AUCTORES
Globalize your Research

Journal of Cancer Research and Cellular Therapeutics

Rahman F *

Open Access

Case Report

Light Chain Disease: A Diagnostic Challenge

Rahman F [1]*, Mekhola M H [2], Rahman M S [2]

[1]Associate Professor, Department of Hematology, Bsmmu.

[2]Medical Officer, Department of Nephrology, Bsmmu.

***Corresponding Author:** Rahman F, Associate Professor, Department of Hematology, Bsmmu.

Received Date: June 01, 2025; Accepted Date: June 09, 2025; Published Date: June 17, 2025

Citation: Rahman F, Mekhola M H, Rahman M S, (2025), Light Chain Disease: A Diagnostic Challenge, *J. Cancer Research and Cellular Therapeutics*. 9(4); **DOI:10.31579/2640-1053/242**

Abstract

Light-chain multiple myeloma (LCMM) is a rare subtype of multiple myeloma (MM) that can affect various organs, with the kidneys being the most commonly impacted. LCMM typically has a more aggressive progression and is associated with a poorer prognosis. Renal dysfunction in LCMM arises due to the buildup of monoclonal immunoglobulin light chains in the kidneys. In this case, we present a 40-year-old male who came in with generalized swelling, decreased urine output, severe anaemia, and significant renal impairment. He underwent five sessions of haemodialysis and received five units of blood transfusion. Initial screening to exclude plasma cell neoplasm by serum protein electrophoresis showed negative results for monoclonal band. But bone marrow examination revealed an abundance of atypical plasma cells, constituting about 80% of the sample. Immunophenotyping identified 70% clonal plasma cells, with a positive lambda light chain marker. Urine analysis confirmed the presence of free light chains. Quantitative immunofixation markedly higher ratio of involved free light chain (instead of Kappa lambda ratio) but heavy chain level is within normal range. A CT scan indicated subtle changes in the axial and proximal appendicular skeleton. Early diagnosis of LCMM is crucial to initiate timely treatment.

Keywords: bone marrow morphology; light chain disease; multiple myeloma (mm); renal impairment

Introduction

One of the most prevalent hematologic tumours, multiple myeloma (MM) accounts for approximately 1% of all malignancies and is becoming more prevalent worldwide [1-2]. Since MM is diagnosed at an average age of about 65, it is more common in middle-aged and older males [1-4]. Its clinical manifestations include lytic bone lesions, hypercalcemia, anaemia, renal failure, coagulation problems, neurological abnormalities, and an elevated risk of infection [1-2,5]. The hallmark of MM is the aberrant growth of clonal plasma cells, which is a malignant condition of B-cells overall [1-2]. In MM, the malignant cells produce abnormal amounts of either monoclonal free light chains, or M-protein, or full immunoglobulins (Ig), which are normally comprised of heavy and light chains and produced by plasma cells [6].

Multiple forms of M-protein exist, but the most common is immunoglobulin G (IgG), which is followed by immunoglobulin A (IgA) and light-chain-only variants [2-4]. One or more myeloma- defining events, a plasmacytoma in biopsy tissue, and the presence of 10% or more clonal plasma cells in a bone marrow sample are used to diagnose MM. These include indicators of end-organ damage (like anaemia, renal impairment, hypercalcemia, or lytic bone lesions) or biomarkers of cancer (like bone marrow containing 60% or more clonal plasma cells, changed serum free light chain ratios, or several focal lesions on MRI that are at least 5 mm in size) [7]. About 15% of instances of light-chain multiple myeloma (LCMM), a less frequent subtype of MM, are kidney-related, however they can also affect other organs [2,8]. Because they are unable to form heavy chains, clonal plasma cells in LCMM only make light chains [2]. The hallmark of LCMM is organ damage brought on by aberrant light chain deposition, regardless of the quantity of light chain synthesis or the load of plasma cells. This results in a worse prognosis and a more aggressive course of the disease [9]. In LCMM, systemic light-chain amyloidosis, bone lesions, and renal failure are frequently seen [2,4]. Similar to MM, autologous stem cell transplantation (ASCT), immunomodulatory medications (like thalidomide and lenalidomide), and proteasome inhibitors (like bortezomib) are commonly used in therapy [8].

Case Study

A 40-year-old man had been experiencing acute dyspnoea, widespread oedema, and decreased urine production for seven days. He did not mention having a fever, vomiting, back discomfort, bodily pains, or uncomfortable or frequent urination in the past. Additionally, he did not have a history of high blood pressure or excessive cholesterol. Upon inspection, his blood pressure and body temperature were normal, but he was noticeably pale, short of breath, and much bloated. In addition to no history of organ enlargement or abdominal fluid accumulation, there was no history of blood loss or ongoing bleeding. The results of his neurological, cardiovascular, and musculoskeletal exams were normal.

