Case Report

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Unusual Presentation of Light Chain Deposition Disease: A Case Report

Pathology Section

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ABSTRACT

Light Chain Deposition Disease (LCDD) is a rare disease characterized by deposition of monoclonal non-amyloid light chains in multiple organs. We report an unusual histologic manifestation of LCDD in a 55-year-old female patient, who presented with nephrotic syndrome and an increased serum creatinine. This case of LCDD had features of cast nephropathy on biopsy which is diagnostic of myeloma kidney, when the patient was clinically asymptomatic. Serum electrophoresis showed no abnormal band. There was no other evidence of a B-cell clonal disorder or amyloidosis. Following chemotherapy, improvement in renal function correlated with a reduction in circulating light-chain levels.

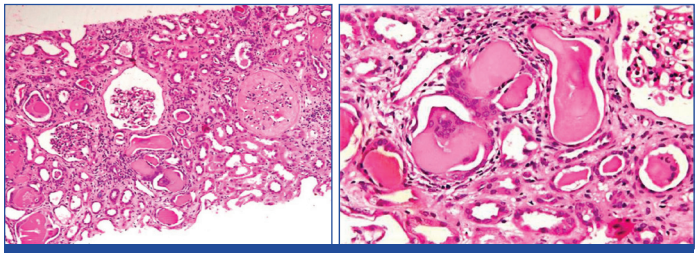
Keywords: Cast nephropathy, Myeloma kidney, Nephrotic syndrome

CASE REPORT

A 55-year-old female was referred to Nephrology OPD with history of lethargy, fatigue and bone pains for one year and photosensitivity to sun for four months. There was history of recent onset hypertension and gradually detoriating renal function. Personal and family history was unremarkable for diabetes and renal disease. Physical examination revealed a haemodynamically stable, thinly built woman. She was pale and was mildly hypertensive at presentation (BP–150/90 mmhg). Laboratory data showed normocytic, normochromic anaemia with decreased haematocrit (23%); increase in blood urea nitrogen (70 mg/dl); increased serum creatinine (6.7 mg/dl), marginal increase in serum calcium levels (11.5 mg/dl) and normal blood sugar levels (Fasting sugar 85mg/dl, HbA1c 5.8%). A 24-hour urine protein excretion was increased (7.6 g); although serum albumin levels were almost normal (2.2 mg/dl). Creatinine clearance was 5 ml/min. Urine dipstick was negative for albumin; urine sulfosalicylic acid test showed flocculation (indicates non-albumin protein, light chain) and urine Bence Jones protein was negative.

Ultrasound showed normal kidney size with increased echogenicity. Loss of corticomedullary differentiation was noticed in both kidneys. There was no hydronephrosis. No organomegaly was noted. Further laboratory work up showed no abnormal band in serum electrophoresis. Serologies for hepatitis B, hepatitis C, anti-neutrophil cytoplasmic antibodies, anti-glomerular basement membrane antibodies, rheumatoid factor, and HIV were negative. C3, C4 complement component were normal. A clinical diagnosis of nephrotic syndrome was made and a diagnostic renal biopsy was performed.

Among the ten glomeruli sampled for histopathology, three showed eosinophilic deposits. 30% of glomeruli were enlarged with mild mesangial widening and having vague nodular deposits [Table/Fig-1]. Glomerular basement membrane showed no thickening. Capillary loops were patent. Tubules were dilated and filled with dense markedly eosinophilic lamellated casts, some of which were surrounded by multinucleated giant cells [Table/Fig-2]. Some tubules also showed flattening of lining epithelium. Interstitium showed mild fibrosis and mild chronic inflammatory infiltrate. Vessels showed no specific changes. Since, there were nodular glomerular lesions, so a differential diagnosis of nodular glomerulosclerosis was made and the following entities were considered and special stains were carried out [Table/Fig-3].



[Table/Fig-1]: H&E, 10X, Low power view showing glomerulus with vague nodular deposits in one glomerulus, other glomerulus shows mesangial widening.
[Table/Fig-2]: H&E, 40X, High power view of tubules showing dense lamellated casts with giant cell reaction.

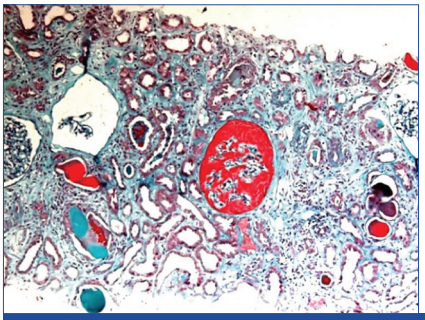
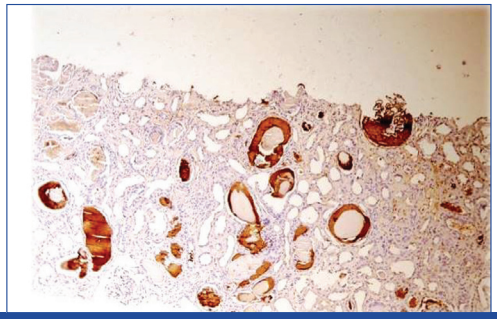
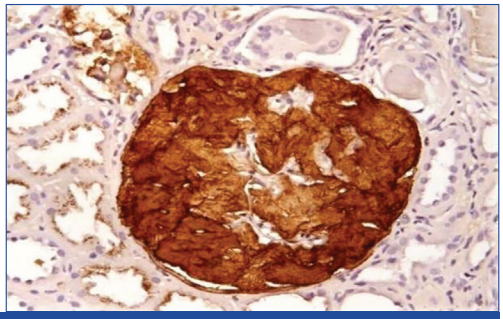
Lesions	PAS	Silver/Jones	Masson Trichome	Congo Red
Immunotactoid	+++	Negative	Blue	Negative
DM	+++	Black	Blue	Negative
LCDD/HCDD	++	Negative	Red	Negative
Amyloid	Negative	Negative	Blue	+++

[Table/Fig-3]: Differential diagnosis of nodular glomerulosclerosis.
*PAS: Periodic acid Schiff, DM: Diabetes mellitus, LCDD: Light chain deposition disease, HCDD: Heavy chain deposition disease.

