colored urine
- Progressive fatigue and unintentional weight loss (8 kg in 2 months)
- Chronic constipation and intermittent upper abdominal discomfort

He denied chest pain, dyspnea, orthopnea, palpitations, or neurological symptoms (tingling, vision changes).

Clinical Findings

Table 1: Physical examination report

Parameter	Findings
Vital Signs	Temp: 96.8°F, BP: 100/60 mmHg, HR: 80 bpm, RR: 12/min, SpO_2: 98% (room air)
General	Moderate pallor, no lymphadenopathy or macroglossia
Cardiovascular	Regular rhythm, no murmurs/jugular venous distension
Respiratory	Clear lung fields bilaterally
Abdomen	Soft, nontender, no hepatosplenomegaly
Extremities	2+ pitting edema bilaterally
Neurological	No focal deficits; cranial nerves intact

Table 2: Laboratory investigations

Test	Result (Reference Range)	Significance
Hemoglobin	8.7 g/dL (12–16 g/dL)	Moderate anemia
MCV	64.2 fL (80–100 fL)	Microcytosis
Serum Creatinine	1.1 mg/dL (0.6–1.2 mg/dL)	Normal GFR
Albumin	3.15 g/dL (3.5–5.0 g/dL)	Hypoalbuminemia
NT-proBNP	3900 pg/mL (<125 pg/mL)	Cardiac strain
Urine Protein	6.75 g/day (<0.15 g/day)	Nephrotic syndrome
Serum Protein Electrophoresis	Monoclonal IgG lambda spike	MM-associated AL amyloidosis
Kappa/Lambda Ratio	0.22 (0.26–1.65)	Lambda dominance
Bone Marrow Biopsy	25–30% plasma cells (2nd biopsy)	Clonal plasmacytosis

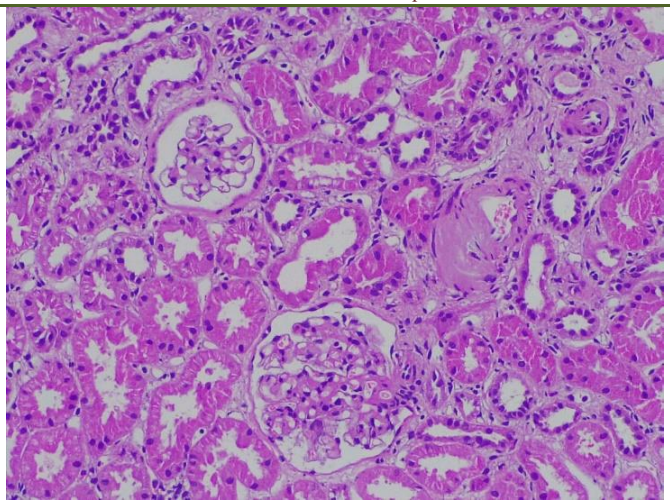

Figure 1 (A): Renal biopsy (H&E) showing pale pink, acellular, glassy amyloid deposits in glomeruli and arterioles

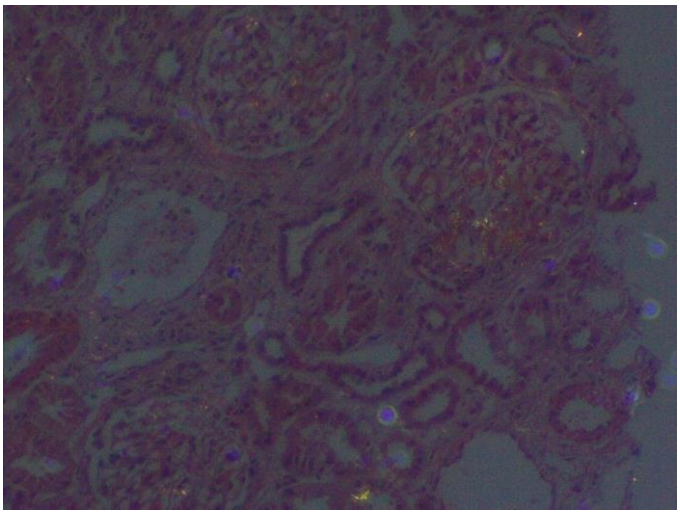

Figure 1 (B): Congo red-stained amyloid deposits appear reddish-orange under light microscopy and show apple-green birefringence under polarized light

