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Bilateral Primary Renal Lymphoma Presented As Homogenous Renal Enlargement And Acute Interstitial Nephritis.

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INTRODUCTION

Primary renal lymphoma(PRL) is an extremely rare form of extranodal lymphoma and exhibits as single (10-20%), multifocal nodules (60%), renal invasion from contiguous retroperitoneal disease (25-30%), diffuse infiltration (20%) or perirenal involvement (10%)[1]. Here we report a case of bilateral primary renal lymphoma in a 13 year-old boy who presented with homogenous nephromegaly and acute interstitial nephritis(AIN). The renal biopsy revealed primary renal T lymphoblastic lymphoma. Hyper-CVAD regimen was initiated and the renal function had been recovered after the first round of chemotherapy. To our knowledge, there have only been three reports of primary renal T lymphoblastic lymphoma including ours so far. All the three patients were young and showed as AIN and bilateral renal enlargement. We also reviewed 16 cases of PRL presenting with AIN and enlarged kidneys that have been reported since 1997. Although PRL is quite rare, it must be taken into account when making a differential diagnosis of AIN. Renal biopsy is the gold standard and intensive chemotherapy can preserve the renal function.

CASE REPORT

A 13-year old boy without any medical history was admitted to our department for fatigue, anorexia, arthralgia and weight loss. Careful physical examination revealed a low-grade fever(38.2°C) and boggy swelling of his joints. There was no peripheral lymphadenopathy or hepatosplenomegaly. The routine blood tests showed elevated

serum creatinine of 3.31mg/dl, uric acid of 42.62mg/dl and lactate dehydrogenase of 367U/L. He had hemoglobin of 103g/l, platelet count $185 \times 10^9/L$, white blood cell count $10.01 \times 10^9/L$ with a differential of 70.4% neutrophils. Twenty-four hour urinary protein was 385mg/dL. Urine analysis revealed the trace protein and no red blood corpuscle. The peripheral blood smear showed no abnormal findings. Abdominal ultrasonography revealed bilateral renal symmetrical enlargement with lengths of 14cm and medulla spongy appearance.

The renal biopsy was performed and showed a diffuse interstitial infiltration with lymphomatous cells compressing tubules and surrounding preserved glomeruli. Additional stainings confirmed T-lymphoblastic lymphoma with CD3+ and CD1a+. Ki-67 stained more than 90% of the cells indicating a high-growth fraction(Figure 1). FDG PET-CT showed a diffusely intense FDG uptake in both kidneys with a standard uptake value of 4.84 and intense patchy uptake in the bone marrow of multiple bones in axial and appendicular skeleton (Figure 2). Bone marrow biopsy evaluation identified 16% lymphoblasts. Flow cytometry of the bone marrow identified a large population of cells expressing CD1a and Tdt. Cerebrospinal fluid specimen analysis was interpreted as unremarkable. Combining the clinical and pathological findings, the patient was diagnosed with primary renal T lymphoblastic lymphoma. Intensive systemic chemotherapy with hyperfractionated cyclophosphamide, vincristine, theraurubicin and dexamethasone (hyper-CVAD) and intrathecal chemotherapy were determined as appropriate treatment. Three weeks after the chemotherapy, a repeated ultrasonography showed the lengths of both kidney decreased to 11cm. His serum creatinine was

1.23mg/dL and uric acid was 6.65mg/dL. The patient's renal function and uric acid kept normal until the last visit. Unfortunately, he died of pulmonary infection after allogeneic bone marrow transplantation at 17 months after diagnosis.

