Case Report

Renal Primitive Neuroectodermal Tumor or Renal Ewing Sarcoma

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Abstract

Renal primitive neuroectodermal tumor (renal PNET) or renal Ewing sarcoma (renal ES) is a rare, rapidly growing malignant small round cell tumor with poor prognosis. A 32-years-old Bangladeshi male patient presented with right loin pain, fever and anemia. On CT imaging a large (18x10.5x10.0 cm) renal mass was discovered. On suspicion of malignancy, a biopsy was taken from the mass. Microscopic evaluation showed features consistent with malignant small round blue cell tumor. Immunohistochemical stains showed diffuse and strong positive reaction to CD-99 and negative for WT-1, CD-3 and CD-20, which confirmed the diagnosis of renal PNET. After 6 cycles of combined chemotherapy, the patient was relatively well and at 6 months follow-up he showed no evidence of metastasis or recurrence.

Key words: *Ewing sarcoma family tumors, Extraskeletal Ewing sarcoma, Renal Ewing sarcoma, Renal primitive neuroectodermal tumor (Renal PNET)*

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Introduction

Ewing sarcoma family tumors (ESFTs) previously called primitive neuroectodermal tumor, Askin's tumor or Ewing sarcoma is a rapidly growing, aggressive malignant round cell sarcoma of presumed neuroectodermal origin.[1] ESFTs occur mostly in bone and soft tissue and rarely occur in extraskeletal location like kidney, urinary bladder, heart, lung, central nervous system and genitourinary system. These organs contain neuroendocrine cells or cells of embryonic neural creast.[2] Primary Ewing sarcoma of kidney or renal PNET was first described by Seemayer and colleagues in 1975.[3] Subsequently, renal PNET has been sporadically reported. Primary renal PNET is a rare entity and representing less than 1% of all renal tumors.[4,5] Till now sporadically reported cases of renal PNET is less than 200 cases. Because of its rare entity and chance of mistaken for other renal tumors, the exact number of cases is difficult to determine.[6]

The clinical presentation of patient is usually not specific. Patient of renal PNET usually present with loin pain, hematuria, dysuria, bulky renal mass, fever, weight loss, anemia and abdominal distension.[7] About 56.7% patient presented with metastasis in lung, liver or bone with or without venous tumor thrombi. The 4 year overall survival rate is 85% in patients without metastasis and with metastasis about 47%.[4] Renal PNET also has no specificity in imaging examination. It often manifest as a heterogenous tumor with median size of 13.76 ± 5.33 cm without obvious boundaries. Renal or inferior venacaval (IVC) tumor emboli is often seen. These clinical and radiological findings may mimic renal cell carcinoma (RCC).[8,9] The diagnosis is usually confirmed by histomorphological evaluation and immunohistochemical findings of strong positive expression of CD-99. It also shows presence of a reciprocal translocation between EWS gene on chromosome 22 and members of ETS family, most commonly FLI-1 or ERG.[4,7,10]

Here, we present an unusual case of renal PNET mimicking RCC in an adult Bangladeshi male patient.

Case Presentation

A 32-years-old Bangladeshi male presented in the Outpatient Department of KhwajaYunusAli Medical College and Hospital with right loin pain, low grade fever, loss of appetite, malaise and weight loss for last 1 month. His medical history was unremarkable. On physical examination, anemia and right costovertebral angle tenderness were found. The urine analysis

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was unremarkable. His blood Hb level was 8.4 gm/dl with the total red blood cell (RBC) count 3.10 million/µl and ESR (Westergreen) was 106 mm/ 1st hour. The ultrasonographical study showed huge enlargement of right kidney with heterogenous echotexture mimicking nephroblastoma (Figure 1). A contrast-enhanced computed tomography (CT) scan showed almost total replacement of right kidney by a heterogenous enhancing mass lesion measuring 18.0 x 10.5 x 10.0 cm with areas of necrosis (Figure 2). It extends medially along the renal vein with thrombosis involving IVC upto the intrathorasic part of it. Other organs were unremarkable. The CT imaging was negative for distant metastasis. Clinically, it was diagnosed as RCC.

The patient was admitted in this hospital for proper evaluation. Due to its extension along IVC, surgical resection could not be done. A CT-guided trucut biopsy (containing two linear pieces of tissue measuring 0.6 cm and 0.3 cm) was obtained from that renal lesion. On histomorphological examination, it showed a malignant neoplasm composed of atypical small round cells arranged in diffuse pattern, clusters, rosettes and pseudorosettes. These cells had hyperchromatic round to oval nucleus with very scanty cytoplasm. Histomorphologically, it was diagnosed as malignant small round cell tumor (Figure 3). Moreover, immunohistochemical analysis showed diffuse strong positive expression of CD-99 on tumor cell cytoplasmic membrane (Figure 4). Immunohistochemical expression of WT-1, CD-3 and CD-20 were negative. Thus, the diagnosis was confirmed as renal Ewing sarcoma or renal PNET.

