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Light Chain Cast Nephropathy in an African-American Woman with Waldenström's Macroglobulinemia

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Abstract Waldenström's macroglobulinemia (WM) is a rare cancer of the lymphatic system due to excess IgM monoclonal protein with a rare renal involvement. We describe a case of MW presenting with acute renal failure. A 63-year-old female who was admitted to our hospital for influenza B complicated by acute renal failure during the hospital stay, with creatinine up to 6 mg/dL, despite adequate hydration. Electrophoresis revealed a monoclonal component in the gamma region, which was classified as an IgM k. A kidney biopsy was performed, showing light cast chains suggested the possibility of myeloma kidney. Furthermore, bone marrow histology was performed, revealing lymphoplasmacytic lymphoma. The patient was treated with bortezomib, dexamethasone, and cyclophosphamide, with complete recovery of renal function (creatinine 1.1 mg/dL).

Keywords: *Waldenström's macroglobulinemia, light cast chain nephropathy*

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1. Introduction

In 1944, Jan Waldenstrom described a novel non-Hodgkin's lymphoma characterized by lymphoplasmocyte, plasma cell, and small B cell proliferation within, among other sites, the bone marrow. The clinical entity, known today as Waldenström's macroglobulinemia (WM), is attributed to excess IgM production. The condition is uncommon with less than 1500 cases diagnosed annually in the US [1,2]. Presentation is non-specific and includes failure to thrive, grade B symptoms, and sequelae of hyperviscosity. Renal involvement is rare with an incidence of 3 cases per million people per year. A minority of patients are women, and only 5% are black. [3,4,5]. Herein, we report a case of an African-American woman diagnosed with WM by kidney biopsy.

2. Case Presentation

A healthy 63-year-old African-American lady presented to the hospital with a multiday history of nausea, vomiting, and cough. She was immediately diagnosed with influenza B and oseltamivir was administered. After three days of intravenous fluids and anti-viral therapy, she felt well and her appetite had returned. However, her creatinine continued to rise (3.5mg/dL from 1.8mg/dL upon admission) and nephrology was consulted. Upon interview, the patient reported a modest decline in appetite and 2-3 ibuprofen tablets in the days prior to admission. She reported no change in weight or grade B symptoms. She was otherwise in good health and without chronic medical conditions. She was normotensive. Daily urine output was greater than 1.5 liters. Physical examination was notable for the absence of hepatosplenomegaly, lymphadenopathy, or edema. Laboratory values (Table 1) upon presentation revealed a creatinine of 1.8 mg/dL, albumin of 2.7g/dL, and a corrected calcium of 9.5 mg/dL. Blood counts were within normal limits. Urine analysis and microscopy revealed 1+ protein and 2+ blood. The fractional excretion of sodium was 3.5%. Urine protein-to-creatinine ratio was 600mg/g. Ultrasonography showed 10cm kidneys without evidence of chronic disease. Given the history and preliminary data did not suggest glomerular disease, no further workup was pursued. On day eight, her creatinine reached 5.74 mg/dL and a kidney biopsy was performed.

Among the eight glomeruli obtained, four were sclerosed with tubular atrophy present involving approximately 40% of the renal cortex. The interstitium was fibrotic and the vasculature was preserved. Light microscopy showed normal glomeruli (Image 1) with no evidence of amyloid by Congo red stain. Tubular lumen was occluded by numerous PAS-negative casts (Image 2). Immunofluorescence showed intense (3+) staining for kappa light chains within the tubular casts. electron microscopy was unremarkable. The renal biopsy was

consistent with light chain nephropathy, likely from Waldenstrom's disease.

Table 1. Lab Values on Admission

Creatinine	1.78 mg/dL	0.6-1.2 mg/dL
BUN	15 mg/dL	7-25 mg/dL
Total protein	5.9 mg/dl	6.4-8.9 mg/dL
Uric acid	8.6 mg/dL	2.3-7.6 mg/dL
Serum albumin	2.7 g/dL	3.5-5.7 mg/dL
hemoglobin	12.1 g/dL	11.5-15.1 g/dL
Calcium	8.9 mg/dL	8.6-10.8 mg/dL
Hepatits C Virus Ab	Negative	
Hepatitis B	Negative	
HIV	Negative	
URINE		
FeNa	3.6%	
RBCs	2+	
WBCs	<5	
protein	1+	
protein	28 mg/dl	Normal range <12 mg/dl
creatinine	42 mg/dl	Normal range 29-226 mg/dl
protein to creatinine	0.66	

