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CASE REPORT

Renal amyloidosis causing nephrotic syndrome: An unusual presentation of light chain myeloma

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ABSTRACT

Light chain myeloma represents 20% of multiple myeloma cases. Renal amyloidosis is one of the manifestations of light chain myeloma. Here, we present a case of nephrotic syndrome which was later diagnosed by kidney biopsy to be renal amyloidosis. Cumulative analysis of routine investigations, bone marrow analysis, immunofixation, and skeletal radiography confirmed it to be a case of light chain myeloma. The patient was later started on VRD regimen (lenalidomide, bortezomib, and dexamethasone) and responded well to the treatment.

KEY WORDS: Light Chain Myeloma; Renal Amyloidosis; Nephrotic Syndrome

INTRODUCTION

Amyloidosis comprises a group of heterogeneous diseases which are characterized by deposition of insoluble misfolded proteins that assume a crossed β-pleated structure to form amyloid fibrils in the extracellular space. Primary systemic amyloidosis (amyloid light chain or AL type), a type of systemic amyloidosis, is a part of the spectrum of plasma cell dyscrasias, where an aberrant clone of plasma cells produces immunoglobulin light chains in excess (commonly lambda) and forms amyloid.[1] Amyloidosis is more prevalent in men between the fourth and seventh decades.[2] In general, amyloidosis can affect any organ except the brain. Its pathophysiology is doubtful: Amyloid accumulation in the extracellular matrix of the blood vessels leading to ischemic damage as well as apoptosis along with mechanical interference.[2,3] The blood vessels are usually affected first, leading to endothelial microcirculatory dysfunction.[3] AL amyloidosis accompanies 10–15% of multiple myeloma cases.[4] Amyloidosis may be asymptomatic in 10–15% of cases.[2,5] The following is the case of a patient with systemic AL amyloidosis presenting with nephrotic syndrome who was later diagnosed to be a case of light chain myeloma.

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CASE REPORT

A 70-year-old male patient presented with gradual onset and progressive bilateral leg swelling. There was no history of orthopnea, paroxysmal nocturnal dyspnea, or decreased urine output. On clinical examination, pulse was 94/min, regular and blood pressure was 100/70 in the right upper arm in supine position. Pallor and pitting type of pedal edema was present on general examination. Systemic examination was within normal limits. The patient was mildly anemic with a hemoglobin of 8.6 g/dL. Type of anemia was of chronic type with a serum lactate dehydrogenase of 218 and iron/total iron-binding capacity of 73/111. GBP was normal and corrected reticulocyte count was 0.97. Bone marrow biopsy revealed (15%) plasma cells. Serum creatinine was 1.2 mg/dL with a creatinine clearance of 17 mL/min. Liver function tests revealed hypergammaglobulinemia along with low serum albumin with A: G ratio of 2.8:3.5. Corrected calcium was 8.2mg/dL. Viral markers were negative. His routine urine

revealed 2+ proteinuria and 24 h urine protein was in the nephrotic range (11 g/24 h).

Abdominal ultrasound revealed coarsened liver echotexture with slightly enlarged kidneys 12.1 and 12.6 cm in length and without hydronephrosis, stones, or any masses. Kidney biopsy and microscopy revealed irregular mesangial expansion with deposition of pale eosinophilic appearance with H&E stain, congophilia, and apple green birefringence in polarized light. Immunohistochemistry revealed dominance of lambda light chains over kappa light chains [Figure 1]. Serum protein electrophoresis was negative for a myeloma band, but serum lambda light chains were raised 169 mg/dL with a kappa/lambda light chain ratio of 0.130. Lateral view of skull revealed multiple lytic lesions [Figure 2].

The patient was started on oral lenalidomide 15 mg every 48 h for 21 days of a 28-day cycle (renal modification was done according to creatinine clearance), dexamethasone 40 mg weekly orally, and bortezomib 1.3 mg/m^2 weekly subcutaneously. At present, the patient is under follow-up and doing well.

