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CASE REPORT

New Onset Nephrotic - Range Proteinuria in a Patient with Chronic Kidney Disease - Not Always What it Seems

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Abstract

Light chain deposition disease (LCDD) is a rare condition that is characterized by the deposition of monoclonal immunoglobulin light chains in glomerular and tubular basement membranes. We report the case of a 72-year-old male with long-standing and stable chronic kidney disease (CKD) presumably due to hypertension and lithiasis who presented with new-onset nephrotic range proteinuria, anemia and rapidly worsening renal function that eventually led to end-stage renal disease (ESRD) requiring dialysis. Radiologic and laboratory workup found enlarged kidneys in the ultrasound and increased kappa/lambda ratio (KLR) suggestive of a plasma cell dyscrasia. The patient underwent bone marrow biopsy, confirming the diagnosis of kappa light chains multiple myeloma (MM). Since exclusion of amyloidosis was essential for determining therapeutic strategies, a kidney biopsy was performed, showing deposition of Periodic acid-Schiff (PAS) positive and silver-negative material in the glomeruli, tubular basement membrane, vessels and interstitium and kappa light chain restriction in the immunofluorescence staining. A diagnosis of kappa LCDD secondary to MM was made, and the patient received a Bortezomib-based regimen directed to the plasma cell disorder.

Keywords

Light chain deposition disease, Monoclonal immunoglobulin Deposition disease, Nephrotic proteinuria, Nodular glomerulosclerosis, Chronic kidney disease, Nephrotic proteinuria

Introduction

Light chain deposition disease (LCDD) is a rare condition that is characterized by the deposition of monoclonal immunoglobulin light chains in glomerular and tubular basement membranes [1]. We report a case of LCDD in a patient with established chronic kidney disease (CKD) presenting with new onset nephrotic-range proteinuria, anemia, and rapidly deteriorating kidney function. We focus on the differential diagnosis of this clinical picture and emphasize the importance of having a low level of suspicion of systemic disorders to timely diagnose and treat them.

Case Description

A 72-year-old Caucasian male, previously followed in the Nephrology clinic, was sent to a hemodialysis (HD) unit to start ambulatory renal replacement therapy (RRT) in May 2021 due to end-stage renal disease (ESRD). His previous medical history included arterial hypertension, obesity (BMI 40 kg/m^2), nephrolithiasis, glaucoma, and iatrogenic hypothyroidism after thyroidectomy at age 26. The patient had been diagnosed with CKD in 2019, which was thought to be a complication of hypertension and lithiasis. He was medicated with olmesartan, amlodipine, bisoprolol, furosemide, simvastatin, and levothyroxine. Renal function was stable (baseline creatinine 1.7 mg/dL) and proteinuria was consistently below 2 g/g until October

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2020, when he presented with worsening renal function (creatinine 3.45 mg/dL), anemia (Hb 9.3 g/dL) and proteinuria in the nephrotic range (8 g/g), without signs of edema, hypoalbuminemia or hypercholesterolemia. At that time, he had unremarkable urinary sediment apart from proteinuria, controlled hypertension, and no other obvious cause of acute-on-chronic kidney disease. His renal ultrasound showed enlarged kidneys, without evidence of obstruction or hydronephrosis. No further investigation was undertaken and he eventually progressed to ESRD, starting HD a few months later.

After initiating HD, he underwent a detailed investigation to determine the cause of nephrotic-range proteinuria. Diabetes was excluded by normal values of glycosylated hemoglobin and serologic tests for HIV, HBV, and HCV were negative. A thorough immunological study comprising anti-phospholipase A2 receptor (anti-PLA2R) antibodies, antineutrophil cytoplasmic antibodies (ANCA) and complement C3 and C4 was performed and showed no anomalies. Serum protein electrophoresis (SPEP) and serum immunofixation were unremarkable, but an increased kappa/lambda ratio (KLR) was found (KLR = 37; normal range 0.26-1.65). Urinary immunofixation showed polyclonal free light chains (FLC) and immunoglobulins. Since the increased KLR could be compatible with dysproteinemia, the patient was referred to the Hematology clinic. He was submitted to a myelogram and bone marrow biopsy, which showed 19% of plasmocytes, confirming the diagnosis of kappa light chain multiple myeloma (MM). No amyloid deposition was found in the bone marrow.