Deposits stained red with Masson Trichrome stain [Table/Fig-4]. Nodules were negative for congo red and silver; and vaguely positive for PAS.

Immunohistochemistry showed kappa chain positivity [Table/Fig-5, 6], and negative for lambda chain. Immunofluorescence for IgG, IgM, IgA, C3 and C4 was negative. So based on clinical features, histopathology, special stains and immunofluorescence a final diagnosis of light chain deposition disease with cast nephropathy was made.

Since, light chain induced renal failure is an emergency situation, dialysis was immediately started. A bone marrow biopsy was performed subsequent to the renal biopsy which demonstrated 20% plasma cells. Serum electrophoresis was negative. However, urine immunoelectrophoresis and immunofixation electrophoresis revealed a monoclonal kappa light chain immunoglobulin. No lytic bone lesions were identified by a skeletal X-ray survey. The patient received a regimen of melphalan and prednisone over the next 8–10 months. After four month interval, serum creatinine values returned to baseline levels and dialysis was stopped. A repeat bone marrow biopsy at that time revealed 6% plasma cells. The patient is currently under follow-up.

[Table/Fig-4]: Low power view showing deposits staining red with Masson Trichrome. **[Table/Fig-5]:** IHC: Low power showing Kappa chain positivity in tubules and glomeruli. **[Table/Fig-6]:** IHC: High power showing kappa chain positivity in glomeruli.

DISCUSSION

Monoclonal Immunoglobulin Deposition Disease (MIDD) is a rare paraproteinemia characterized by deposition of monoclonal immunoglobulin deposits in renal basement membrane manifesting between 5th – 6th decades of life. MIDD is further sub-classified into Light Chain Deposition Disease (LCDD), Heavy Chain Deposition Disease (HCDD) and Light and Heavy Chain Deposition Disease (LHCDD), depending on the composition of the deposits. Among these, LCDD constitutes the most common form (75-80%) [1].

True incidence of LCDD is unknown. LCDD occurs most frequently in older men, and the average age at presentation is 55-60 years. Nephrotic-range proteinuria is common, but full-blown nephrotic syndrome occurs only in one-quarter of patients [2]. Patients usually present with proteinuria, microscopic haematuria, hypertension, and variable degrees of renal insufficiency [2-4].

Histopathologic features include nodular sclerosing gomerulopathy, which is seen in about 60% of the patients. The deposits in LCDD are composed of monoclonal light chains, mainly of kappa subtype. These deposits do not stain with congo red, since they are non-amyloid and do not exhibit fibrillar structure ultrastructurally [1]. The nodules are a mixture of light chains and mesangial protein.

LCDD typically occurs in association with Multiple Myeloma (MM) or other lymphoplasmacytic disorders. The incidence of LCDD in patients with plasma cell dyscrasia is approximately 5%. Many patients with LCDD are associated with MM, but upto 50% of patients do not have concurrent MM [5].

Light chain multiple myeloma (LCMM) accounts for around 20% of all cases of MM. Its clinical diagnosis is confirmed by the presence of monoclonal free light chains (FLCs) in the serum orurine, in the absence of intact monoclonal immunoglobulins, alongside clonal bone marrow plasma cells and the presence of end organ damage.

Bone marrow involvement in LCDD is common and the criteria for MM are met in 40-50% of cases [6]. The clonal production of nephrotoxic FLCs is the predominant cause of renal injury associated with MM and related gammopathies [7].

Compared with LCDD alone, LCDD in combination with cast nephropathy follows a more severe course of disease [1]. The incidence of cast nephropathy, also known as myeloma kidney, waxy casts form in the distal tubules of the nephron due to the aggregation of FLC with Tamm Horsfall protein [7]. Casts in addition to obstructing tubular flow in affected nephrons, incite a giant cell or foreign body reaction and can lead to tubular rupture resulting in interstitial fibrosis.

Serum creatinine level greater than 4 mg/dl is a poor prognosis sign for future progress to end stage renal disease in this disease [5]. A timely diagnosis is critically important in order to initiate treatment regimens to rapidly reduce FLC concentrations in patients with myeloma kidney. Such early FLC reductions are associated with improved survival [7]. The 5 year survival rate for LCDD is approximately 70%, but is less if there is coexistent myeloma.

It is recommended that patients with ESRD should not undergo transplantation unless their synthesis of monoclonal protein has been controlled through effective therapy, otherwise it will lead to recurrence [6].

CONCLUSION

Light Chain Deposition Disease was first described almost three decades ago. Here we present a case of light chain deposition disease with features of cast nephropathy which is diagnostic of myeloma kidney. Due to varied clinical presentations and many differential diagnoses on morphology; it is possibly both under-recognized and under-reported. Thus, recognition and knowledge of varied presentations can help in early diagnosis and treatment of the disease.

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