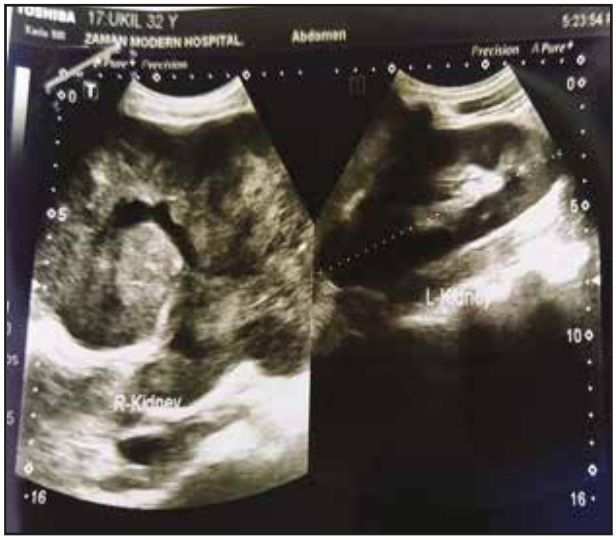

Figure 1: USG of both kidneys showing right renal mass.

Then combined chemotherapy was started including: vincristine (2 mg/ m2, day1), doxorubicin (90 mg/ m2, day1), cyclophosphamide (1500mg/m2, day1) at 3 weeks interval for 6 cycles. The patient completed 6 cycles of chemotherapy and at the end of the 6 months follow up, no evidence of metastasis or recurrence was noted.

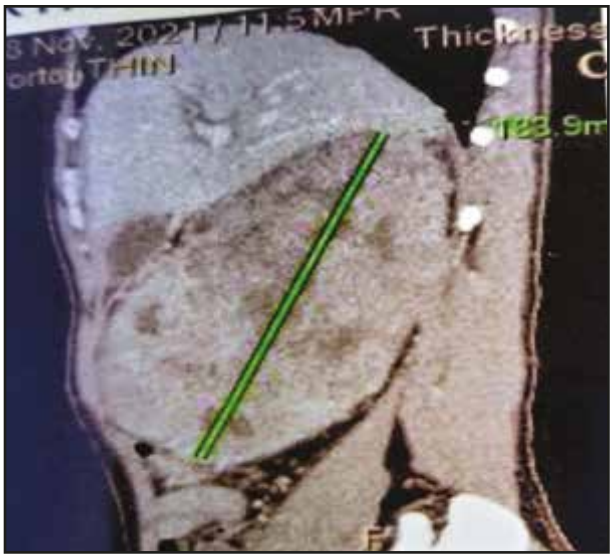

Figure 2: Axial contrast-enhanced CT scan image showing a large heterogeneously enhancing mass lesion in right kidney.

Discussion

Renal ES/ renal PNET is a relatively rare tumor of kidney. The differential diagnosis includes other round cell tumors of kidney including Wilms tumor/ nephroblastoma, neuroblastoma, renal cell carcinoma, malignant lymphoma, desmoplastic small round cell tumor, clear cell sarcoma, synovial sarcoma and metastatic small round cell tumor from other site.[11,12] This differential diagnosis is further complicated by the overlapping morphological features and the relatively rare occurrence of most of these entities in the kidney.[10] Reportedly, renal PNET usually occur in young adults with a mean age of 30.5 years having 66.7% male predominance.[4] In this case, our patient was a 32-years-old male.

Patient with renal PNET usually presents with malaise, abdominal pain, renal colic, dull flank pain, hematuria, weight loss, dysuria and abdominal distension. These symptoms simulate the presentation of renal cell carcinoma.[7] Our patient presented with complaints of flank pain, fever, pallor, anemia, loss of appetite, malaise and weight loss, which are often seen in the patients of renal PNET. Imaging study usually reveal a hypoenhancing tumor having endophytic growth pattern with mean size of 13.76 ± 5.33 cm. Extension of the tumor in the renal vein is noted in 89.4% and in the IVC about 42.1% of the renal PNET patients.[8] The CT imaging of our patient noted a 18.0x 10.5x 10.0 cm heterogeneously enhancing endophytic neoplastic lesion in right kidney which extends along renal vein and tumor thrombosis was found in IVC.