The decision to undergo a kidney biopsy was taken since the cause of ESRD, which would dictate treatment options, was still unknown, and because there was a high suspicion of amyloidosis. The biopsy was performed on a non-dialysis day and heparin was stopped in the previous and subsequent sessions to avoid hemorrhagic complications. The procedure was uneventful.

The kidney biopsy (Figure 1 and Figure 2) showed deposition of Periodic acid-Schiff (PAS) positive and silver-negative material in the glomeruli, tubular basement membrane, vessels, and interstitium. In the glomeruli, the deposits had a characteristic nodular pattern. Congo red staining was negative. Immunofluorescence (IF) showed light chain restriction, with a linear basement membrane staining for monotypic kappa light chain

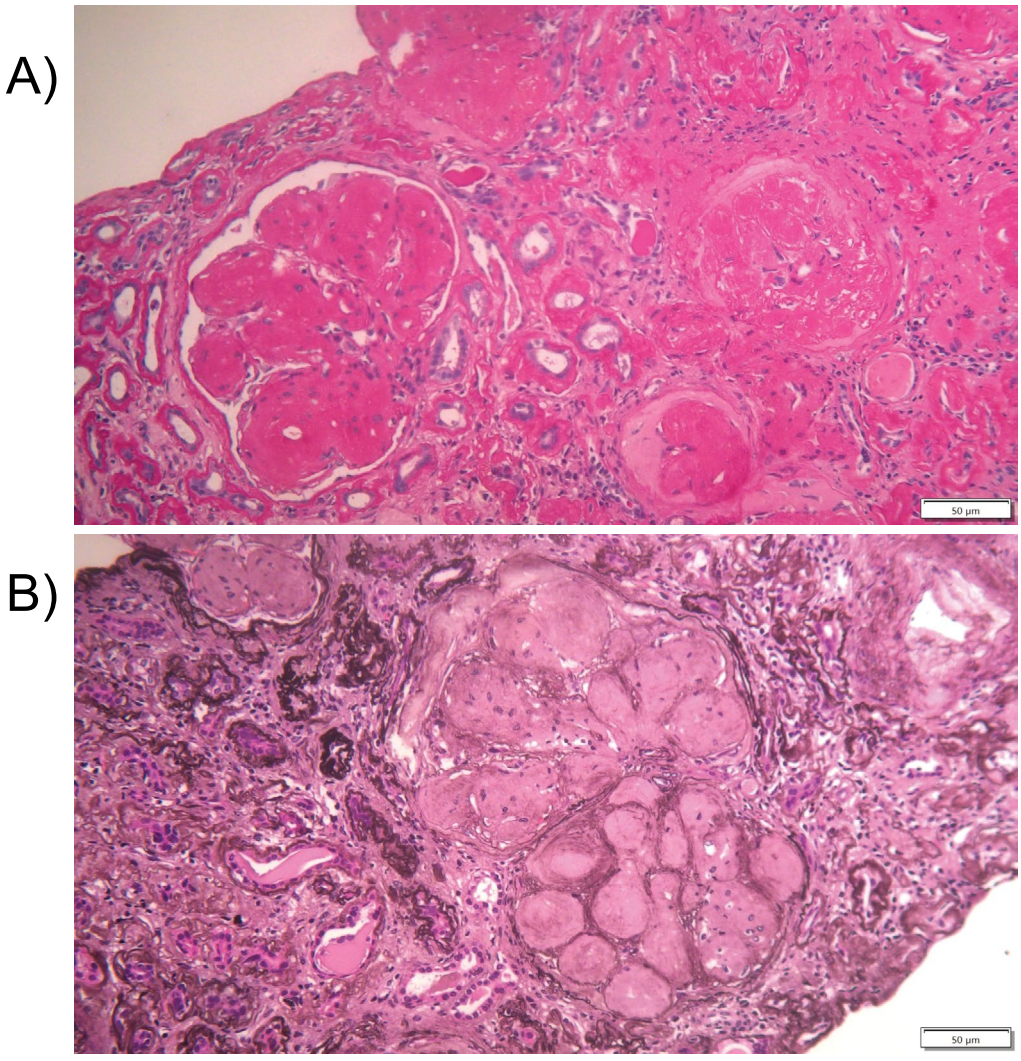

Figure 1: Kidney biopsy. (A) Periodic acid-Schiffstain; (B) Silver stain.