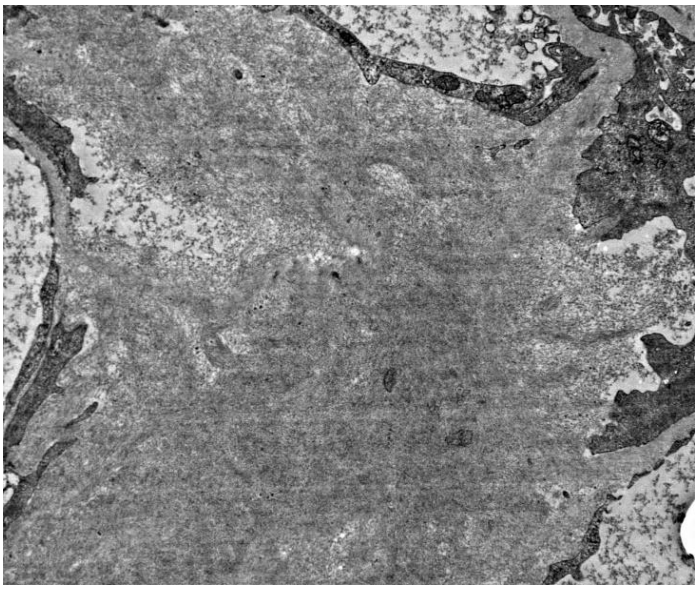

Figure 1 (C): Electron microscopy reveals randomly oriented, non-branching thin fibrils in the mesangium

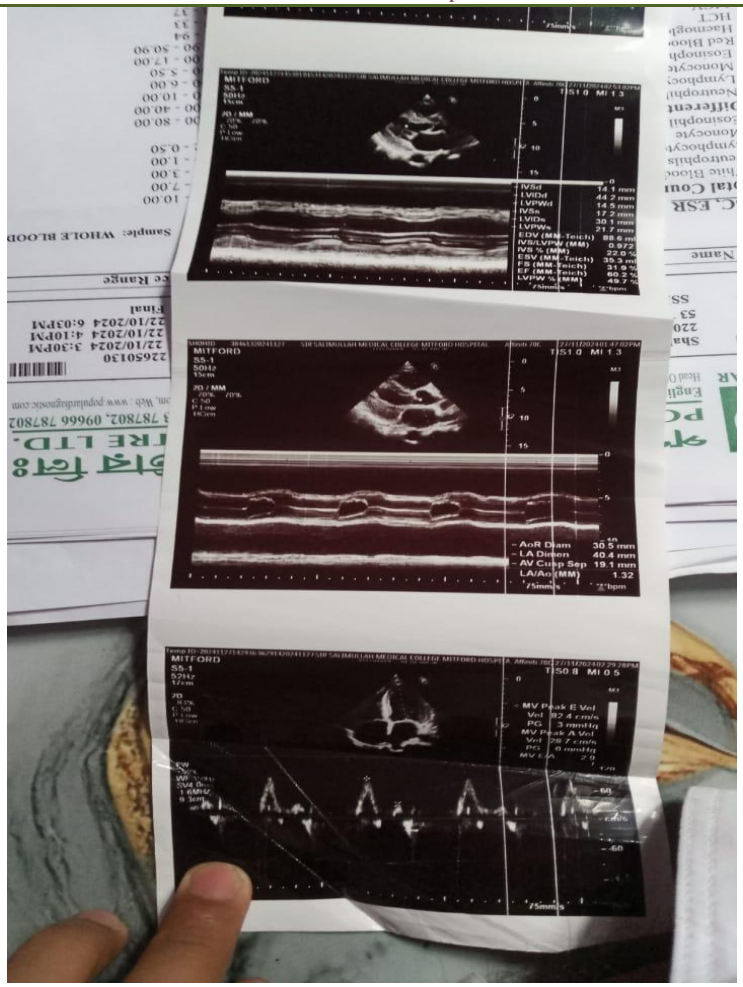

Figure 2: 2D echo shows RA, LA engagement with features of restrictive cardiomyopathy with Apical sparing pattern

