Taylor & Francis
Taylor & Francis Group

CASE REPORT

OPEN ACCESS | Check for updates

Acute kidney injury on chronic kidney disease: from congestive heart failure to light chain deposition disease and cast nephropathy in multiple myeloma

Sana Shaikh [a], Christian Nwankwo[b], Alexandre Lacasse[a] and Steven Cheng[c]

aDepartment of Internal Medicine, SSM St. Mary's Hospital, St. Louis, St. Louis, MO, USA; bDepartment of Nephrology, SSM St. Mary's Hospital, St. Louis, St. Louis, MO, USA; cDepartment of Nephrology, Washington University School of Medicine, St. Louis, MO, USA

ABSTRACT

Acute on chronic renal failure is a common but notably broad diagnosis. We present a 64-year-old man with a history of diastolic heart failure and chronic kidney disease, admitted for an elevated creatinine. History and physical examination were suggestive of decompensated heart failure; however, the careful interpretation of urinalysis rendered the diagnosis of multiple myeloma. On renal biopsy, the patient was found to have light chain deposition disease with cast nephropathy. Combination lesions in multiple myeloma are rare and require diligent histopathology for detection, including light microscopy, immunofluorescence and electron microscopy. These patients portray different demographics, renal manifestations, oncologic characteristics and outcomes, and hence, further studies isolating these combined lesions are warranted.

Abbreviations: CKD: chronic kidney disease; CN: cast nephropathy; CT: computerized tomography; EDD: electron-dense deposits; EM: electron microscopy; IF: immunofluorescence; FLC: free light chain; LC: light chain; LCDD: light chain deposition disease; MIDD: monoclonal immunoglobulin deposition disease; MM: multiple myeloma; LM: light microscopy; NGS: nodular glomerulosclerosis; κ: kappa; λ: lambda.

1. Introduction

Free light chains (FLCs) are overproduced by abnormal B-cells in plasma cell dyscrasias and other lymphoproliferative disorders [1]. They are filtered by the glomeruli, reabsorbed in the proximal tubules and degraded in the tubular cells, making the kidney a prominent deposition target [2]. Light chain (LC) deposition contributes to renal insufficiency in multiple myeloma (MM) by causing three main patterns of injury: cast nephropathy (CN), monoclonal immunoglobulin deposition disease (MIDD) and amyloidosis [3]. Light chain deposition disease (LCDD) is the most prevalent variant of MIDD. Lesions in combination are scarcely observed, with LCDD-CN being relatively more frequent and LCDD-amyloid being rare [1,3,4].

2. Case report

A 64-year-old man with past medical history of diastolic heart failure, stage 3 chronic kidney disease (CKD) of unknown etiology, interstitial lung disease and pulmonary hypertension with chronic hypoxemic respiratory failure, recurrent nephrolithiasis, morbid obesity and 65-pack-year tobacco abuse presented with an elevated creatinine on outpatient laboratory investigation. Associated symptoms included progressive lower extremity swelling, weight gain and chronic, spontaneous and intermittent gross hematuria. Vital signs were stable. Physical examination was pertinent for jugular venous distention and symmetric bilateral pitting pedal edema. Laboratory data was significant for creatinine of 5 mg/dl [0.8–1.3 mg/dl] from baseline value of 1.4 mg/dl a month prior to encounter, elevated blood urea nitrogen (42 [8–25 mg/dl]), hyperphosphatemia (6.2 [2.3–4.5 mg/dl]), elevated N-terminal pro B-type natriuretic peptide (7162 [0–299 pg/ml]), normocytic normochromic anemia (10.8 [13–17.5 gm/dl]) and normal albumin. Urine studies disclosed proteinuria (2+), gross hematuria (3+), transient normoglycemic glycosuria (1+), spot protein/creatinine ratio of 4.7 and a calculated fractional excretion of urea of 52%. Chest X-ray showed bilateral reticular opacities, traction bronchiectasis and bullous apical disease. Noncontrast computerized tomography (CT) of the chest confirmed bibasilar nonspecific interstitial pneumonia pattern, combined pulmonary fibrosis and emphysema and bibasilar cystic changes representing amyloidosis or pneumatoceles. Retroperitoneal ultrasound demonstrated a 16-cm right kidney, 16.4-cm left kidney, right-sided renal parenchymal disease and bilateral nonobstructing nephrolithiasis.

Further investigations revealed an abnormal restricted peak in the gamma region on serum protein electrophoresis, elevated kappa (κ)-FLC (477 [0.33–1.94 mg/dl]), elevated κ- to lambda (λ)-FLC