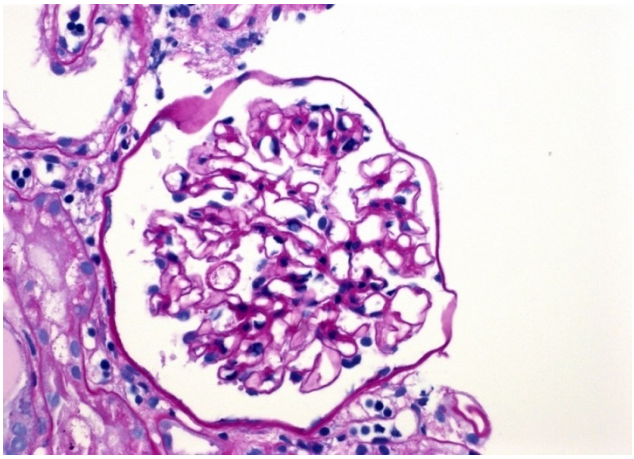

Image 1. Light microscopy: PAS staining, normal glomeruli

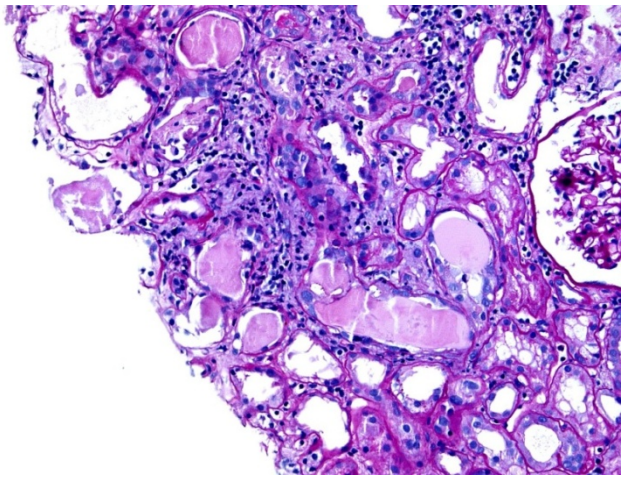

Image 2. Light microscopy, PAS staining, tubules filled with casts and lymphocytic infiltrates within tubules

Subsequent monoclonal studies identified an IgM kappa gammopathy with a size of xxx by SPEP. Free kappa light chain level of 41mg/dL (normal range 0.33-1.9 mg/dL) with kappa/lambda ratio of 10.9 (normal range 0.26-1.65). IgM level of 1,019 mg/dL (normal 45-281 mg/dl), Bence-Jones proteins were absent. Bone marrow histology demonstrated the involvement of a lymphoplasmacytic lymphoma or marginal zone lymphoma with plasmacytic differentiation. This was consistent with the diagnosis of Waldenstrom macroglobulinemia. Therapy with bortezomib, dexamethasone, and cyclophosphamide was initiated. At a three-month follow-up, her disease was in remission and creatinine returned to 1.1mg/dL.

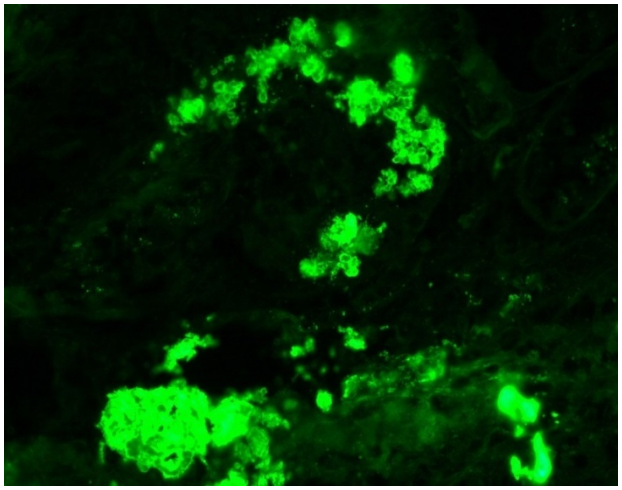

Image 3. immunofluorescence. Stained positive for kappa light chains

3. Discussion

Waldenstrom macroglobulinemia, also known as lymphoplasmacytic lymphoma first described in 1944 by JanWaldenström. It is a type of non-Hodgkin lymphoma (NHL) that produces a large amount of an abnormal protein (named a macroglobulin). Overall, renal manifestations are not commonly seen in WM. Approximately one-third of patients are asymptomatic at the time of diagnosis [6]. Like our patient who did not have renal symptoms and AKI discovered serendipitously. Nevertheless, nephrotic syndrome secondary to amyloid deposition and Light chain cast nephropathy has been reported in WM [7]. Another Immune-mediated glomerulonephritis, in consequence of cryoglobulinemia or IgM deposition, has been discussed [8]. Furthermore, there are anecdotal reports of deposits of IgM in the glomerular basement membrane that may be noticeable, and the infiltration of lymphocytes or plasmacytoid cells could occur [9,10]. Given the fact that the patient does not have a significant past medical history, with a steadily rising serum creatinine despite adequate hydration with bland urine analysis and urine microscopy. A decision was made to perform a renal biopsy at day six of hospitalization, which was consistent with a light chain cast nephropathy.

MYD88 is a molecule that plays a role in interleukin-1 receptor and Toll-like receptor signaling, which leads to expanded B cell survival. An activating point mutation of MYD88 L265P has been involved in the pathogenesis of Lymphoplasmacytic lymphoma. MYD88 mutation status was performed in these patients and was positive studies have shown that MYD88 L265P mutation is present in almost 70-90% of WM patients [11,12]. On the other hand, other studies indicated that 20-30% of patients also harbor

a CXCR4 WHIM mutation, which was not routinely performed in this patient [13,14]. FISH and cytogenetic studies were negative in our reported patient.

Studies showed that patients with considerable renal poorly functioning at presentation have a propensity to have worse outcomes than those without, despite aggressive therapy [15]. In contrast, reported rates of full renal recovery following adequate treatment are almost more than 50 percent [16]. Patients with reversibly renal failure had longer median survival compared with patients who did not restore renal function [17]. Our patient kidney function recovered completely three months following chemotherapy and supportive therapy.

In summary, we report the etiology, genetic association, response, and outcome of a rare renal involvement observed in a patient with WM with complete renal recovery. Further studies to define tailored management for WM with kidney involvement are warranted.

Abbreviation

WM: Waldenström's macroglobulinemia
IG: Immunoglobulin
PAS: Periodic Acid Schiff
NHL: non-Hodgkin lymphoma
AKI: Acute Kidney Injury.

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