DISCUSSION

Acute interstitial nephritis has a large variety of etiologies including drugs, infections, autoimmune disorders and hematological diseases. Although extremely rare, acute interstitial nephritis can be a primary clinical manifestation of renal lymphoma. Drug-induced or allergic interstitial nephritis and other systemic diseases (IgG4 related disease, Sjogren syndrome etc.) should be considered in the differential diagnosis with PRL presenting with massive lymphomatous infiltration. Criteria to diagnose PRL can be concluded by the following four features: renal enlargement, lymphomatous infiltration, no nodal or extranodal involvement, and improved renal function after chemotherapy[2,3]. PRL is quite rare as no more than 70 cases have been reported so far[4]. Due to a relatively aggressive behavior and delayed diagnosis, most of the patients had a poor prognosis[5]. Therefore, the early diagnosis and rapid intensive treatment are essential to preserve the renal function.

Majority of patients with T-LBL present with stage IV disease (80%), B symptoms (50%) and elevated serum lactate dehydrogenase (LDH) levels[6]. There have been only two cases of primary renal T lymphoblastic lymphoma[7,8], both with young age and enlarged kidneys, which were similar with ours. Our patient had severe hyperuricemia without hyperkalemia, hyperphosphatemia or hypocalcemia, are probably due to the high metabolite state of tumor cells, other than the tumor lysis

syndrome. FDG PET-CT is an unspecific tool for the diagnosis of lymphoma due to that physiologic FDG excretion in the kidneys makes the interpretation of the tracer uptake in this organ difficult. However, it shows superiority on the diagnosis of primary renal lymphoma by excluding the nodal or extranodal lymphoma and staging of the disease.

The present study reviewed 16 cases of bilateral primary renal lymphoma presenting with acute interstitial nephritis since 1997[7-22](Table 1.). There were more male patients than female patients, with a gender ratio of 11:5. These patients aged from 5 to 70 years old, of which 10 were young patients (age <28 years). Weight loss(7/16), fever(7/16) and flank or abdominal pain(5/16) are most common symptoms. The average renal size was 15.6cm. Most of the patients had increased LDH level. Three patients combined with HCV, HBV or HIV infections. Preponderance of the cases(11/16) are B-cell lineage, and diffuse large B cell lymphoma are the most common histological type(8/16). After chemotherapy, most patients had improved renal functions. However, their prognoses were not clear with limited information.

It was postulated that the pre-existing inflammation recruits lymphoid cells into the renal parenchyma[27]. However, the exact mechanisms underlying the different patterns of malignant cells infiltrating to the kidney (diffuse or focal, bilateral or unilateral) remain unknown. Bilateral primary renal lymphoma presented as acute interstitial nephritis and symmetrical nephromegaly is believed to be a unique entity with specific manifestations of acute kidney injury and elevated LDH and uric acid level. In this setting renal biopsy and FDG PET-CT are useful modalities greatly contributing to the early diagnosis of PRL.

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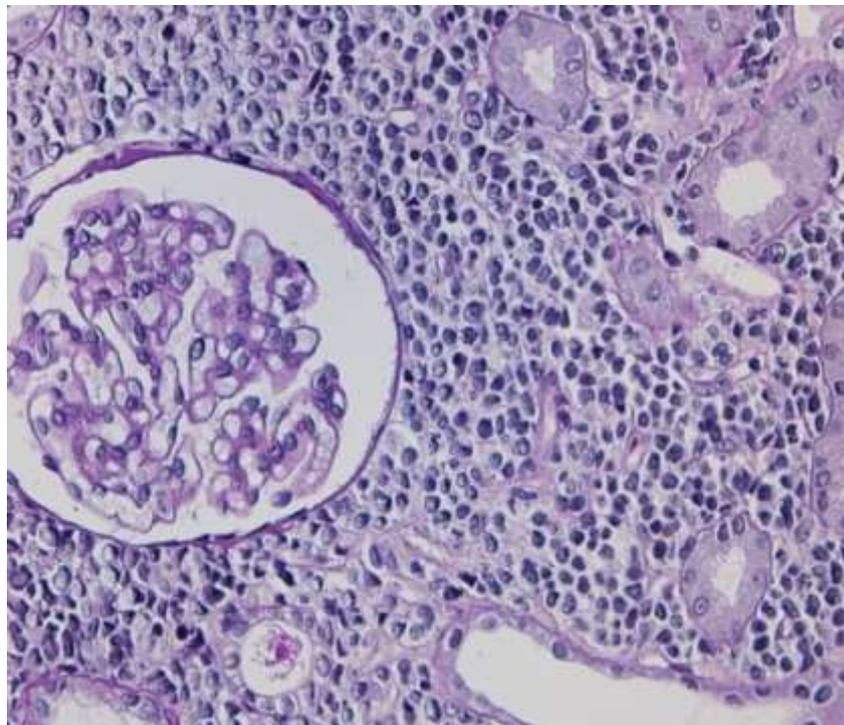


