Lymphomatous Infiltration of the Kidney Associated with Glomerulopathy Presenting as Acute Renal Failure

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Acute renal failure due to diffuse bilateral parenchymal infiltration is a rare initial manifestation of lymphoma [1]. Paraneoplastic glomerulopathy is described in the literature as a complication of malignancy, including lymphoma [2]. Prompt recognition of lymphoma as the cause of nephropathy is crucial since it is potentially a treatable disease and responds well to chemotherapy.

We describe here a rare case of acute renal failure due to diffuse lymphomatous infiltration of the kidneys associated with glomerulopathy of mesangial proliferative glomerulonephritis with crescent formation in 3 of 13 glomeruli, presenting as the first manifestation of lymphoma. Chemotherapy resulted in rapid improvement of renal function and disappearance of the nephritic sediment. To the best of our knowledge this is the first report in the literature of simultaneous occurrence of interstitial and glomerular renal involvement in lymphoma.

Patient Description

A 55 year old man was admitted to the internal medicine department because of general weakness, weight loss (10 kg over a 6 month period), macroscopic hematuria, nasal bleeding and progressive renal failure. Serum creatinine was 1.1 mg/dl (97.24 μmol/L) and 1.5 mg/dl (132.6 μmol/L) 4 years and 8 months respectively, prior to his current admission. The patient reported that he had suffered several episodes of macroscopic hematuria and renal colic 4 years previously. At that time, ultrasound examination raised the suspicion of a small stone in the left kidney, which was not present on repeated ultrasound a few days after the renal colic resolved.

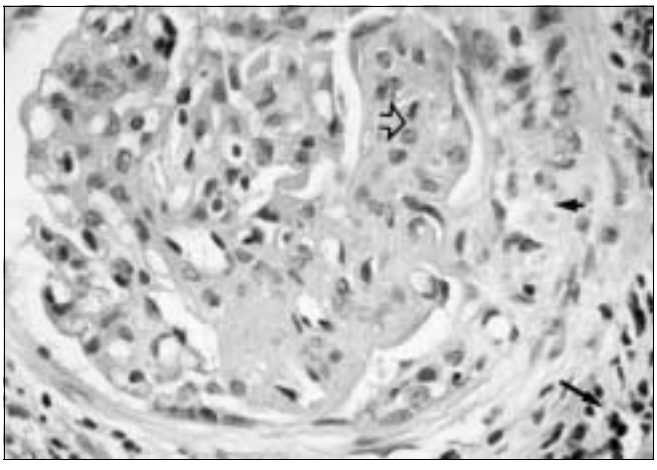
On physical examination the patient did not appear to be in any distress. Blood pressure was 130/80, heart rate 82 beats/minute, the lungs were clear and the neck veins flat. The liver was of normal size and the tip of the spleen was palpable. Several axillary lymph nodes, 1 cm in size, were palpated bilaterally. Complete blood count showed leukocytosis 17.0 x 10^9/L, lymphocytes 43%, normocytic normochromic anemia with hemoglobin 9.4 g/dl, mild thrombocytopenia 119×10^9/L and rouleaux formation. Urinalysis showed macroscopic hematuria with many dysmorphic red blood cells, red blood cell casts, granular casts and 2+ positive dipstick for protein. Urinary protein excretion was 1.66 g/24 hours and the test for urinary Bence-Jones protein was negative. Initial serum biochemistry results were: urea 254 mg/dl (90.7 mmol/L), creatinine 10.16 mg/dl (898.1 mol/L), calcium 7.4 mg/dl (1.85 mmol/L), phosphorus 8.1 mg/dl (2.6 mmol/L), albumin 38 g/L, and globulin 55 g/L. Serum protein electrophoresis revealed polyclonal hypergammaglobulinemia 32.6% (normal range 10–19%). Serology for C3, C4, rheumatoid factor, antinuclear antibodies and ANCA was normal. Serology for hepatitis B and C was negative. Chest X-ray was normal. Renal ultrasound revealed normal sized kidneys without signs of hydronephrosis. Computed tomography of the abdomen and chest (not shown), performed without contrast dye, showed evidence of bilateral axillary lymphadenopathy, mild mediastinal lymphadenopathy, small left para-aortal lymph nodes, splenomegaly and two kidneys of normal size and position. Bone marrow biopsy demonstrated predominantly B cell lymphocytosis and was consistent with involvement by a small lymphocytic lymphoma. A kidney biopsy demonstrated severe focal interstitial infiltration with small atypical lymphocytes positive for CD20-B cells. Most glomeruli showed proliferation of mesangial cells and expansion of mesangial matrix [Figure]. Of 13 glomeruli 3 had a crescent formation and 1 had foci of fibrinoid necrosis. Two glomeruli showed lobulation, synechia, thickening of membranes, expansion of mesangial matrix and proliferation of mesangial cells. Immunofluorescence microscopy revealed weak IgG staining in mesangial and paramesangial areas, and granular C3 staining in mesangial areas. On electron microscopy two glomeruli showed expansion of mesangial matrix with accumulation of electron-dense material and proliferation of mesangial cells.

