

Renal Lymphoma: Primary or First Manifestation of Aggressive Pediatric B-cell Lymphoma

Abstract

Renal lymphoma is an uncommon renal tumor in children. Unlike renal lymphomas presenting as bilateral disease and renal failure, we report a boy who presented with unilateral renal involvement. After initial nephrectomy, he achieved remission with multiagent chemotherapy but relapsed systemically within 3 months. He was initiated on salvage chemotherapy with autologous bone marrow transplant. Even though the initial manifestation was localized lymphoma eventually, it turned out to be a systemic disease. He succumbed to disease at 14 months from diagnosis.

Keywords: *Chemotherapy, nephrectomy, renal lymphoma*

Introduction

Primary renal lymphoma (PRL) is an uncommon renal tumor and constitutes 0.7% of extranodal lymphomas.^[1] PRL is a rare diagnosis in pediatric age group.^[2,3] Secondary involvement of kidneys in lymphoma is very common entity but primary involvement is rare.^[4] PRL in pediatric age groups manifest as bilateral renal involvement, renal failure, and anemia.^[2,3] There is no standard treatment approach in case of PRL in children.^[2,5] We report a very interesting case in a 10-year-old boy presenting as unilateral renal involvement, without any symptoms. With a suspicion of Wilms tumor, he underwent nephrectomy. In spite of aggressive treatment, he relapsed systemically and succumbed to disease.

Case Report

A 10-year-old boy presented to outside facility with complaints of a diffuse lump in the left flank, incidentally noticed by his mother. There is no history of fever, chills, pain, nausea, vomiting, diarrhea, constipation, urinary complaints, chronic infections, or any other palpable masses. Preliminary physical examination showed no fever, dysmorphic features, hypertension, or lymphadenopathy. There was a ballotable left flank mass that was firm to hard in consistency with ill-defined border. An abdominal sonogram revealed a large, solid,

reniform mass with heterogeneous echo pattern in the left renal fossa. Hemogram, metabolic, and liver functions were within normal limits, and blood urea was 22 mg/dl and creatinine was 0.7 mg/dl. He was negative for HIV, HbsAg, and HCV. A contrast-enhanced computed tomography study of the chest and abdomen showed an enlarged left kidney, measuring 17.9 cm × 11.5 cm × 10.5 cm, with loss of internal morphological architecture, uniform hypoattenuation, and few areas of heterogeneous enhancement. There were no calcific foci. The renal artery was encased by the mass while the renal vein was patent. There were a few subcentimeter left paraaortic nodes. Lungs and mediastinum were normal. A provisional diagnosis of Wilms tumor was made. The boy was transferred to the care of a surgical oncologist. He underwent a left radical nephrectomy. Postoperative histopathological examination of the specimen was reported as malignant small round cell tumor, without capsular infiltration or vascular emboli, not involving the ureter, possibly Wilms tumor with the diffuse blastemal pattern. The resected lymph nodes were free of metastases. Postoperatively, he received locoregional radiation therapy (RT) to the tumor bed with three-drug regimen as per National Wilms Tumor Study Group IV.

A month later, the boy developed enlargement of the right tonsil and

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Table 1: Common Pediatric Renal Tumors

Renal Tumor	Age Range and (Peak age)	Imaging findings	Immunohistochemistry (positive marker)
Wilms' tumor Unilateral Bilateral	1-11y (3.5y) 2mo-2yr (15mo)	Intrarenal solid mass with pseudocapsule with heterogeneous enhancement +/- calcification +/- regional LN +/- vascular invasion/thrombus +/- liver or lung metastasis	Blastemal -CD56 , CD57 Epithelial- CK22 , CK18 , CK8 , EMA Stromal - SMA, actin WT-1
Mesoblastic nephroma	0-1 y (1-3mo)	Large solid intrarenal lesion moderately enhancing - involves the renal sinus +/- necrosis, hemorrhage, cysts +/- perinephric extension similar to uterine leiomyoma or infantile fibrosarcoma	Common translocation: t (12;15) (p13;q25), involving the <i>ETV6</i> and <i>NTRK3</i> genes
Clear cell sarcoma	1-4y (2y)	Solid intrarenal demarcated mass+necrosis +/- bone metastasis without vascular invasion	vimentin and CD-99
Rhabdoid tumor	0.5-9y (6-12mo)	Centrally located lobulated solid mass with indistinct borders involving the renal hilum with subcapsular fluid collections, lobules separated with necrosis, calcification and hemorrhage vascular invasion +/- lung, brain metastasis	loss of INI1 expression in malignant cells
Renal cell carcinoma (Von Hippel Lindau syndrome)	0.5-60 y (10-20y)	Relatively small infiltrative solid mass, hyperintense+necrosis, hemorrhage, Calcification +/- cystic degeneration +/-retroperitoneal LN +/- lung, bone, liver brain	vimentin, AE1/AE3 keratins, CD10, RCC marker, and carbonic anhydrase IX
Neuroblastoma (adjacent organ)	0-5 (40% before 1yr and 90% before 5 yr)	Heterogeneous mass+highly vascular+necrosis+calcification+displacing other organs+encasing aorta	CD56, chromogranin A, and synaptophysin
Nephroblastomatosis	Any age (6-18 mo)	Nephromegaly with multiple bilateral subcapsular lesions - loss of corticomedullary differentiation	Similar to blastemal cells
Renal medullary carcinoma	10-39 y (20 y)	Intrarenal heterogeneous mass with loss of corticomedullary differentiation+hydronephrosis +/- bone metastasis. Associated with sickle cell trait	CK7, CK19, CAM 5.2, EMA, Vimentin, AE1/AE3
Primary Renal Lymphoma	Any age child (<10) y	Homogeneous, hypoattenuated multiple nodules or masses indistinct margins associated lymphadenopathy	LCA, B-cell - CD20 and CD79a, T-cell -CD3 and CD5
Angiomyolipoma	6-41 y (10 y)	Imaging findings are diagnostic depending on fat - multiple fat attenuated foci in B/L kidneys, heterogeneous enhancing Syndromic association (TS, VHL, NF)	HMG 45, Melan A