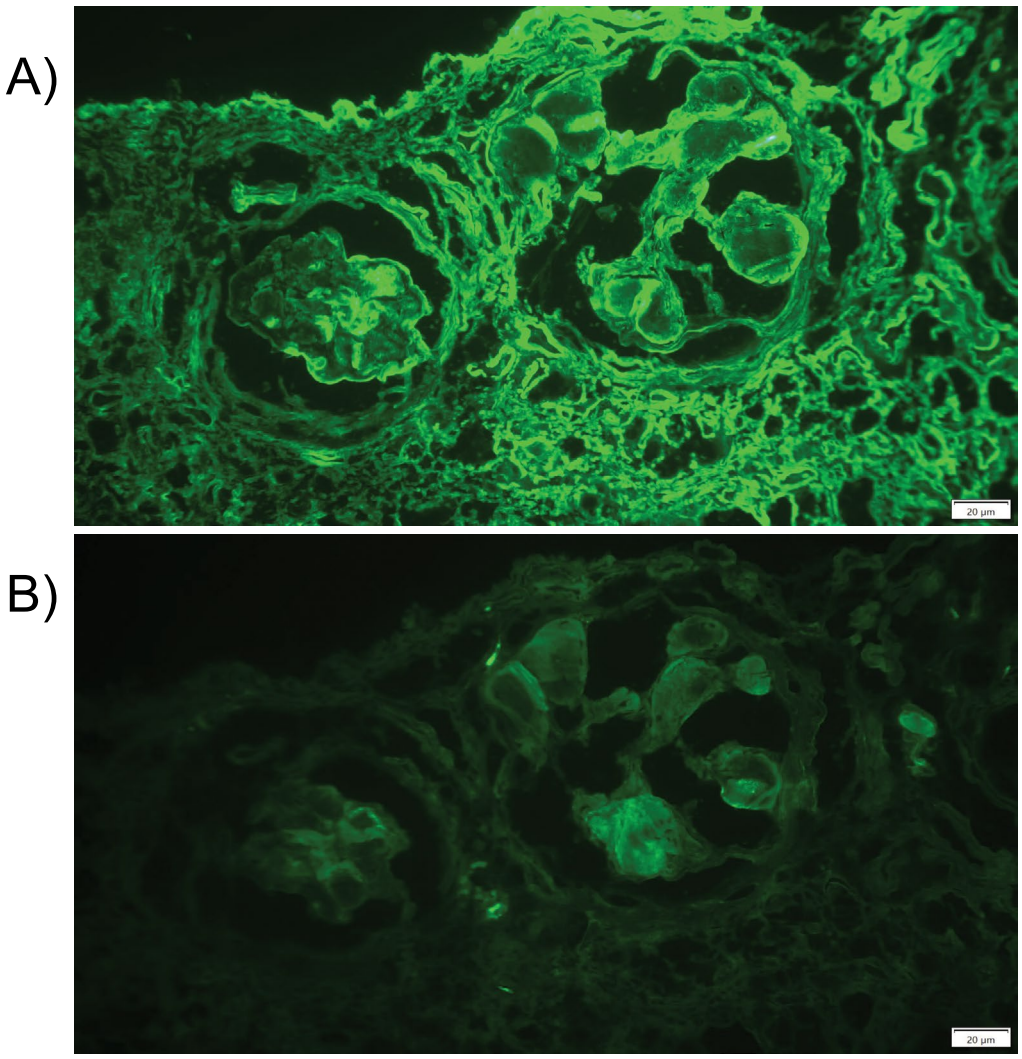

Figure 2: Immunofluorescence for kappa (A) and lambda (B) light chains.

only. These findings made the final diagnosis of kappa LCDD secondary to MM.

A therapeutic regimen with Bortezomib, cyclophosphamide, and dexamethasone (VCD) was started, aiming to treat the underlying MM. Although a hematologic response was achieved, there was no recovery of renal function and the patient remained on HD.