The diagnosis of small cell lymphocytic lymphoma grade 4 was confirmed by axillary lymph node biopsy. The patient was started on CHOP chemotherapy (cytoxan, adriamycin, vincristine, prednisone). Six months later urea had decreased to 54.3 mg/dl (20.35 mmol/L) and creatinine to 1.69 mg/dl (149.4 μmol/L).

Comment

In this report we describe a patient with lymphoma presenting as acute renal failure with nephritic sediment. The presence of nephritic urinary sediment in the context of acute renal failure suggests acute or rapidly progressive glomerulonephritis. However, weight loss, splenomegaly, lymphadenopathy, peripheral lymphocytosis and roleaux formation, as well as polyclonal hypergammaglobulinemia suggested hematological malignancy subsequently confirmed to be small cell lymphocytic lymphoma.

Acute renal failure is rare in malignant lymphomas, with an incidence reported to be as low as 0.5% [3], and appears even more rarely as the first clinical manifestation of the lymphoma [1]. LIK is the most common extra-nodal site for metastatic lymphoma and has been observed in 34% of 696 autopsies [3]. However, in only 14% of 142 patients was LIK diagnosed prior to death [3] and in only 2.7–10% by radiological studies [4], reflecting the generally silent course and late occurrence of LIK manifestations. Gross hematuria was detected in only 18% of cases of renal failure due to LIK [5] and was believed to be the result of hemorrhagic necrosis of the kidney [1]. In our patient the hematuria was feasibly of glomerular origin because of the presence of dysmorphic red blood cells and red blood cell casts, and the glomerular lesion found on kidney biopsy that was consistent with mesangioproliferative glomerulonephritis with few crescents. Paraneoplastic glomerulonephritis asso-



Glomerulus with cellular crescent (head of arrow), expansion of mesangial matrix with mild mesangial proliferation (open arrow), and severe focal renal interstitial infiltration by small atypical lymphocytes (black arrow).

ciated with lymphoma is a well-known clinical entity [2]. The most frequent glomerulopathies associated with non-Hodgkin lymphoma are membranoproliferative and crescentic glomerulonephritis [2]. In our patient the glomerular lesion consisted of a unique combination of mesangioproliferative glomerulonephritis with local crescent formation. Our impression was that the macroscopic hematuria a few years before was due to stone disease. Our belief that glomerular lesion in this patient was probably of paraneoplastic nature is supported by the fact that his dysmorphic macroscopic hematuria rapidly disappeared after introduction of anti-tumor therapy. The presentation of severe acute renal failure in this patient was probably the result of the unusual combination of glomerular and tubulointerstitial involvement.

In conclusion, we present an unusual combination of glomerulonephritis and lymphomatous infiltration of the kidneys induced by lymphoma presenting as acute renal failure with nephritic urinary sediment.

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