Case Report

Primitive neuroectodermal tumor of kidney with Level III inferior vena cava thrombus

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Abstract

Primitive neuroectodermal tumor (PNET) of the kidney is an extremely rare renal neoplasm with only about 50 reported cases in the literature. These tumors behave aggressively and carry a poor prognosis. A 22 years female patient presented with right lumber and right hypochondrium lump of 4 months duration. Commutated tomography revealed large right renal mass with renal vein and inferior vena cava (IVC) thrombus. Magnetic resonance imaging abdomen demonstrated the extension of tumor thrombus up to the junction of hepatic vein and IVC. Preoperative percutaneous needle biopsy was performed. Histopathology demonstrated small round to oval cells with scanty cytoplasm and cells are arranged in clusters. Immunohistochemical staining demonstrated a highly specific cluster of differentiation 99, confirming the diagnosis of a PNET.

Keywords: Cluster of differentiation 99, inferior vena cava thrombus, primitive neuroectodermal tumor

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INTRODUCTION

The term primitive neuroectodermal tumor (PNET) is used for a group of small round cell neoplasm which are a type of sarcoma. They have been considered to be neural crest derivatives.[1] They were first described by Stout in 1918 in the case report that involved an ulnar nerve tumor.[2] In 1994, Mor described the first case of a renal Ewing's sarcoma (ES)/PNET.[3] These tumors are closely related to ES due to the same chromosomal abnormality: t(11;22) (q24:q12).[4,5] PNET/extraskeletal ES (PNET/ES) rarely present as organ based neoplasm rather, it is seen typically in the soft tissue of extremities, chest wall (Askin's tumor) and paravertebral region. ES/PNET is an extraordinarily rare primary tumor in the kidney with only about 50 cases described in the literature.[6] The majority of the patients present in the second and third decades of life with nonspecific signs and symptoms similar to those of other renal mass lesion. Both males and females have been shown to be affected by some work documenting a predominance in males,[7] although, this has not been universally confirmed.[8] Patients with renal PNET may present with malaise, an increase in abdominal circumference, weight loss, renal colic, fever, flank pain, hematuria, and night sweats.[8-11] Dysuria, testicular pain, and varicocele have also been reported.[9,10] Dyspnea and dizziness may also be seen if the tumor features atrial involvement.[12]

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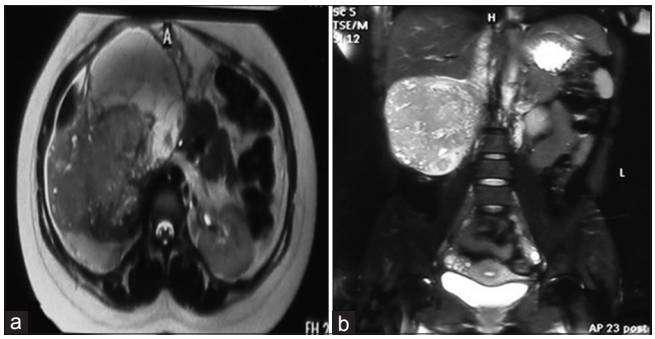

Figure 1: On MRI (a) Tumor shows heterogenous signal; intensity on Axial T2 -Weighted image (b) coronal Recostruction on gadolinium enhanced T2- weighted image the tumor thrombus invading right renal vein and inferior vena cava up to junction of inferior vena cava with hepatic vein

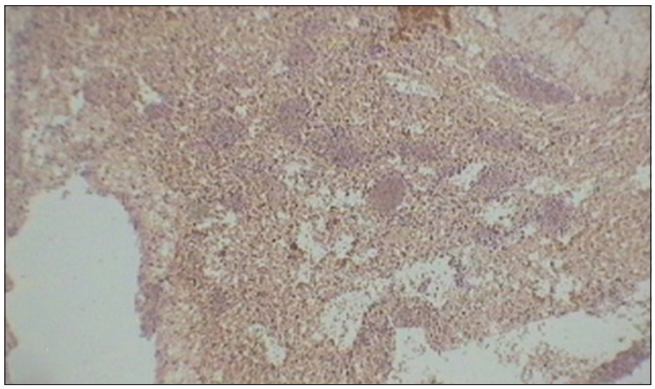

Figure 3: An immunohistochemical stain for CD99 was positive in the tumor cells. (Immunohistochemistry, ×400)