A high erythrocyte sedimentation rate, raised calcium and phosphate levels, severe anaemia, and acute renal failure were all found during the first examinations (see Table 1). Traces of protein with positive Bence Jones protein were found in a urinalysis, but there were no active sediments. Studies on serum iron were normal. He got five units of blood and three haemodialysis procedures due to acute renal failure. His anaemia was resolved, and his blood creatinine level increased to 5.6 mg/dL. Corticosteroids and hydration were used to treat elevated calcium levels. Electrophoresis of serum proteins was normal. His significant anaemia was submitted to a haematologist for further assessment.

Following a bone marrow aspiration, both normal and atypical plasma cells were found in large quantities (around 80%) (Figure 1). A myeloma panel's immunophenotyping revealed 70% clonal plasma cells with lambda light chain restriction, positive expression of CD38, CD138, CD56, and CD28, negative expression of CD19 and CD45, and no kappa chains (Figure 2).

A free light chain ratio of 0.008:1 was obtained using a serum free light chain test, which showed a much higher lambda light chain (1398.5 mg/L) and a smaller kappa light chain (11.3 mg/L) (see Table 2). Immunofixation revealed good findings for lambda light chains but negative results for heavy chains such as IgG, IgA, and IgM (Figure 3).

Low-grade tracer uptake and mild lytic alterations in the axial and proximal appendicular skeletal systems were detected by a PET/CT scan. These results led to the diagnosis of lambda light chain multiple myeloma, even though the serum protein electrophoresis was normal. Following two cycles of the VCD treatment, the patient's serum creatinine level improved to 1.2 mg/dL. With normal serum creatinine levels, he was subsequently moved to the continuing VRD regimen.

The renal biopsy was not performed due to the involved serum free light chain level exceeding 1000 mg/L, signifying monoclonal gammopathy of renal significance (MGRS). Following flow cytometry immunophenotyping from a bone marrow sample, which revealed 70% clonal plasma cells with lambda light chain restriction and positive CD38, CD138, CD56, CD28, and cyLambda, but negative CD19 and cyKappa, the patient was ultimately diagnosed with multiple myeloma.

He underwent autologous bone marrow transplantation after achieving complete remission following six cycles of the VRD (bortezomib/Velcade, lenalidomide, dexamethasone) protocol and is currently on maintenance treatment.

