Bilateral Primary Renal Lymphoma

Kenneth Richard Kindle, DO, V.O. Speights, DO, and Craig Warren Clanton, MD

The frequency of immunodeficiency syndromes and patients at risk for these syndromes is increasing. These patients can come to their family physicians with unusual infections and neoplasms. The following is a case of an unusual disease, primary renal lymphoma, in a patient with a history of drug abuse and chronic hepatitis. Primary renal lymphoma, a lymphomatous involvement of the kidney with no detectable lymphoma elsewhere in the body, is unusual in that the renal parenchyma is normally devoid of lymphoid tissue. We describe a case of bilateral primary renal lymphoma in which the patient experienced acute renal failure. In addition, we briefly review the cases described in the literature.

Case Report

A 49-year-old man, who had a history of ethanol and intravenous drug abuse, came to his family physician complaining of right flank pain, dysuria, and gross hematuria of 10 days' duration. He had no fever, night sweats, or weight loss. His physical examination was remarkable for right upper quadrant and right flank tenderness. The patient responded with voluntary guarding, but there were no peritoneal signs, hepatosplenomegaly, or lymphadenopathy.

The patient was admitted to the hospital for further tests. The initial laboratory data are summarized in Table 1. Because of the predominant urinary symptoms, the examination focused on the genitourinary tract. An upright abdominal radiograph was negative for renal lithiasis. A renal sonogram showed a rounded, hypoechoic lesion measuring 2.8 cm in the midpole of the left kidney and a similar 2-cm lesion in the right kidney. There was no hydronephrosis. Computed tomography (CT) showed many abnormal soft tissue densities involving both kidneys (Figure 1). In addition, there were rounded areas of abnormal decreased attenuation within the right and left lobes of the liver; both of these lesions measured approximately 4 cm in diameter. The multiple lesions suggested metastatic disease. Lung neoplasm, melanoma, and lymphoma were considered probable causes.

Results of a CT-directed needle biopsy of the liver showed chronic active hepatitis on two separate procedures, with no evidence of malignancy. CT-directed needle biopsies of the kidney showed an infiltrating tumor mass that surrounded a number of residual glomeruli and tubules (Figure 2). The tumor cells had enlarged, and irregular hyperchromatic nuclei with some scattered nucleoli but minimal cytoplasm were noted. Because undifferentiated carcinomas can sometimes mimic lymphoma histologically, immunohistochemical stains were performed using well-established methods. The keratin AE1-3 (Hybritech, San Diego, CA) was negative, indicating that the tumor

Table 1. Laboratory Data.

Test	Patient Value	Normal Value
Complete blood count		
Leucocytes (mm^3)	8600	4800–10,800
Hemoglobin (g/dL)	12.3	13.0–18.0
Hematocrit (%)	36	39–54
Urinalysis		
Leucocytes (/hpf)	0–2	0
Erythrocytes (/hpf)	2–5	0
Casts	0	0
Protein	0	0
Serum chemistries		
Sodium (mEq/L)	141	136–145
Potassium (mEq/L)	4.6	3.5–5.3
Bicarbonate (mEq/L)	27	22–33
Calcium (mg/dL)	8.1	8.4–10.3
Phosphorus (mg/dL)	4.2	2.5–4.2
Uric acid (mg/dL)	9.2	2.4–7.9
Blood urea nitrogen (mg/dL)	15	10–20
Creatinine (mg/dL)	2.0	0.4–1.4
Albumin (g/dL)	2.6	3.0–5.5
Total protein (g/dL)	6.1	6.0–8.5
Liver enzymes		
Aspartate aminotransferase	63	0–40
γ-glutamyl transferase	75	0–65
Lactate dehydrogenase	321	60–200

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From the Departments of Family Medicine (KRK, CWC) and Pathology (VOS), Scott & White Clinic and Memorial Hospital, Scott, Sherwood and Brindley Foundation, Texas A&M University College of Medicine, Temple. Address reprint requests to V.O. Speights, DO, Scott & White Clinic, 2401 South 31st Street, Temple, TX 76508.