Figure 1. Histopathological examination of core biopsy specimen showing diffuse infiltration of interstitium by monomorphic atypical lymphocytes(H&E, x200 magnification)

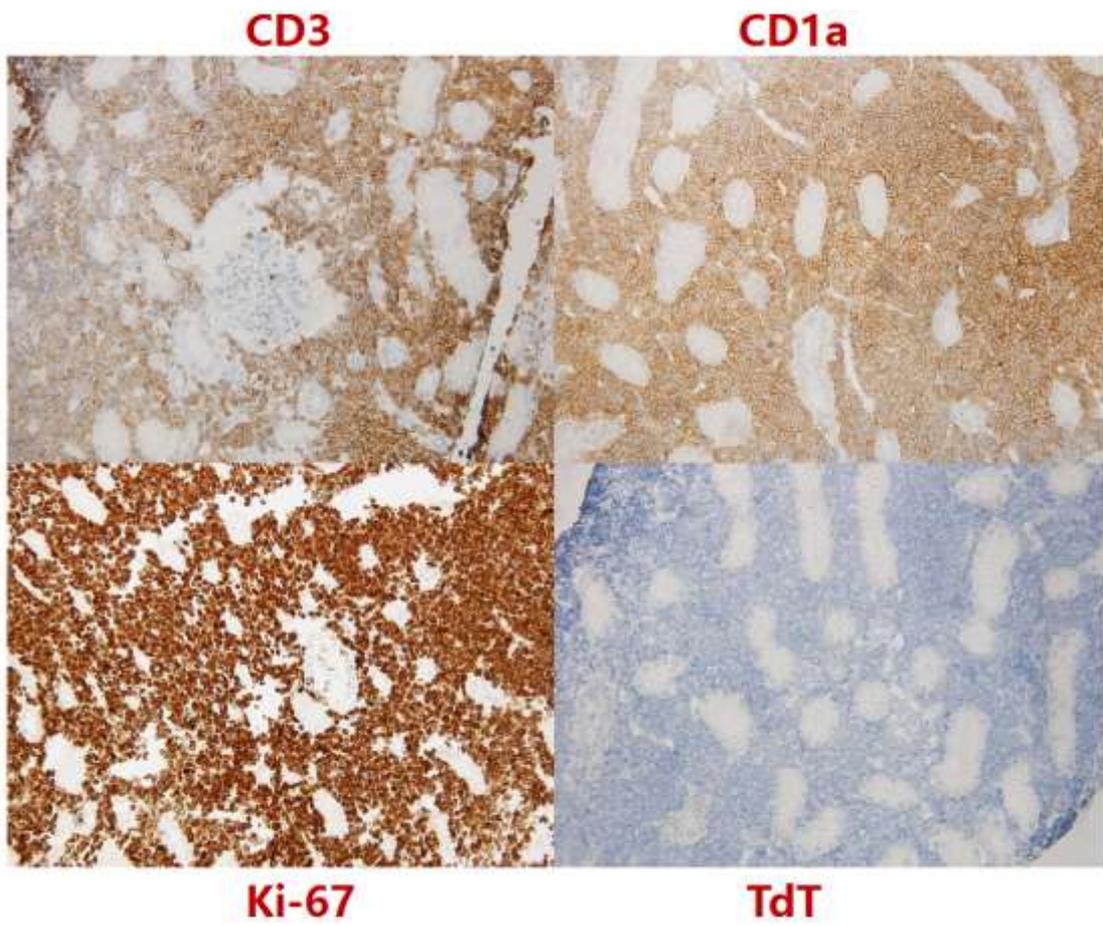


Figure 2. Immunohistological stainings showed that the neoplastic cells were positive for CD3+,

CD1a+ and Ki-67 and negative for Tdt. (x200 magnification).