Discussion

The authors report a case of a patient with established CKD, presumably due to hypertension and lithiasis, who presented with new onset nephrotic-range proteinuria, rapidly deteriorating renal function, and anemia. Those abrupt changes in a previously stable patient should have raised the suspicion of an underlying systemic disease with glomerular involvement. Consequently, a careful evaluation was carried out to exclude diseases that could present with nephrotic-range proteinuria and kidney dysfunction in an elderly patient.

The most common causes of nephrotic-range proteinuria or nephrotic syndrome in patients above 65-years-old are membranous nephropathy, minimal change disease, and amyloidosis, accounting for approximately 60% of all cases. Other common etiologies include focal segmental glomerulosclerosis (FSGS), proliferative glomerulonephritis (GN), and diabetic nephropathy. Additionally, the incidence of dysproteinemic kidney disease also increases with age and should be taken into account. Crescentic GN is also common in the elderly but usually presents with multisystemic involvement, hematuria, and rapidly progressive renal failure. The diagnosis of these conditions is confirmed by a kidney biopsy [2].

Besides proteinuria, this patient also had enlarged kidneys in the ultrasound, which were highly suggestive of amyloidosis. The laboratory workup was suggestive of dysproteinemia, which was confirmed by the presence of 19% of plasmocytes in the bone marrow biopsy. Despite the absence of amyloid deposits in the bone marrow tissue, the suspicion was high and its diagnosis had important therapeutic and prognostic implications. So, the patient underwent a kidney biopsy that ruled out this hypothesis.

The histopathology result showed a nodular glomerulosclerosis pattern which can be found in

Table 1: Differential diagnosis of nodular glomerulosclerosis.

Condition	Light microscopy	Immunofluorescence
Diabetic nephropathy	PAS positive Silver positive	Linear staining for albumin and IgG
Monoclonal immunoglobulin deposition disease	PAS positive Silver negative	Diffuse deposits of either kappa or lambda and, in rare cases, heavy chains
Membranoproliferative glomerulonephritis	Duplicated glomerular basement membrane	Immunoglobulin and/or C3 deposits
Amyloidosis	Congo red positive Silver negative	Monoclonal light chain in AL
Fibrillary glomerulonephritis	Congo red negative	IgG and C3 deposits in mesangium and along GBM; kappa = lambda
Immunotactoid glomerulonephritis	Congo red negative	Predominant IgG deposits; majority have light chain restriction
Idiopathic nodular glomerulosclerosis	PAS and silver positive	Negative

AL - Light chain amyloidosis; C3 - Complement component 3; GBM - Glomerular Basement Membrane; IgG - Immunoglobulin G

several conditions, including diabetic nephropathy, monoclonal immunoglobulin deposition disease (MIDD), membranoproliferative glomerulonephritis (MPGN), amyloidosis, immunotactoid and fibrillary glomerulonephritis, and idiopathic nodular glomerulosclerosis in patients with a history of smoking and hypertension [3]. IF is the most useful test in differentiating the aforementioned conditions (Table 1). In this case, it showed light chain restriction, with a linear basement membrane staining for monotypic kappa light chain only, which confirmed the diagnosis of LCDD [4].

LCDD is the most common form of MIDD and it is characterized by the deposition of monoclonal immunoglobulin light chains along glomerular, tubular, and vascular wall basement membranes [5]. It affects predominantly males in the fifth to sixth decade of life and can occur in association with an underlying plasma cell dyscrasia or as monoclonal gammopathy of renal significance [6]. Kidney is the principal organ involved in this systemic disease and it usually presents with nephrotic syndrome and renal dysfunction that frequently progresses to ESRD requiring RRT [7].

The main goal in the treatment of LCDD is to suppress the production of light chains, avoiding more damage to the kidney and other organs involved. However, patients with ESRD on dialysis are less likely to recover renal function [8]. The association with multiple myeloma confers a poor prognosis and treatment should be directed at this underlying condition, usually consisting of systemic chemotherapy with or without autologous stem cell transplant. Bortezomib-based regimens were associated with high hematological response rates and prolonged survival in those patients [9]. Daratumumab, an anti-CD38 monoclonal antibody, is a promising drug that showed a rapid and significant hematologic response in around 7 out of 8 patients with refractory disease [10].

Conclusion

Through this case report, we aimed to demonstrate the importance of closely monitoring kidney function deterioration, even in a patient with long-standing CKD, as new systemic diseases can manifest through renal involvement and may dictate a different therapeutic approach.

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None.

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