

# Acute Renal Failure and Bilateral Kidney Infiltration as the First Presentation of non-Hodgkin Lymphoma

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Diffuse bilateral infiltration of the kidneys by lymphoma is probably the rarest cause of renal insufficiency. Moreover, acute renal failure as the initial manifestation of the lymphoma is reported only in a few cases. A 44-year-old man complaining of bilateral flank pain and weakness for 2 months was admitted with acute renal failure. Ultraonography revealed hyperechoic bilaterally enlarged kidneys and an enlarged spleen. Fat pad aspiration was negative for amyloidosis and serum protein electrophoresis was normal. Needle biopsy of the kidney and pathologic examination showed diffuse infiltration of the interstitium with lymphocytes and atypical cells. Bone marrow aspiration and biopsy were negative for malignant cells. Open kidney biopsy was performed and infiltrated cells positive for CD20 and negative for CD3 markers were observed based upon which diagnosis of diffuse large B-cell type non-Hodgkin lymphoma was made.

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## INTRODUCTION

Infiltration of the kidneys with primary renal lymphoma is very rare, because this organ is normally free of lymphoid tissue.<sup>1</sup> Renal involvement with bilateral infiltration is often secondary to rapid-growing hematological malignancies such as systemic lymphoma or acute leukemia.<sup>2,3</sup> Widespread infiltration of the kidney is present in almost one-third of patients with lymphoma at autopsy,<sup>4</sup> but acute renal failure is an unusual manifestation of lymphoma infiltration of the kidney and is rarely the presenting sign of a hematological malignancy.<sup>4,5</sup> In this report, we describe a patient whose initial presentation of lymphoma was acute renal failure and bilateral enlarged kidneys.

## CASE REPORT

A 44-year-old man was admitted to our hospital with acute renal failure. He complained of bilateral flank pain, weakness, and anorexia since 2 months earlier. He was a cigarette smoker (20 pack.years)

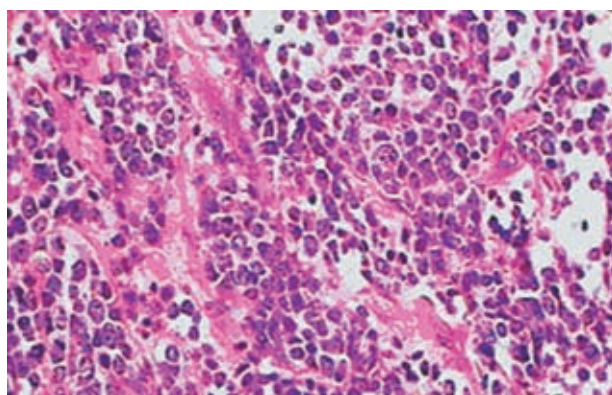
and he had once been exposed to a chemical product (mustard chemical weapon) during the war between Iran and Iraq in 1980s.

Physical examination revealed a blood pressure of 140/70 mm Hg, a heart rate of 80 beats per minute, and a body temperature of 36.9°C. The examination was remarkable for left upper quadrant tenderness and splenomegaly, but neither hepatomegaly nor lymphadenopathy was present. Laboratory data disclosed a leukocyte count of  $12 \times 10^9/L$  (75% neutrophil, 4.5% lymphocyte, 18% monocyte, and 1.5% eosinophil) and a platelet count of  $220 \times 10^9/L$ . Serum creatinine concentration was increased to 5.5 mg/dL. Other laboratory data were as follows: hemoglobin, 13.1 g/dL; hematocrit, 40%; blood urea, 200 mg/dL; and serum uric acid, 7 mg/dL. Liver enzymes, plasma bilirubin, and coagulation tests were in their reference ranges. Urinalysis showed 6 to 8 erythrocytes and 3 to 4 leukocytes per high-power field, but there was no cast on urine microscopy, and no discrepancies between

dipstick and sulfosalicylic acid results was seen. Twenty-four-hour urine contained 900 mg of protein. Serum and urine protein electrophoresis for light chain and monoclonal gammopathy were negative.

Renal and abdominal ultrasonography showed bilateral enlarged kidneys (right kidney, 160 × 77 mm; left kidney, 153 × 76 mm) and splenomegaly (142 mm). Computed tomography showed no abnormality in the chest and the mediastinum, but bilateral enlarged kidneys without hydronephrosis and a large spleen in the abdomen and pelvis. There was no lymphadenopathy in the hilum of the kidneys or the retroperitoneum (Figure 1). Peripheral blood smear, fat pad aspiration for amyloid substance, bone marrow aspiration, and bone marrow biopsy were all negative for amyloidosis and malignancy. Needle biopsy of the kidney was performed and light microscopy revealed infiltration of the interstitium and atypical cells with normal glomeruli. Then, open-wedge biopsy was performed, and heterogeneous neoplastic cells were observed on pathologic examination (Figure 2). However, large cells with vesicular and prominent nucleoli were prominent. Immunohistochemistry showed infiltrated cells positive for CD20 and leucocyte common antigen, and negative for CD3, CD15, and CD30 markers. According to these, malignant diffuse large B-cell type non-Hodgkin lymphoma was diagnosed.