CASE REPORT

A 22-year-female patient presented with right lumber and right hypochondrium lump 4 months duration. On physical examination, a large solid mass was palpable with restricted mobility. Initial ultrasonography of kidney revealed 8.5 cm × 8.5 cm renal mass predominantly cystic with mixed echogenicity. Computed tomography revealed heterogeneously enhancing soft tissue right large renal mass crossing midline with renal vein and inferior vena cava (IVC) thrombus. Magnetic resonance imaging (MRI) abdomen demonstrated the extension of tumor thrombus up to the junction of hepatic vein and IVC [Figure 1a and 1b]. Based on physical examination and imaging studies tumor was found to be unresectable. Preoperative percutaneous needle biopsy was performed. Histopathology demonstrated small round to oval cells with scanty cytoplasm and cells were arranged in clusters [Figure 2]. Immunohistochemical staining showed a highly specific cluster of differentiation (CD99) [Figure 3], thus confirmed the diagnosis of a PNET. Neoadjuvant chemotherapy (adriamycin, vincristine, ifosfamide with mesna; four cycle) was planned in this patient and completed safely with a resolution of radiographic

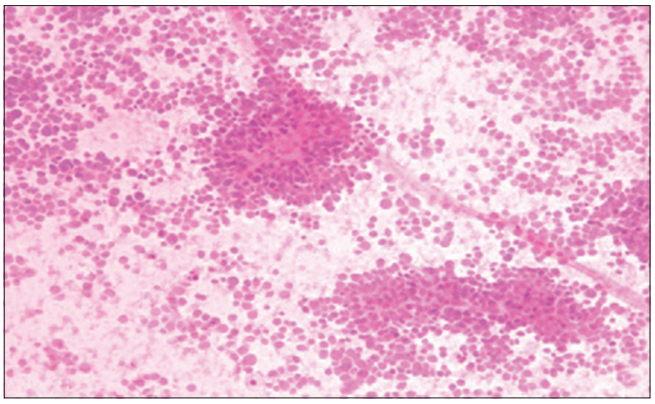

Figure 2: High power vision of smear shows lobules made of all round cells with indistinct cytoplasm, round nuclei with vesicular chromatin arranged around eosinophilic fibrillary materials and cells were arranged in clusters. (H and E, ×400)

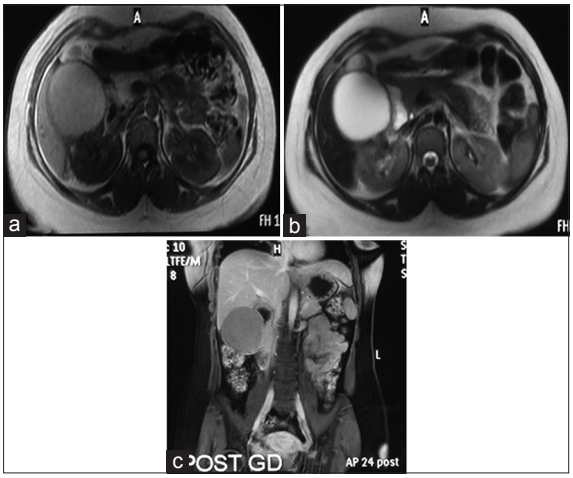

Figure 4: After completion of four cycle of neoadjuvant chemotherapy (IVAD regimen) MRI shows (a) bright signal intensities on T1-weighted and T2-weighted imaging (b); (c) No extension of tumor thrombus seen in right renal vein and inferior vena cava, and on gadolinium contrast no abnormal enhancement seen

disease. MRI abdomen demonstrated hemorrhagic cystic mass (bright signal intensities on T1 and T2 image) and no tumor thrombus extension visualized renal vein or IVC [Figure 4a-c]. Radical nephrectomy was performed with the anterior subcostal approach. The patient is disease free at 6 months of follow-up.

DISCUSSION

PNET of the kidneys are exceedingly rare. The exact number of cases is difficult to determine because these tumors are sometimes not clearly differentiated from extraskeletal ES.[13] PNETs of the kidney are found equally in both sexes and tend to occur in relatively young patients and often with metastatic disease.[14] Patient present with flank and abdominal pain hematuria or palpable mass.