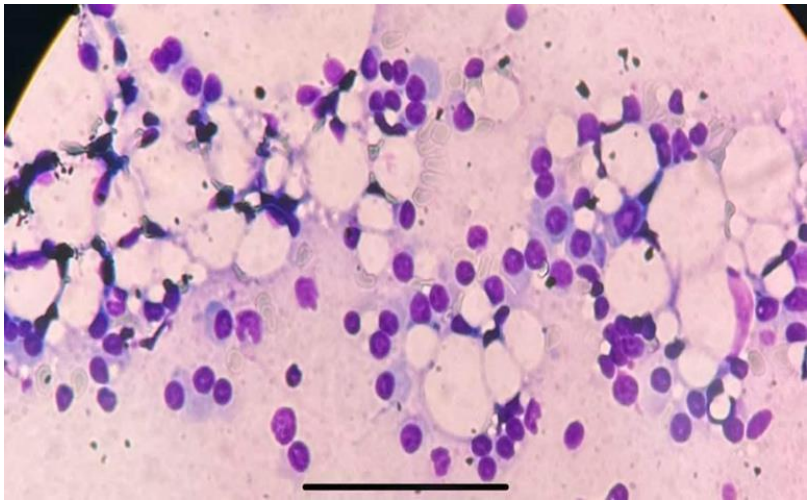

Figure 1: Bone Marrow Morphology showing plenty of plasma cells

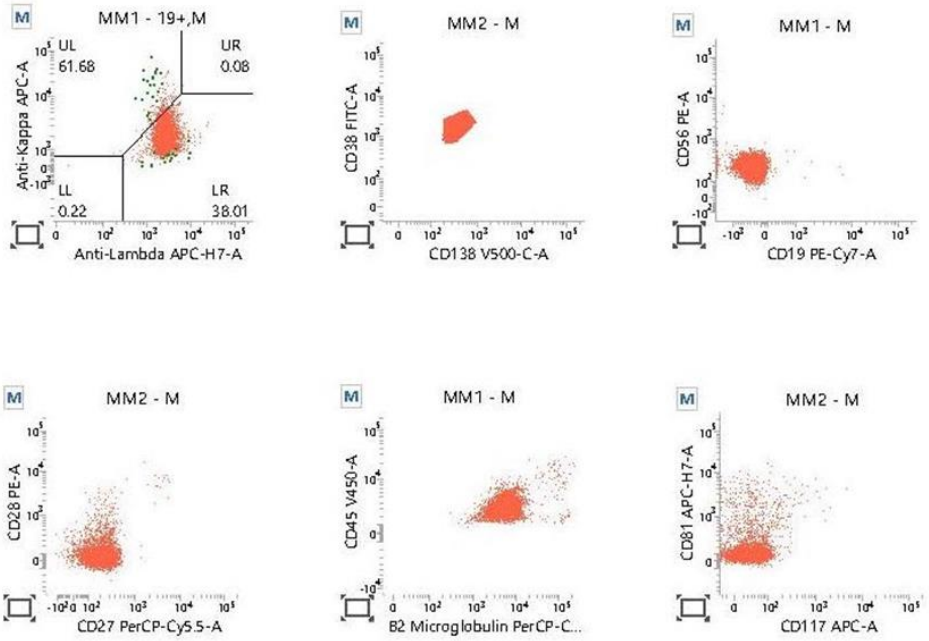

Figure 2: Bone marrow flow cytometry

Analyte (Unit)	Initial Test Outcome	Reference Standard
Hemoglobin (g/dL)	3.2	12.0–16.0
Mean corpuscular volume (fL)	85.4	83–103
Mean corpuscular hemoglobin (pg)	29.3	28–34
Mean corpuscular hemoglobin concentration (g/dL)	34.3	32–36
White blood cells	12.6 × 103/µL	4.8–10.8 × 103/µL
Neutrophils	10.3 × 103/µL	1.8–7.7 × 103/µL
Eosinophils	0.1 × 103/µL	0.00–0.49 × 103/µL
Basophils	0.0 × 103/µL	0.0–0.1 × 103/µL
Lymphocytes	1.0 × 103/µL	1.0–4.8 × 103/µL
Monocytes	1.1 × 103/µL	0.12–0.80 × 103/µL
Platelets	203 × 103/µL	150–350 × 103/µL
Erythrocyte sedimentation rate (mm/h)	75	0–35
Urea (mg/dL)	230	15–39
Creatinine (mg/dL)	12.40	0.57–1.11
Sodium (mEq/L)	135	135–146
Potassium (mEq/L)	4.79	3.5–5.1
Phosphorus (mg/dL)	7.0	2.5–4.9
Albumin (g/dL)	4.1	3.4–5.0
Serum calcium	13.7 mg/dl	8.5-10.5 /dl
Iron studies		
Serum iron (g/dL)	9	50–170
Total iron binding capacity (g/dL)	241	250–450
Serum ferritin (ng/mL)	152	8–252
Urine routine microscopic examination		
Protein	Trace	Nil
Bence jones protein	Present	Absent
Red blood cell (RBC)	0-3	0-5
White blood cell (WBC)	3-5	Nil
Cast	Nil	Nil

Table 1: Preliminary laboratory tests

Test	Result	Reference value
Kappa Light Chain	11.3 mg/L	200-440 mg/dl
Lamda Light Chain	1398.5 mg/L	110-240 mg/dl
Kappa:Lamda	0.008:1	0.31-1.56

Table 2: The serum free light chain assay

Discussion

An uncommon hematologic condition, LCMM (Light Chain Multiple Myeloma) makes up 15% of all instances of multiple myeloma (MM)2. Information for a thorough case report on LCMM is scarce in the existing literature. The deposition of monoclonal immunoglobulin light chains in different organs is what defines it [10]. Depending on which organs are impacted, LCMM might present with different clinical symptoms [11].

The clinical features of LCMM are similar to other forms of MM, with bone pain and kidney impairment being the most common presenting symptoms. Over the course of the disease, patients may also develop lytic bone lesions, hypercalcemia, anaemia, pleural effusion, and extramedullary involvement [2,4]. In cases where the kidneys are involved, monoclonal light chains produced by clonal plasma cells in the bone marrow are deposited in the glomeruli, leading to characteristic nodular glomerulosclerosis [12]. A hallmark feature of LCMM is the absence of complete clonal immunoglobulin production by malignant plasma cells [2]. This is important because the absence of an M-spike in serum electrophoresis can lead to misdiagnosis. Therefore, evaluating serum and urine free light chains is critical when LCMM is clinically suspected.

Patients with LCMM are more likely to have renal involvement than those with other types of MM [2,4]. Significant morbidity, a worse overall survival rate, and increased rates of early mortality have all been linked to renal impairment at diagnosis in LCMM [13-15]. Supportive care and the timely start of antimyeloma medication are the cornerstones of treatment for LCMM with renal insufficiency [16]. For LCMM with renal impairment, boratezolomib-based regimens are the recommended course of therapy [13-16], since they have been shown to be more effective than alternative approaches [2,4].