Figure 3. PET demonstrated enlarged kidneys with abnormal intense cortical FDG accumulation and intense patchy uptake in the bone marrow of multiple bones in axial and appendicular skeleton.

Table 1. Literature review of the 16 cases of bilateral primary renal lymphoma presenting with acute

interstitial nephritis since 1997.

Age/sex	Clinical manifestations	Scr (mg/dL)	UA (mg/dL)	Pro (mg/d)	LDH (U/L)	RenalSize (cm)	Histology	Treatment	Renal function	Follow-up	Ref
57/M	dyspnoea, anemia	-	-	-	-	-	DLBCL	R-CHOP	↑	-	9
27/F	nausea, vomiting, fever	5.18	9.23	-	644	-	DLBCL	R-CHOP	-	-	10
14/M	headache, flank pain, emesis, weight loss	5.4	17.2	-	622	28/26	DLBCL	CCG-5942	↑	alive at 2 weeks	11
68/F	flank pain , dysuria	2.4	-	472	1820	14/14.5	DLBCL	-	↓	died at 10 days	12
5/M	hypertension	2.0	10.3	-	6354	16.6/17.4	T-LBL	CCG-1961	-	died at 2 months	7
21/F	fever, weight loss, abdominal pain	14.60	-	-	1124	13.6/13.7	DLBCL	VACOP-B	-	-	13
47/M	fever, weakness	1.79	-	390		16.7/14.6	DLBCL	CHOP	↑	alive at 1 year	14
28/M	asymptomatic	9.11	-	-	408	-	DLBCL	R-CHOP	↑	alive at 3 months	15
70/M	confusion	9.42	-	-	-	-	B-LBL	-	-	-	16
23/M	chest pain, weight loss	-	-	230	-	15/15	T-LBL	VDCLP	↑	alive at 2 year	8
62/M	lumbar pain, oliguria, renal failure	8.0	-	1220	919	-	DLBCL	-	-	-	17
17/M	weight loss, joint pain, flank pain, fever	5.3	9.2	-	696	20.7/19.8	NHL of B cells	COP+COPA DM	↑	-	18
52/M	ankleswelling , weight gain ,	4.11	-	400	-	15/15	T cell lymphoma	VAPEC-B	↑	-	19
22/M	fever, weight loss	3.8	-	-	528	15/15	B-LBL	COPADEM	↑	died at 1 year	20
11/F	anorexia, vomiting, weight loss, flank pain	5.79	10.1	-	-	17/17	Birkitt's lymphoma	COP+COPA DM	↑	died	21
6/F	abdominal pain, fever	2.8	-	-	-	-	Peripheral T cell lymphoma	-	-	-	22

Abbreviations: -, not provided; N, normal; ↑, improved; ↓, worsened; Scr, serum creatinine; UA, uric acid; Pro, proteinuria; LDH, lactate dehydrogenase; DLBCL, diffuse large B cell lymphoma; B-LBL, B lymphoblastic lymphoma; T-LBL, T lymphoblastic lymphoma; NHL, Non-Hodgkin's Lymphoma; R-CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone and rituximab; VDCLP, vincristin, prednisolone, daunorubicin, cyclophosphamide, L-Asparaginase, prednisolone; COP, cyclophosphamide, vincristine, prednisolone; COPADM, cyclophosphamide, vincristine, prednisolone, adriamycin, methotrexate; Ref., reference.