Figure 1. A computed tomography section shows irregularly shaped kidneys and multiple soft tissue densities.

was not a carcinoma. The common leukocyte antigen stain was strongly positive in the tumor cells, which indicated that they were of hematopoietic origin. The cells stained universally positive for the L26 marker (Dako, Carpinteria, CA), which is a marker for B lymphocytes. The cells stained negative for UCHL-1 (Dako, Carpinteria, CA), which is a T lymphocyte marker. These findings were indicative of the monoclonal population of a B-cell lymphoma.

Additional evaluation for metastatic disease included a bone marrow biopsy, which was negative for lymphoma. Findings from chest radiogram, pelvic CT, and urine protein electrophoresis studies were unremarkable. In addition, the human immunodeficiency virus test by the ELISA method was nonreactive and remained nonreactive during chemotherapy. As a result, the Western blot test was not performed. The antihepatitis C virus test was reactive, which indicated a past or recent infection.

On day 3 of hospitalization, the serum creatinine was 5.6 mg/dL. The patient was thought to have acute renal failure secondary to lymphomatous infiltration of the renal parenchyma. A 12-week chemotherapeutic regimen was initiated that included adriamycin, cyclophosphamide, etoposide, vincristine, and bleomycin. The patient had a dramatic improvement in renal function, and his serum creatinine returned to normal 4 weeks into therapy. A CT scan showed complete resolution of the renal lesions 4 weeks into therapy. Eighteen months after the diagnosis, the patient remained in clinical remission.

Discussion

A diagnosis of primary renal lymphoma requires lymphoma to be present in the kidney with no detectable lymphoma elsewhere in the body. Since a 1987 summary of 28 cases was published,[1] 12 additional cases have been reported. After reviewing the literature, we concluded that not all cases were primary renal lymphoma. Exclusion of cases with evidence of extrarenal disease by autopsy or surgical exploration would greatly reduce the

Table 2. Cases of Primary Renal Lymphoma.

Reference	Sex, Age (years)	Histology	Kidney(s) Involved	Treatment	Confirmation
Kandel, et al.[1]	M, 76	Large immunoblastic	L	N, C	SE, BM, R
Truong, et al.[2]	M, 59	Large cleaved	B	C	BM, R
	M, 26	Large cleaved	B	C	BM, R
Osborne, et al.[3]	M, 71	Large cell	L	C, R	BM, R
Leoncini, et al.[4]	M, 47	B cell	Rt	N, C	SE, BM, R
	F, 50	B cell	B	C	BM, R
Barr, et al.[5]	M, 61	Large cell	B	C	BM, R
Clifton & Baily[6]	M, 48	Lymphoplasmacytoid	Rt	Unknown	BM, R
Sheil, et al.[7]	F, 29	B cell	L	C	BM, R
Knoepp[8]	M, 58	Lymphosarcoma	Rt	N, RT	SE
Silber & Chang[9]	F, 57	Large cell	Rt	N, RT	SE, BM, R
Harris & Lager[10]	M, 80	Mixed	L	N, RT, C	SE, BM, R
Our case	M, 49	B cell	B	C	BM, R

Rt = right, L = left, B = both, N = nephrectomy, RT = radiation therapy, SE = surgical exploration, BM = bone marrow, C = chemotherapy, R = radiographic.