In our case, a 40-year-old man presented with generalized swelling (anasarca), severe anaemia, hypercalcemia, and severe renal insufficiency. Our initial diagnosis focused on MM. Serum protein electrophoresis showed a flattened gamma zone with no visible M-spike. A bone marrow study confirmed the diagnosis of kappa LCMM. The patient was immediately referred to a haematologist for prompt initiation of treatment.

Conclusion

The hallmark of LCMM, a rare kind of multiple myeloma (MM), is the absence of full clonal immunoglobulin production by the cancerous plasma cells. Serum protein electrophoresis in LCMM typically does not show an M-spike. Patients presenting with symptoms suggestive of MM, such as anaemia and renal impairment, should be carefully evaluated during assessment. Since LCMM has a worse prognosis than more common forms of MM, early identification and prompt initiation of treatment are crucial for improving patient outcomes.

Authors contribution

Each author provided valuable input during the article's development and critical editing for noteworthy intellectual content, and they all approved the final version.

Conflicts of interest

All authors declared that they have no conflict of interest regarding this publication.

References

1. Rajkumar SV. (2020), Multiple myeloma: 2020 update on diagnosis, risk-stratification and management. *Am J Hematol*. 95(5):548-567.
2. Rafae A, Malik MN, Zar MA, Durer S, Durer C. (2018), An overview of light chain multiple myeloma: clinical characteristics and rarities, management strategies, and disease monitoring. *Cureus*. 10(8).
3. Dimopoulos MA, Moreau P, Terpos E, Mateos MV, Zweegman S, et al., (2021), Multiple myeloma: EHA- ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Hemasphere*.1;5(2)
4. Zhang JJ, Sun WJ, Huang ZX, Chen SL, Zhong YP, et al., (2014), Light chain multiple myeloma, clinic features, responses to therapy and survival in a long-term study. *World J Surg Oncol*. 12:1-4.
5. Munshi NC, Longo DL, Anderson KC. (2018), Harrison's Principles of Internal Medicine. New York: McGraw Hill Education; *Plasma cell disorders*; p. 793–802.
6. Rao M, Yu WW, Chan J, et al. (2012), Serum free light chain analysis for the diagnosis, management, and prognosis of plasma cell dyscrasias. Agency for Healthcare Research and Quality (US), *Rockville (MD)*; PMID: 23016162.
7. Moreau P, San Miguel J, Sonneveld P, Mateos MV, Zamagni E, (2017), Multiple myeloma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 1;28.
8. Masood A, Ehsan H, Iqbal Q, Salman A, Hashmi H. (2022), Treatment of light chain deposition disease: a systematic review. *J Hematol*. 11(4):123.
9. Dhodapkar MV, Merlini G, Solomon A. (1997), Biology and therapy of immunoglobulin deposition diseases. *Hematol Oncol Clin North Am*. 1;11(1):89-110.
10. Randall RE, Williamson Jr WC, Mullinax F, Tung MY, Still WJ. (1976), Manifestations of systemic light chain deposition. *Am J Med*. 1;60(2):293-299.
11. Pozzi C, Locatelli F. (2002), Kidney and liver involvement in monoclonal light chain disorders. *Semin Nephrol*. 1;22(4):319-330.
12. Preud'homme JL, Aucouturier P, Touchard G, Striker L, Khamlichi AA, et al. (1994), Monoclonal immunoglobulin deposition disease (Randall type). Relationship with structural abnormalities of immunoglobulin chains. *Kidney Int*.;46(4):965-972.
13. Uttervall K, Duru AD, Lund J, Liwing J, Gahrton G, et al., (2014), The use of novel drugs can effectively improve response, delay relapse and enhance overall survival in multiple myeloma patients with renal impairment. *PLoS One*. Jul 8;9(7)
14. Khan R, Apewokin S, Grazziutti M, Yaccoby S, Epstein J, et al., (2015), Renal insufficiency retains adverse prognostic implications despite renal function improvement following Total Therapy for newly diagnosed multiple myeloma. *Leukemia*. 29(5):1195- 1201.
15. Dimopoulos MA, Delimpasi S, Katodritou E, Vassou A, Kyrtsonis MC, et al., (2014), Significant improvement in the survival of patients with multiple myeloma presenting with severe renal impairment after the introduction of novel agents. *Ann Oncol*. 1;25(1):195-200.
16. Dimopoulos MA, Sonneveld P, Leung N, Merlini G, Ludwig H, et al., (2016), International Myeloma Working Group recommendations for the diagnosis and management of myeloma-related renal impairment. *J Clin Oncol*. May 1;34(13):1544-1557.

DOI:10.31579/2640-1053/242