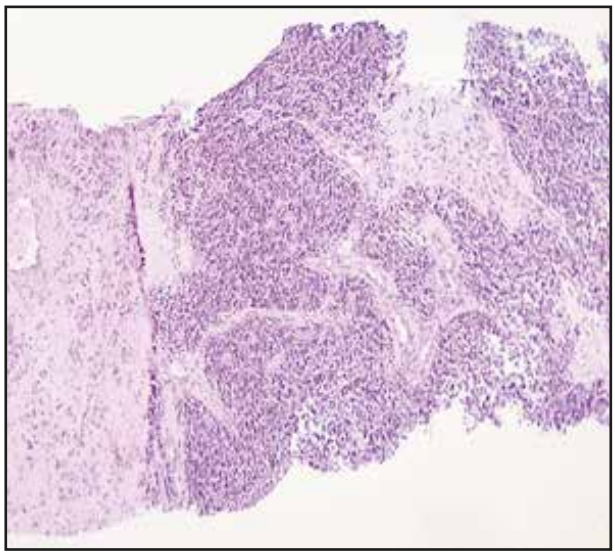

Figure 3: Photomicrograph showing H&E stained slide exhibiting features of malignant small round blue cell tumor.

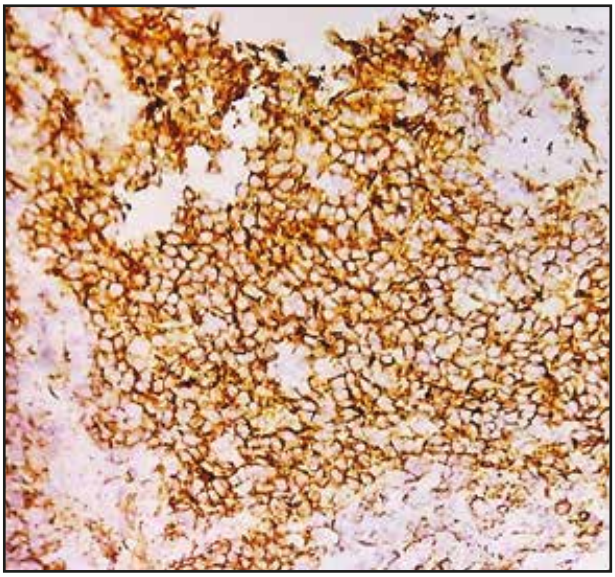

Figure 4: Photomicrograph showing diffuse and strong immunohistochemical expression of CD-99.

Diagnosis of renal PNET is generally done by the combination of histomorphological and immunohistochemical findings. Molecular genetic study also help in the confirmation of the diagnosis.[10-13] In this case, the histomorphological findings revealed some atypical small dark round cells arranged in clusters, nests, rosettes as well as pseudorosettes. Immunohistochemical expression of CD-99 in the cell membrane is universal in renal PNET. Application of immunohistochemistry helps in differentiating from other small round cell tumor of kidney like nephroblastoma, neuroblastoma and desmoplastic small round cell tumor.[2,11,12] Our case showed diffuse and strong positivity of CD-99. The expression of WT-1, CD-3 and CD-20 were negative in these tumor cells.

Renal PNET is a highly aggressive tumor with a tendency of local recurrence and metastasis to lungs, liver, bone and regional lymph nodes. The 4 years overall survival rate is 85% in patients without metastasis and with metastasis declines to 47%.[4] Other authors observed that, 45-55% patient with metastasis showed 5-yr disease free survival.[2] Multimodal therapeutic approaches consisting of surgical resection, chemotherapy and radiotherapy are required depending on the primary site and stage.[1] The most commonly administered chemotherapy is vincristine-doxorubicin-cyclophosphamide, followed by itoposide-ifostamid.[14]

The outcome is significantly associated with disease group of patient, tumor size, presence of tumor thrombus, distant metastasis and the use of chemotherapy. Our patient underwent biopsy followed by chemotherapy and is alive without relapse/metastasis for last 6 months follow up.

Conclusion

Renal PNET is a rare aggressive malignant tumor with poor prognosis. Due to the rarity of the disease and potential for misdiagnosis, we feel that it is crucial to generate more widespread awareness of renal PNET. Pathologist should always be cautious for renal PNET when presenting a large endophytic renal mass of small round blue cell morphology, specially in adolescent or young adult. Due to limited information on clinical behavior, no definite treatment protocol have been designed. So, early diagnosis and prompt multidisciplinary approach can ultimately improve the outcome of the disease.

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