Light microscopy
(A) - PAS positive and (B) - silver positive nodular glomerulosclerosis
(C) - PAS negative fuchsinophilic casts within tubular lumens
(D) - Cortical tubulointerstitial tissue with interstitial edema
Immunofluorescence
(E) - κ-LC stain: tubular casts and TBM and (F) - λ-LC stain: tubular casts only
Electron microscopy
(G) - GBM with punctate granular subendothelial electron dense deposits
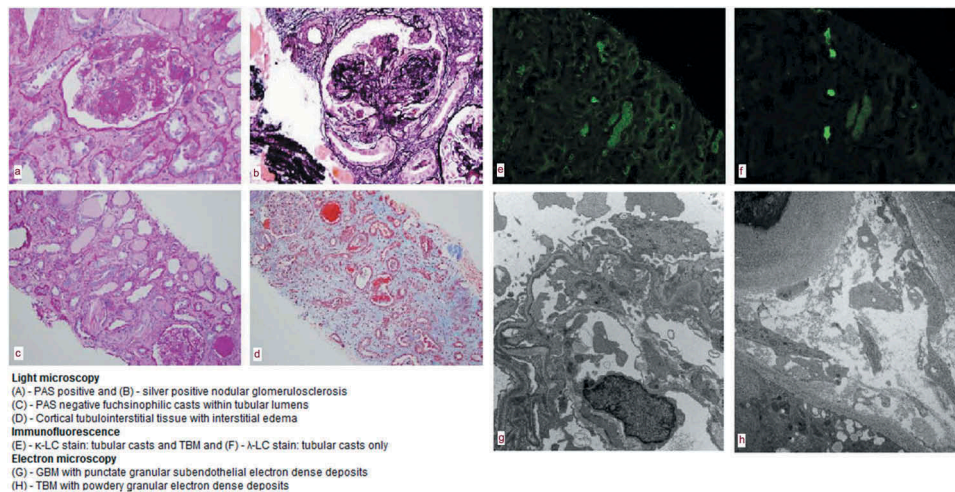(H) - TBM with powdery granular electron dense deposits

Figure 1. Histopathology seen on renal biopsy.

Light microscopy – The non-sclerotic glomeruli show nodular glomerulosclerosis. The nodules are Periodic acid-Schiff (PAS) (a) and silver positive (b). Numerous periodic acid-Schiff-negative fuchsinophilic casts are present within the tubular lumens, some of which have a cracked appearance and associated inflammation (c). The cortical tubulointerstitial tissue has moderate interstitial edema (d). Immunofluorescence – Frozen sections of tissue submitted show no glomeruli. On a scale of 0–3+, tubular casts stain with kappa light chain (3+, focal) (e) and lambda light chain (1+, focal) (f). Tubular basement membranes stain with kappa light chain (2+) (e) and are negative for lambda light chain (f). Electron microscopy – The two glomeruli evaluated show punctate granular subendothelial electron-dense deposits that have a linear distribution throughout the glomerular basement membranes (g). The tubular basement membranes show similar powdery granular electron-dense deposits (h).

ratio (229 [0.26–1.65]), presence of immunoglobulin G κ monoclonal protein on immunofixation, elevated beta-2 microglobulin (21.4 [1–2.5 mg/L]), high normal immunoglobulin G (1568 [700–1600 mg/dl]) as well as anemia of chronic disease. Renal biopsy was consistent with the diagnosis of κ-LCDD, CN and focal global glomerulosclerosis (3/19, 16%) (Figure 1). Bone marrow aspirate and core biopsy affirmed plasma cell neoplasm comprising 30% of marrow cellularity. Flow cytometry showed 6% of events in the plasma cell gate which were κ restricted (96%), CD19 negative (95%) and CD56 positive (97%). Positron emission tomography-CT was without bony lytic lesions. Kidney function steadily declined and after the onset of oliguria, intermittent hemodialysis was initiated. The patient was discharged with nephrology and hematology follow-up. As an outpatient, therapy with cyclophosphamide, dexamethasone and bortezomib was administered. Renal function, including serum creatinine and urine output, began to improve. Hemodialysis was discontinued after five months. At one year, serum creatinine was 2.5 mg/dl, κ-FLC was 8.64 and κ/λ ratio was 2.65.

3. Discussion

Admission diagnosis for this patient was acute cor pulmonale or decompensated right-sided congestive heart failure. Following intravenous diuresis, subjective improvement was reported and there was an appropriate response in the urine output. However, certain subtle laboratory findings pointed towards an alternative diagnosis. Serial creatinine measurements continued to trend upwards in spite of several diuretic regimen adjustments. Urine protein quantification showed nephrotic-range proteinuria, although falsely elevated by concomitant red blood cell lysis. Hematuria was attributed to trauma from renal calculi, but nephritic syndromes could not be excluded. The presence of glycosuria in the setting of normoglycemia and normal hemoglobin A1c was concerning for proximal tubular dysfunction. Despite preexisting CKD, both kidneys were paradoxically enlarged on ultrasound. In an attempt to find a unifying diagnosis, serum and urine protein electrophoresis and immunofixation were sent, and findings were consistent with an immunoglobulin overproduction process. Diagnosis of MM was thus obtained in the absence of hypercalcemia, albuminocytologic dissociation, bony lytic lesions, weight loss or fatigue. Renal lesion identified on biopsy was a combination of LCDD and CN. Amyloidosis was suspected based on kidney size, potential amyloid-associated cystic lung disease and presence of diastolic heart failure, but this was not settled by biopsy.