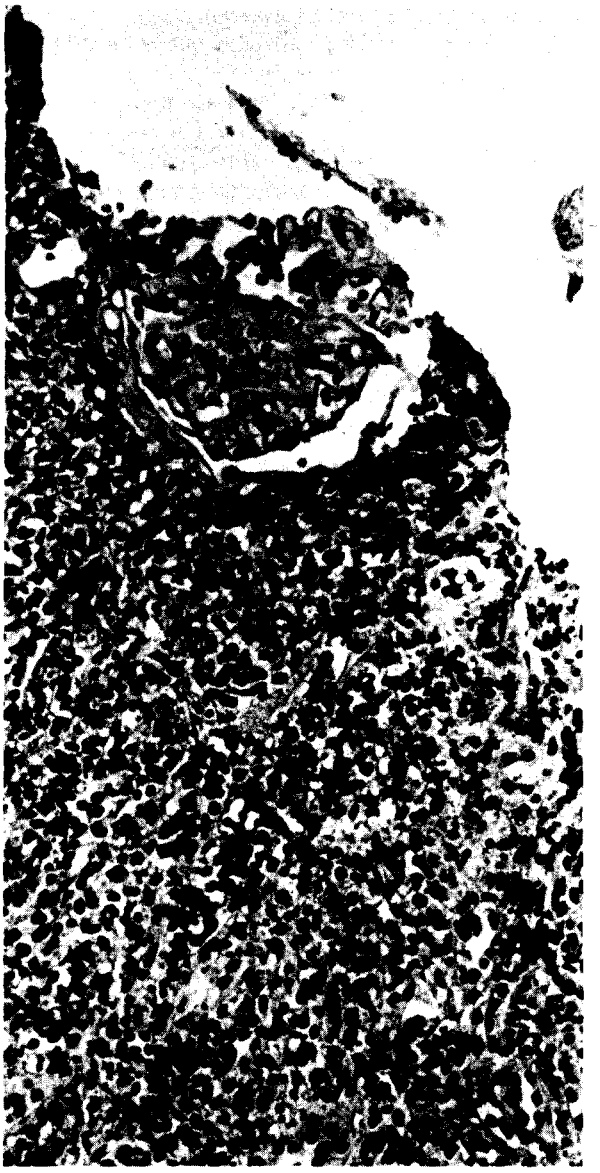

Figure 2. Renal biopsy shows heavy infiltration by large neoplastic lymphoid cells surrounding a glomerulus (Hematoxylin and eosin stain, 100 × magnification).

number of cases of purported primary renal lymphoma (Table 2).[1-10] Primary renal lymphoma was confirmed by modern radiographic techniques and bone marrow biopsy in seven reported cases.[2-7] Primary renal involvement was confirmed by surgical exploration in five reported cases,[1,4,8-10] and one was confirmed by autopsy.[11]

Although only 3 percent of all patients scanned during routine staging of known lymphoma have evidence of renal involvement,[12] autopsy studies have shown a 47 percent incidence of renal involvement of malignant lymphoma.[13] Primary renal lymphoma has been disputed because the kidneys are thought to be devoid of lymphoid tissue. It has been postulated that lymphoid cells are harbored in the kidney as a result of chronic inflammation. An alternate source could be the capsule, which is rich in lymphatics.[7] Whether the first malignant cell originates in the renal parenchyma or migrates to the kidney from another hematopoietic tissue is undetermined.

Primary renal lymphoma is usually not suspected in the work-up of a renal mass or masses. The renal lesions in our case were multiple and bilateral. Bilateral renal masses can be primary or secondary, benign or malignant. Bilateral disease occurs in only 1 percent of the most common renal cell carcinoma, whereas 50 percent of metastatic renal disease is bilateral.[4] Of the reported cases of primary renal lymphoma outlined in Table 2, many are bilateral.

Our case was one of five that involved acute renal failure. Lymphomatous infiltration is a rare cause of acute renal failure. The usual causes have included dehydration, hypercalcemia, sepsis, amyloidosis, drug-induced nephropathy, or those secondary to complications of treatment.[14,15] Because no other potential causes of acute renal failure were found in our case, we concluded that the acute renal failure must have been the result of lymphomatous infiltration. The dramatic return of renal function following chemotherapy would also support that assertion.

It was interesting to note that the liver lesions improved following chemotherapy. The liver enzymes remained elevated, however. The CT-directed needle biopsies of the liver on two separate occasions showed no evidence of malignancy. Nevertheless, lymphomatous involvement cannot be unequivocally eliminated.

Conclusion

Malignant lymphomas occurring in extranodal sites have been rare. Their frequency is increasing, however, because of the spread of human immunodeficiency virus.[16] Although this patient had a history of drug abuse, he was not infected with the human immunodeficiency virus. The relation of hepatitis C to lymphoma is uncertain. Family physicians should be aware of the possibility of lymphoma appearing in the kidney or other extranodal sites, especially in patients with a history of drug abuse or other risk factors for immunosuppression. Primary renal lymphoma should be

included in the differential diagnosis for a renal mass or masses. As is typical in other reported cases of primary renal lymphoma, in our case no extrarenal involvement could be found using modern techniques. Bilaterality of disease and acute renal failure are commonly associated with primary renal lymphoma. Because effective chemotherapeutic regimens are available for non-Hodgkin's lymphoma, a biopsy of a renal lesion can prevent unnecessary surgery.

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