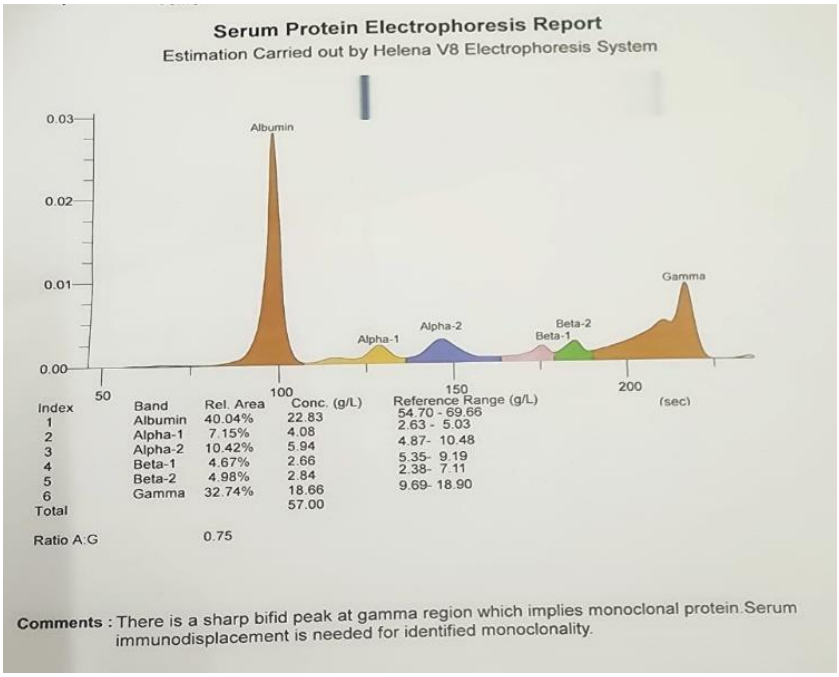

Figure 3: There is a sharp bifid peak at the gamma region, which implies monoclonal protein. Serum immuno-displacement is needed for the identified monoclonality

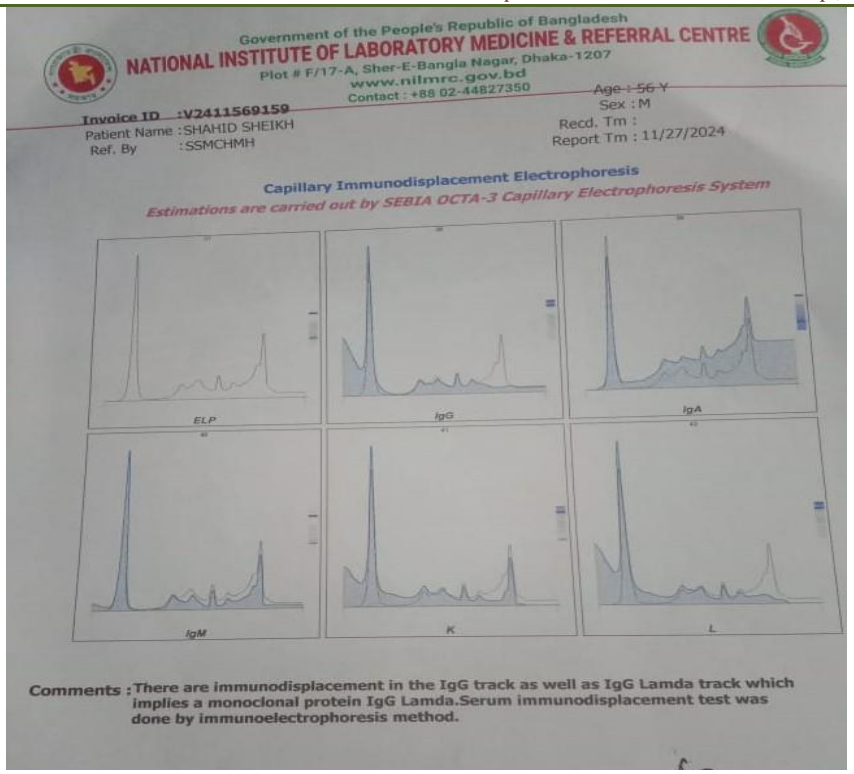

Figure 4: There is immune-displacement in both the IgG track and the IgG Lambda track, which implies a monoclonal protein, IgG Lambda. Serum immune-displacement test was done by the immunoelectrophoresis method