swelling in the right groin. Physical examination showed mild pallor, a right tonsillar mass that was 5 cm × 5 cm and displacing the uvula to other side and right inguinal lymphadenopathy of 3 cm × 3 cm. A fine needle aspiration of the right inguinal lymph node showed metastatic deposits of a malignant round cell tumor. At this point of time, he was referred to our center for further management. The histopathology of the nephrectomy specimen was reviewed. Morphology and immunohistochemistry showed small, round, relatively undifferentiated cells in sheets positive for CD20 and negative for WT-2 and pancytokeratin. A diagnosis of B-non-Hodgkin lymphoma (B-NHL) of

the kidney was made. Staging investigations with the whole body 18F fluorodeoxyglucose (18F-FDG) positron emission tomography (PET) showed hypermetabolic large residual disease in the right renal bed and multiple hypermetabolic right tonsil, mediastinal, abdominal and inguinal lymphadenopathy. Bone marrow biopsy was normal. He was diagnosed as B-NHL Stage III A. He was started on chemotherapy with NHL-BFM 95 protocol. He tolerated chemotherapy well and responded well. At the end of six cycles of chemotherapy, he was in complete remission. After 3 months, he again presented with bilateral cervical lymphadenopathy, and biopsy confirmed

relapse of B-NHL. Staging workup showed disease on both sides of diaphragm and bone marrow biopsy was negative. He was given salvage treatment with 4 cycles of ifosfamide, etoposide, and carboplatin. He had a very good partial response. In view of limited options and guarded prognosis in a case of early relapsed extranodal NHL in a child, parents consented for autologous bone marrow transplant. After evaluating for the organ reserve, a standard myeloablative regimen of BCNU, etoposide, cytarabine, and melphalan was used. He tolerated the procedure well with mucositis and myelosuppression as main toxicity. At end of 1 month, he was clinical in remission. Two months after autologous BMT, he once again had florid relapse and succumbed to disease, 14 months after diagnosis.

Discussion

Most common causes of benign enlargement of kidneys are hydronephrosis, polycystic kidney disease, mesoblastic nephroma, multilocular cystic nephroma, multicystic dysplastic kidneys, renal abscess, mesoblastic nephroma, and medullary cystic disease complex. Common malignant kidney tumor is Wilms tumor, neuroblastoma [Table 1].^[6]

Involvement of kidneys in NHL is common and presents as hypodense nodular lesions on imaging or autopsies.^[4] Primary involvement of kidney is rare and its existence has been doubted.^[7] Based on a report of nine cases in adults, one group suggested the following criteria (1) renal failure as the initial presentation, (2) bilateral enlargement of the kidneys without obstruction and other organ or nodal involvement, (3) diagnosis only made by renal biopsy, (4) absence of other causes of renal failure, and (5) rapid improvement of renal function after radiotherapy or systemic chemotherapy.^[8] In this present case, the diagnosis was established in nephrectomy specimen and response to chemotherapy with first-line drugs.

Even though the most common manifestation is bilateral renal involvement, acute renal failure, anemia, hematuria, fatigue, and musculoskeletal pains there are few case reports of unilateral involvement.^[2,3] Both T- and B-cell renal lymphoma has been reported.^[2,9] In this present case, it manifested as single kidney involvement with no systemic symptoms or renal failure. The patient was 10-year-old, on initial radiological findings, there was suspicion of Wilms tumor, and he underwent nephrectomy. In a case of WT, the common radiological findings are intrarenal heterogeneous mass with pseudo capsule with calcification and involvement of renal vein or inferior vena cava with or without lymphadenopathy, but in a case of lymphoma, there is some hypodense nodular lesion with homogenous involvement with our distinct borders and \pm nodal involvement [Table 1]. There are case reports of PRL who underwent nephrectomy, based on radiological features.^[10]

Aggressive lymphomas fall into the differential diagnosis of small blue round cells tumors and may be confused with other round cells tumor like neuroblastoma or blastemal component of WT, where immunohistochemistry (IHC) is of great help. The differential diagnoses of the renal mass with common IHC markers are presented in Table 1. There is growing evidence that a renal mass in a doubtful situation can be subjected to ¹⁸F-FDG PET especially before contemplating nephrectomy. ¹⁸F-FDG PET may be useful in differentiating lymphomas as they have more avid uptake.^[11]

In most cases, pediatric renal lymphomas are treated as in adults with six cycles of chemotherapy \pm rituximab with varied outcome.^[2,5] Patients with renal lymphoma rarely survive more than 1 year.^[12]

The interesting lesson learnt from our patient is that PRL can manifest initially with an asymptomatic renal mass and can relapse later with systemic disease. Better radiological, nuclear imaging and comprehensive pathology could have established an earlier and accurate diagnosis. We have treated with multiagent protocol NHL-BFM-95 and autologous transplant, but still, the patient could not be salvaged. Pediatric renal lymphomas are an aggressive form of lymphoma with guarded prognosis.

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Conflicts of interest

There are no conflicts of interest.

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