LCDD-CN is a histopathologic diagnosis. It can be easily missed without meticulous and sequential light microscopy (LM), immunofluorescence (IF) staining for κ- and λ-LC and electron microscopy (EM) (Table 1, Supplementary material). The various permutations and combinations of microscopic findings make the diagnosis challenging. First, the LM findings associated with LCDD-CN are dominated by the CN component, with the presence of fractured periodic acid-Schiff-negative tubular casts [3,5]. Nodular

glomerulosclerosis (NGS), the lesion most suggestive of LCDD, is infrequently identified [2,5,6]. This could be due to an earlier presentation with CN-induced renal failure and insufficient NGS development time or decreased sclerogenicity of the pathogenic LC in this entity [6]. Second, IF is the most sensitive technique for detecting LC deposition, but EM oftentimes reveals typical finely granular electron-dense deposits (EDDs) in IF-negative cases [2,5]. Structural changes in the antigenic sites on the LC and masked antibody recognition epitopes may play a role [2]. Third, EM alone may conceal the diagnosis due to differences in LC structure. EDDs are more likely with κ-LC than λ-LC [2]. Deposits may be focally distributed and absent in the available EM sample or the LC aggregation may be insufficient for visualization at an ultrastructural level [2,5]. Repeat renal biopsies may show persistent LC deposits in treated and transplanted patients [7].

Lin et al. reported differences in demographics, presenting renal manifestations, oncologic characteristics and outcomes in patients with LCDD-CN in comparison to pure MIDD [6]. Several indices varied: mean age was higher (67.1 versus 57.4 years), mean 24-hour proteinuria was lower (2.2 versus 4.2 g/day), incidence rates of acute kidney injury and dialysis dependence at the time of renal biopsy were higher (82% versus 30% and 64% versus 26%, respectively) and the incidence of MM was also higher (91% versus 39%). Pozzi et al. found LCDD-CN to be the only histological feature associated with a worse renal outcome [2]. Zand et al. had similar findings in patients with LCDD-CN as compared to those with LCDD alone [8]. The rate of acute renal failure at the time of renal biopsy was higher (54% versus 30%), as was the incidence of MM (100% versus 69%) and overall mortality (69% versus 29%). Treatment goals for LCDD-CN include improvement and stabilization of renal function as well as prevention of extrarenal deposits [7]. These may be seen in the heart, liver, spleen and peripheral nervous system [2,7,9]. Therapy for MM has been well described in oncology literature. In those requiring renal replacement therapy, both hemodialysis and peritoneal dialysis offer similar survival statistics [2]

4. Conclusion

LCDD-CN has not been well characterized or distinguished as a group in previous studies. Establishing diagnosis requires diligent LM, IF and EM evaluation. Patients tend to have worse renal as well as overall survival. Although reported to be a prevalent combination of renal lesion, LCDD-CN remains sporadically documented in the medical literature.

Disclosure statement

ORCID

Sana Shaikh http://orcid.org/0000-0003-1979-4392

References

[1] Paueksakon P, Revelo MP, Horn RG, et al. Monoclonal gammopathy: significance and possible causality in renal disease. Am J Kidney Dis. 2003;42 (1):87–95.

[2] Pozzi C, D'Amico M, Fogazzi GB, et al. Light chain deposition disease with renal involvement: clinical characteristics and prognostic factors. Am J Kidney Dis. 2003;42(6):1154–1163.

[3] Lorenz EC, Sethi S, Poshusta TL, et al. Renal failure due to combined cast nephropathy, amyloidosis and light-chain deposition disease. Nephrol Dial Transplant. 2010;25(4):1340–1343.

[4] Gowda KK, Joshi K, Nada R, et al. Light chain proximal tubulopathy with cast nephropathy in a case of multiple myeloma. Indian J Nephrol. 2015;25 (2):119–122.

[5] Gokden N, Cetin N, Colakoglu N, et al. Morphologic manifestations of combined light-chain deposition disease and light-chain cast nephropathy. Ultrastruct Pathol. 2007;31(2):141–149.

[6] Lin J, Markowitz GS, Valeri AM, et al. Renal monoclonal immunoglobulin deposition disease: the disease spectrum. J Am Soc Nephrol. 2001;12 (7):1482–1492.

[7] Ganeval D, Noël LH, Preud'homme JL, et al. Light-chain deposition disease: its relation with AL-type amyloidosis. Kidney Int. 1984;26(1):1–9.

[8] Zand L, Nasr SHGertz MA, et al. Clinical and prognostic differences among patients with light chain deposition disease, myeloma cast nephropathy and both. Leuk Lymphoma. 2015;56(12):3357–3364.

[9] Pirani CL, Silva F, D'Agati V, et al. Renal lesions in plasma cell dyscrasias: ultrastructural observations. Am J Kidney Dis. 1987;10(3):208–221.

[10] Qian Q, Leung N, Theis JD, et al. Coexistence of myeloma cast nephropathy, light chain deposition disease, and nonamyloid fibrils in a patient with multiple myeloma. Am J Kidney Dis. 2010;56 (5):971–976.

[11] Lam KY, Chan KW. Unusual findings in a myeloma kidney: a light- and electron-microscopic study. Nephron. 1993;65(1):133–136.