Table 3: Imaging and histopathology

Study	Findings
Echocardiography	Restrictive cardiomyopathy, preserved EF (67%), granular sparkling myocardium
Renal Biopsy	LM: Glomerular/arteriolar amyloid deposits
	DIF: Lambda-dominant staining
	EM: 9–12 nm fibrils
Bone Marrow Biopsy	Hypercellular with 25–30% CD138+ plasma cells (lambda-restricted)
Ileocolonoscopic	Normal (no amyloid deposits)
Thyroid Ultrasound	Post-thyroidectomy, residual tissue in the bed

Timeline of Diagnostic Workup

The patient initially presented with nephrotic syndrome, characterized by bilateral edema, hypoalbuminemia (3.15 g/dL), and severe proteinuria (6.75 g/day), prompting a thorough evaluation. Given his monoclonal IgG lambda spike on serum immunofixation electrophoresis and elevated NT-proBNP (4583 pg/mL), systemic AL amyloidosis with cardiac involvement was strongly suspected. To confirm the diagnosis, a renal biopsy was performed, revealing Congo red-positive amyloid deposits with lambda-dominant staining on immunofluorescence. Electron microscopy further identified 9–12 nm fibrils, pathognomonic for amyloidosis. A repeat bone marrow biopsy demonstrated 25–30% clonal plasma cells, confirming multiple myeloma (MM) as the underlying cause.

Other potential etiologies were systematically excluded:

- Autoimmune causes (ANA, anti-CCP) were negative.
- Bence Jones proteinuria was absent, ruling out free light chain-related disease.
- Post-thyroidectomy calcitonin levels were normal (<2 pg/mL), indicating no recurrence of medullary thyroid carcinoma (MTC).

Overall Treatment Procedures & Outcomes

The supportive therapies were continued during the diagnostic process, including the administration of diuretics (furosemide, spironolactone), salt-poor Albumin, prophylactic antibiotics, and vasopressors (non-epinephrine, vasopressor). However, generalized oedema, hypotension didn't improve. At this point, circulating NT-pro-BNP (4583 pg/mL), troponin T (0.5 mg/mL), S. Albumin 2.4, S. creatinine level around 2.4 mg/dl compared to that the time of admission. Soon, patients were referred to the Hematology Department for definitive management. After proper screening for infection on the 25th hospital admission day, they started dexamethasone 40mg/day, 4 days a week (D_{1-4}, D_{9-12},

D_{17-20}). Cyclophosphamide (50 mg in 2 divided doses) 1 day in a week and lenalidomide (25 mg), D_{1-21}/monthly and supportive therapy (acyclovir, cotrimoxazole, fluconazole, and others) on the 35th hospital admission day, patient developed severe chest-pain, fever, cough, respiratory distress and progressively demonizing O_2 sat (<80%) and radiological evidence of bilateral pneumonia, rise of NT Pro-BNP> 30.000 pg/ml, Sev >5.2 ng/dl. The sequential organ failure assessment (SPFA) sum was 16 points (range: 0–24). The patient did not show any farther improvement and died of multiple organ failure on 47th hospital admission day after refusing additional life sustaining therapy.

Table 4: Clinical and laboratory progression

Parameter	Baseline	1-Month Follow-up	Clinical Significance
NT-proBNP (pg/mL)	3,900	6,800	Worsening cardiac strain
Serum Albumin (g/dL)	3.15	2.7	Refractory hypoalbuminemia
Edema	2+ bilateral	3+ generalized	Diuretic resistance
Serum Creatinine (mg/dL)	1.1	2.4	Acute kidney injury

The rise in serum creatinine to 2.4 mg/dL indicated the development of acute kidney injury superimposed on amyloid nephropathy.