The patient was treated with cyclophosphamide, doxorubicin, vincristin, and prednisolone, in combination with rituximab. Six to 8 cycles of

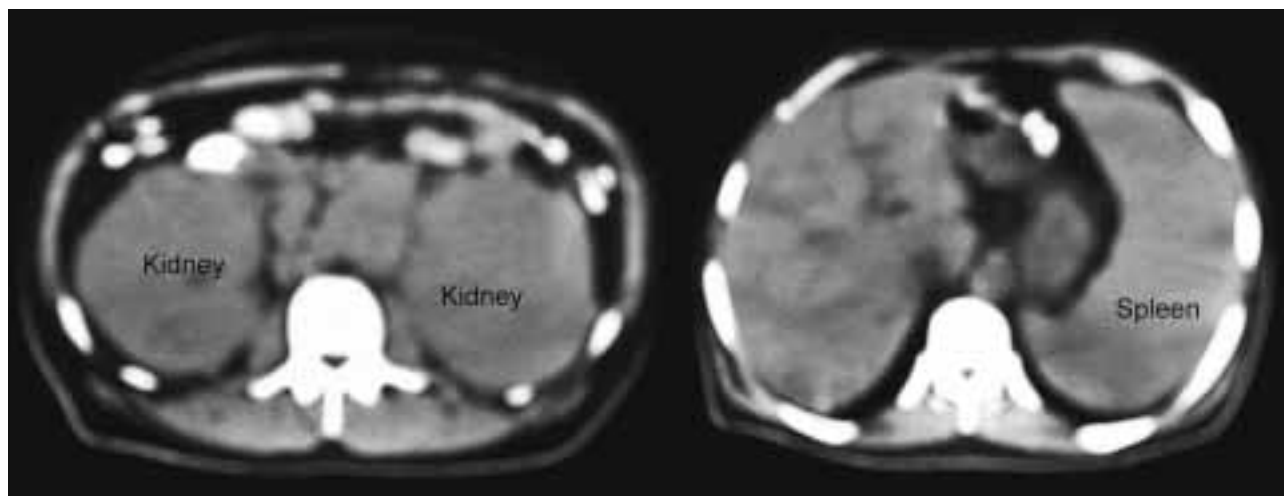


**Figure 2.** Atypical monomorph lymphoid infiltration with large nuclei (hematoxylin-eosin, × 300).

therapy with a combination of chemotherapy and hemodialysis were planned, but the patient died due to septic shock 6 weeks later after initiation of the treatment.

#### DISCUSSION

The absence of other causes of acute renal failure together with massive enlarged unobstructed kidneys on renal ultrasonography strongly suggested an infiltrative process in our patient, and biopsy of the kidney established the diagnosis of non-Hodgkin lymphoma (diffuse large B-cell type). This type of the disease is one of the clinically aggressive and the most common histologic subtypes that constitutes about 30% of all non-Hodgkin lymphomas.<sup>6</sup> Lymphomas are usually of B-cell or T-cell subtype, and peripheral T-cell lymphoma, which usually occurs in patients aged 60 years or older, can most often involve the kidney



**Figure 1.** Left, Bilateral enlarged kidneys without hydronephrosis. Right, Huge splenomegaly.

as a systemic process. Immunohistochemistry pattern, however, will show B-cell infiltration which is less consistent with primary renal B-cell lymphoma.

Patients with non-Hodgkin lymphoma who are generally middle-aged or older (mean age of 64 years) typically present with rapidly enlarging symptomatic mass which is usually due to nodal enlargement, specially in the neck or the abdomen; however, the disease may present with extranodal involvement in 40% of cases including upper gastrointestinal tract, colon, testis, breast, nasal cavity, and paranasal sinuses.<sup>7-10</sup> The kidneys may be involved during the course of the disease. Renal involvement is more common in non-Hodgkin lymphoma than in Hodgkin disease.<sup>11</sup> However, glomerular disease is diverse and more common in Hodgkin disease. In both types, the most common characteristic lesion is minimal change disease.<sup>11</sup>

There are many different causes of impairment of kidney function in patients with lymphoma, including direct effects (eg, obstruction of the ureters and infiltration of the kidneys), indirect effects (eg, hypercalcemia, tubular obstruction by light-chain precipitation, and amyloidosis), and treatment-related effects.<sup>2-4,12</sup> Spread of the primary tumor to the kidney is not uncommon. However, involvement severe enough to impair kidney function is unusual and occurs primarily with hematological malignancies such as lymphoma.<sup>12</sup> Rarely, kidney failure is the presenting sign of lymphoma, and probably kidney failure due to bilateral infiltration of the kidneys is the rarest cause of acute renal failure in lymphoma.<sup>13,14</sup>

Most patients with lymphomatous infiltration of the kidney have no clinical evidence of renal involvement. When present, renal manifestations are nonspecific and may include flank pain, hematuria, abdominal distention or a palpable mass, and hypertension presumably resulting from renal ischemia caused by compression by the tumor. Urinalysis usually reveals mild proteinuria, few erythrocytes and leukocytes, and occasional hyaline and granular casts.<sup>15</sup> In our patient, obstructive nephropathy was promptly excluded by ultrasonography. The absence of extreme hyperuricemia (serum uric acid >20 mg/dL), oliguria, and uric acid crystals in the urinary sediment argued against acute urate nephropathy. Compression of the renal arteries by lymphoma was

ruled out by the absence of severe hypertension, and there was no sign such as ascites or anuria suggesting rupture of the renal pelvis or the ureters. In addition, serum protein electrophoresis did not reveal monoclonal gammopathy, and there were no light chains on pathologic examination.

Kidney biopsy is indicated in patients in whom examination of the lymph nodes or bone marrow fails to confirm the diagnosis, as well as in those in whom tissue sources are not easily accessible. Kidney biopsy not only established the diagnosis in our patient, but also provided valuable information regarding the immunophenotype of the lymphoma and allowed prompt initiation of therapy.

In conclusion, although kidney failure as a result of lymphomatous parenchymal infiltration is uncommon, it should be suspected in any patient presenting with unexplained acute renal failure and enlarged kidneys, especially if the patient is known to have lymphoma.

#### CONFLICT OF INTEREST

None declared.

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