Histologically, the tumor is composed of small dark cells arranged in cords, nets or clusters with or without rosettes

Table 1: Combination of therapy of surgery and chemotherapy of renal PNET

Study	Age year	Gender	Diagnosis	Metastasis	Treatment	Chemotherapeutic agents	Follow-up	Outcome
Habermann *et al*.	16	Female	Right renal PNET	No	Nephrectomy + chemotherapy	Ifosfamide vincristine Vinblastine dactinomycin Adriamycin	>4 year	Alive with complete remission
Wu *et al*.	26	Female	Right renal PNET	Lung metastases 2 months after nephrectomy	Nephrectomy + chemotherapy, after metastases: Sorafenib	Vincristine adriamycin Cyclophosphamide Ifosfamide etoposide	17 months	Alive with stabilized lung metastases
Ohgaki *et al*.	21	Female	Right renal PNET	Liver metastases 6 months after nephrectomy	Nephrectomy, after metastases: Chemotherapy + partial hepatectomy	Doxorubicin ifosfamide Etoposide	21 months	Alive
Kuczynski *et al*.	9	Male	Right renal PNET	No	Nephrectomy + chemotherapy	Vincristine doxorubicin Cyclophosphamide Ifosfamide etoposide	10 months	Relapse in the paraspinal cervical region

PNET: Primitive neuroectodermal tumor

and pseudorosettes. The most important histologic criterion is the formation of rosettes like structures formed by tumor cells [Figure 2].[15,16] Well-formed rosettes can also be identified in neuroblastoma, therefore carefully selected immunohistochemical panel is important for differentiating this tumor from other small round cell tumors of the kidney such as rhabdomyosarcoma, neuroblastoma, desmoplastic small round cell tumor, nephroblastoma, and ES.[16,17] Immunohistochemically PNET cells express vimentin, NSE, and CD99. S-100 protein, synaptophysin neurofilament protein, CD57, and chromogranin show variable reactivity. CD99 (MIC-2 gene product) positivity is a universal features of PNET.

On computed tomography PNETs typically presents as a large heterogenous mass with central low density areas due to necrosis. Areas of high attenuation with in tumor, presumably due to hemorrhage have been observed. Intratumoral calcification, multiple, peripheral, or linear have been reported. Tumor extension into the renal vein, IVC, right atrium have been described in few reports. There are at least two reports of psoas muscle invasion. Hepatic metastases, when present, manifest as low attenuation lesions.[18-20]

PNET belongs to Ewing's family of tumors. A series of well planned, prospective randomized multicenter trials, clearly document the evolution of modern multimodality treatment regimens and have shown the advantages of multidisciplinary approach to treatment, including chemotherapy "up front" and using surgery where possible for local control.[21] Verrill *et al.* recorded 34 patients with ES/PNET, received the IVAD chemotherapy regimens. Drug dose intensity, toxicity, and survival data were collected. Author concluded that although the IVAD chemotherapy regimens are myelotoxic in adults, they can be given safely.[22]

The current treatment for renal PNET include a combination of surgery, chemotherapy, and radiotherapy [Table 1].[23-26] Cavotomy and thrombectomy have also been performed in cases with a IVC tumor thrombus.[19] In addition to nephrectomy surgical resection of other involved organs or vasculature are occasionally indicated.[18,19] Chemotherapy recommendations to treat PNET include alternating cycles of ifosfamide and etoposide with vincristine, doxorubicin, or dactinomycin.[27] Radiotherapy have been reported for locally advanced disease or when there is involvement of Gerota's fascia.[20]

The 5 years disease free survival rate for patients presenting with well confined extraskeletal PNET is around 45–55%, and cases with advanced disease at presentation have a median relapse free survival of only 2 years.

CONCLUSION

Although most authors recommend surgery followed by multidrug chemotherapy, we suggest that chemotherapy prior to surgery (IVAD regimen: Adriamycin, vincristine, ifosfamide with mesna; four cycle) is safe in locally advanced, inoperable PNET of kidney with good response.

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Conflicts of interest
There are no conflicts of interest.

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