Table 5: Predictors of poor prognosis

Factor	Patient's Value	High-Risk Threshold	Clinical Implication
NT-proBNP	6,800 pg/mL	>1,800 pg/mL	Advanced cardiac involvement
Troponin T	0.05 ng/mL	>0.025 ng/mL	Myocardial injury
Kappa/Lambda Ratio	0.22	<0.26 or >1.65	Lambda light chain dominance
Bone Marrow Plasma Cells	35%	≥10%	High tumor burden

Table 5 highlights the high-risk features that portended the patient's poor outcome. The markedly elevated NT-proBNP (6,800 pg/mL) and troponin T (0.05 ng/mL) placed him in the highest risk category by established staging systems. The profoundly abnormal kappa/lambda ratio of 0.22 confirmed lambda light chain predominance, known to correlate with more aggressive disease. The bone marrow plasmacytosis of 35% indicated a significant plasma cell burden, further compounding the prognosis. These objective measures collectively explained the rapid clinical decline observed. The cardiac biomarkers suggested progressive amyloid infiltration of the myocardium, while the hematologic parameters demonstrated uncontrolled plasma cell dyscrasia. The renal dysfunction reflected both the direct effects of amyloid deposition and the consequences of worsening cardiac function. This multidimensional progression ultimately led to the development of refractory cardiorenal syndrome and the patient's demise within nine weeks of diagnosis, underscoring the aggressive nature of his disease variant.

DISCUSSION

This case highlights the aggressive clinical course of multiple myeloma-associated AL amyloidosis with multisystem involvement, particularly emphasizing the diagnostic and therapeutic challenges in such complex presentations. The patient's rapid deterioration despite early detection underscores the poor prognosis associated with cardiac and renal amyloidosis, especially when accompanied by lambda light chain dominance and elevated cardiac biomarkers (NT-proBNP >1,800 pg/mL, troponin T >0.025 ng/mL), consistent with Mayo Stage III disease [24]. The diagnostic challenges in this case were significant. The initial presentation with nephrotic syndrome and fatigue lacked specificity, leading to delays in definitive diagnosis [25]. While monoclonal gammopathy (IgG lambda) raised suspicion for AL amyloidosis, the absence of overt cardiac symptoms initially obscured the severity of myocardial involvement [8]. Only through comprehensive evaluation with echocardiography and NT-proBNP testing was restrictive cardiomyopathy identified [9]. This diagnostic trajectory aligns with existing literature showing that 30-40% of AL amyloidosis patients experience diagnostic delays due to variable organ manifestations [2]. The renal biopsy proved crucial in confirming the diagnosis, demonstrating lambda-predominant amyloid deposits and reinforcing its role as the diagnostic gold standard [15]. The prognostic implications were particularly concerning. The patient exhibited several high-risk features, including lambda light chain dominance (κ/λ ratio: 0.22) and high plasma cell burden (35%), both markers of poor survival in AL amyloidosis [26]. The markedly elevated NT-proBNP (>5,000 pg/mL) placed the patient in the highest risk category, with expected median survival <4 months [24, 27]. The development of refractory edema, persistent hypoalbuminemia, and progressive acute kidney injury further demonstrated the systemic nature of amyloid deposition [28]. Therapeutic management presented significant challenges. Despite prompt diagnosis, hemodynamic instability precluded chemotherapy initiation [29]. The standard bortezomib/dexamethasone regimen could not be safely administered due to deteriorating clinical status [2]. This reflects real-world challenges in treating high-risk patients where organ dysfunction limits therapeutic options [1]. While novel

agents like daratumumab show promise in early-stage disease, access remains limited [30]. The patient's history of medullary thyroid carcinoma adds complexity, as both conditions are associated with amyloid deposition (AL-type in MM vs. calcitonin-derived in MTC) [20]. While no MTC recurrence was found, this association raises questions about shared pathogenic mechanisms [31].

CONCLUSION

This case underscores the aggressive nature of MM-associated AL amyloidosis, particularly with cardiac and renal involvement. While diagnostic tools like serum biomarkers and organ biopsies aid early detection, treatment remains challenging in advanced stages. Future efforts should focus on novel therapies and early intervention protocols to improve outcomes.

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