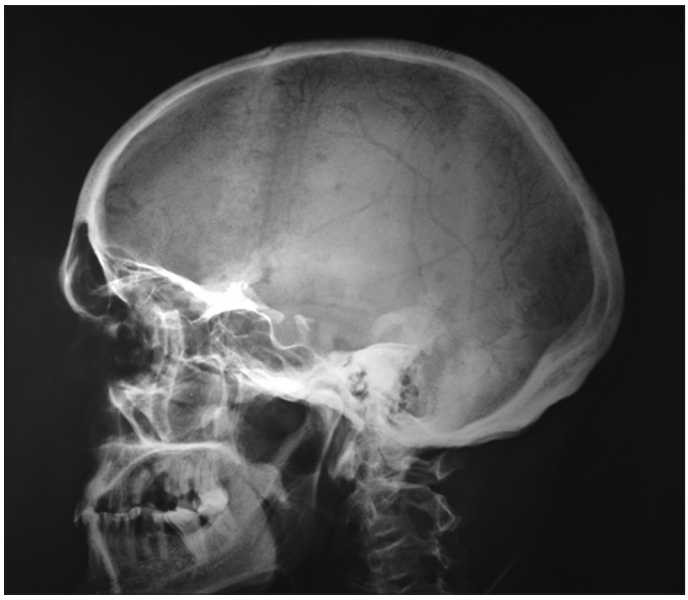

Figure 1: Lateral view of skull

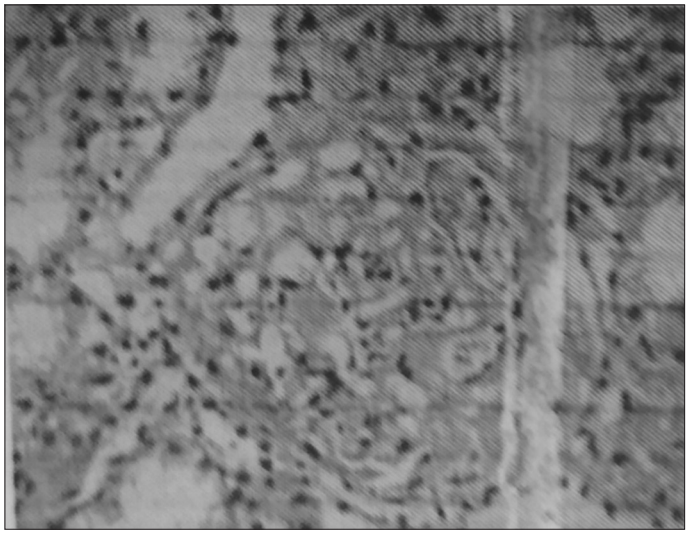

Figure 2: Microscopy of kidney biopsy

DISCUSSION

This patient was diagnosed with light chain myeloma with lambda light chain predominant systemic AL amyloidosis with biopsy-proven involvement of the kidney and bone marrow. The clinical case presented here is part of 15% of AL amyloidosis cases associated with multiple myeloma.[4] However, this case is relevant due to its unique clinical presentation, including severe involvement of kidney as nephrotic syndrome, onset with amyloidosis symptoms, and carbapenem-resistant *Acinetobacter baumannii* features on admission. In a retrospective study conducted by the Mayo Clinic, a cohort of 51 patients with AL amyloidosis treated between January 1995 and December 2015, 22% myopathy only, 65% cardiac symptoms, 31% peripheral/autonomic neuropathy, 25% renal symptoms, 8% liver symptoms, and 4% gastrointestinal symptoms.[6]

Diagnosis includes confirmation of paraproteinemia (present in 90% of patients). Sensitivity of serum or urine electrophoresis is approximately 50%, increasing to 80–90% with immunoelectrophoresis.[7] Biopsy confirmation of the affected organ or subcutaneous fat has a sensitivity of 70–80%.[2] Hematoxylin and eosin staining demonstrates eosinophilic amorphous material, salmon red coloration in Congo red, and apple green birefringence in polarized light. Immunohistochemistry detects up to 92% amyloid subtype depending on the availability of antibodies. There is some limitation for the determination of AL amyloid, due to various attributes, in the detection of conformational differences of light chains and the characteristics of the antibody used[8] as well as limited availability of a very sensitive method such as immunofluorescence in some centers.[9] At present, the gold standard is a proteomic analysis of amyloid deposits by mass spectrometry, after microdissection of Congo red-positive deposits.[2]

CONCLUSION

AL amyloidosis is a plasma cell dyscrasia which might be associated with multiple myeloma. Its spectrum of onset is variable. Timely diagnosis with appropriate investigations and early chemotherapy aids in improving survival.

REFERENCES

1. Blancas-Mejía LM, Ramirez-Alvarado M. Systemic amyloidoses. Annu Rev Biochem 2013;82:745-74.
2. Falk RH, Alexander KM, Liao R, Dorbala S. AL (light-chain) cardiac amyloidosis: A review of diagnosis and therapy. J Am

Coll Cardiol 2016;68:1323-41.
3. Gertz MA, Kyle RA. Myopathy in primary systemic amyloidosis. J Neurol Neurosurg Psychiatry 1996;60:655-60.
4. Kourelis TV, Kumar SK, Gertz MA, Lacy MQ, Buadi FK, Hayman SR, *et al*. Coexistent multiple myeloma or increased bone marrow plasma cells define equally high-risk populations in patients with immunoglobulin light chain amyloidosis. J Clin Oncol 2013;31:4319-24.
5. Pereira M, Afonso L, Fernandes G, Araú-jo R. Multiple myeloma and amyloidosis pre-senting as a restrictive lung disease with respiratory failure. Clin Med Rev Case Rep 2016;3:91.
6. Muchtar E, Derudas D, Mauermann M, Liewluck T, Dispenzieri A, Kumar SK, *et al*. Systemic immunoglobulin light chain amyloidosis-associated myopathy: Presentation, diagnostic pitfalls, and outcome. Mayo Clin Proc 2016;91:1354-61.
7. Chapin JE, Kornfeld M, Harris A. Amyloid myopathy: Characteristic features of a still underdiagnosed disease. Muscle Nerve 2005;31:266-72.
8. Schönland SO, Hegenbart U, Bochtler T, Mangatter A, Hansberg M, Ho AD, *et al*. Immunohistochemistry in the classification of systemic forms of amyloidosis: A systematic investigation of 117 patients. Blood 2012;119:488-93.
9. Wechalekar AD, Gillmore JD, Hawkins PN. Systemic amyloidosis. Lancet 2016;387:2641-54.

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