

Case Report

Primitive Neuroectodermal Tumor (PNET) of Kidney - A Rare Entity

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ABSTRACT

Primitive neuroectodermal tumor (PNET) of kidney is an extremely rare renal neoplasm with only about fifty reported cases in literature. Presumably, of neural crest origin, these tumors behave aggressively and carry a poor prognosis. We report a case of 22-year old female patient complaining of left loin pain with recurrent hematuria for last 3 months. On clinical examination, the abdomen was soft and no palpable mass was felt. She underwent ultrasonography and computed tomography, which revealed a left renal mass. A left radical nephrectomy was performed. Histopathological examination of the nephrectomy specimen showed features of primitive neuroectodermal tumor arising from left kidney, which was confirmed by immunohistochemistry (IHC). The patient was treated with post-nephrectomy chemotherapy and was symptom-free at six-month follow-up.

Keywords: Primitive Neuroectodermal Tumor, Kidney

Introduction

Primitive neuroectodermal tumor/ Extraskelatal Ewing's sarcoma (PNET/ES) first described by Arthur Purdy Stout in 1918, rarely present as organ based neoplasm-rather, it is seen typically in soft tissue of extremities, chest wall and paravertebral region. ES/PNET is an extraordinarily rare primary tumor in kidney with only about fifty cases described in literature (1). Similar to PNET/ES at other sites, approximately 90% of these tumors have a specific 11:22 translocation that re-

sults in a chimeric EWS-FLI-1 protein. So these tumors have overlapping clinical features due to the common histogenesis and cytogenetic abnormality; t (11:22) (q24;q12) (2). Majority of the patients present in the second and third decades of life with non-specific signs and symptoms similar to those of other renal mass lesion. Indeed preoperative diagnosis of PNET of kidney is very difficult. There are almost about 50 cases reported in the medical literature, although it is difficult to estimate the exact number

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since often it has not been clearly differentiated from Ewing's Sarcoma (1). Very few cases have been reported in literature with a variable, nonspecific presentation and aggressive behavior particularly in children and young adults (3).

Case Report

A 22 years old female presented with left loin pain for the last three months. The physical examination revealed a soft abdomen with no palpable mass. Urine analysis revealed microscopic hematuria. Ultrasonographic examination of the abdomen revealed a solid appearing heterogeneous mass arising from the left kidney. Post contrast computed tomography (CT) of the abdomen showed a 7.3 x 6.3 cm well defined, heterogeneously enhancing mass arising from infero-medial aspect of lower pole of left kidney with areas of hemorrhage and necrosis. The mass was infiltrating into the left renal pelvis causing gross dilatation of calyces. Left renal vein appeared opacified. Right kidney and other intra-abdominal organs scanned were normal. CT guided Fine Needle aspiration Cytology (FNAC) was performed and cytological features were suggestive of a small round cell tumor with a possibility of monophasic Wilm's tumor. Routine hematological investigations were as follows: hemoglobin - 10.2 gm/dl, serum urea 22mg/dl, creatinine 0.9mg/dl and fasting blood sugar- 90 mg/dl. The patient underwent left radical nephrectomy. No site of metastasis could be identified pre-operatively.

Grossly, the nephrectomy specimen weighed 500 gm and measured 10x7x6cm, totally covered by renal capsule and partially with perinephric fat. The cut section revealed a

6.5 x 6.0 x 5.5cm well circumscribed, solid, variegated mass with areas of hemorrhage and necrosis in the lower pole of the resected left kidney. Normal kidney tissue measured 4.0 x 4.0 x 2.5 cm. The pelvicalyceal system was dilated. The renal vein appeared solidified but the ureter was free from any tumor invasion grossly. No lymph nodes were identified grossly (Fig. 1). Microscopic examination of hematoxylin and eosin stained slides showed that the tumor was composed of loosely cohesive sheets of small to medium sized undifferentiated small round cells of with hyperchromatic nuclei and scanty cytoplasm (Fig. 2), divided by fibrovascular septae into lobules with a tendency to form rosettes. Perivascular pseudorosette formation, areas of hemorrhage and necrosis were present with a mitotic count of 8-10/high power field. Periodic Acid Schiff's (PAS) stain show focal cytoplasmic positivity. The perinephric fat and renal vein was involved by the tumor cells (Fig. 3). No lymph node involvement could be identified.

Immunohistochemistry was then performed using avidin-biotin complex technique and diaminobenzidine as chromogen with suitable positive and negative controls. The tumor cells showed uniformly diffuse strong membrane positivity for CD 99 (MIC-2 gene product) (Fig. 4) and negative staining for cytokeratin, vimentin and chromogranin. A diagnosis of primitive neuroectodermal tumor of kidney was made based on the characteristic morphological and immunohistochemical appearance.

Post-nephrectomy, the patient was treated with adjuvant chemotherapy comprising of vincristine/ifosfamide/doxorubicin and etoposide and was free of symptoms in six-month follow-up. No evidence of metastasis was seen.

Figure 1



Fig. 1- Gross appearance of the tumor at the lower pole of the kidney

Figure 2

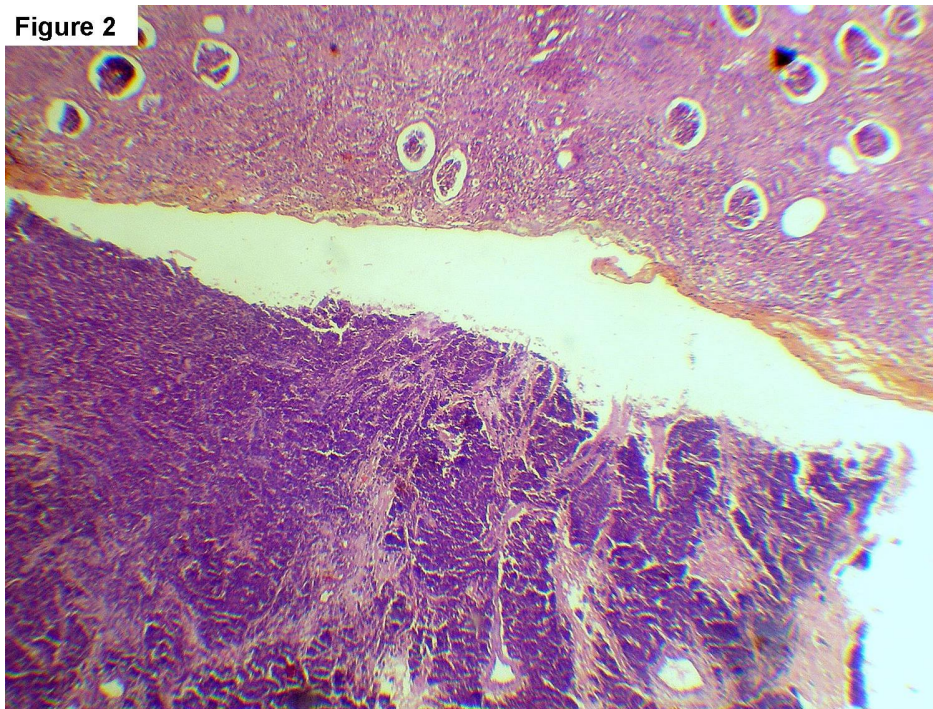


Fig. 2 - Microphotograph showing the PNET of kidney with small, round tumor cells with round uniform nuclei and scanty cytoplasm with the normal kidney above (X100 H&E stain)

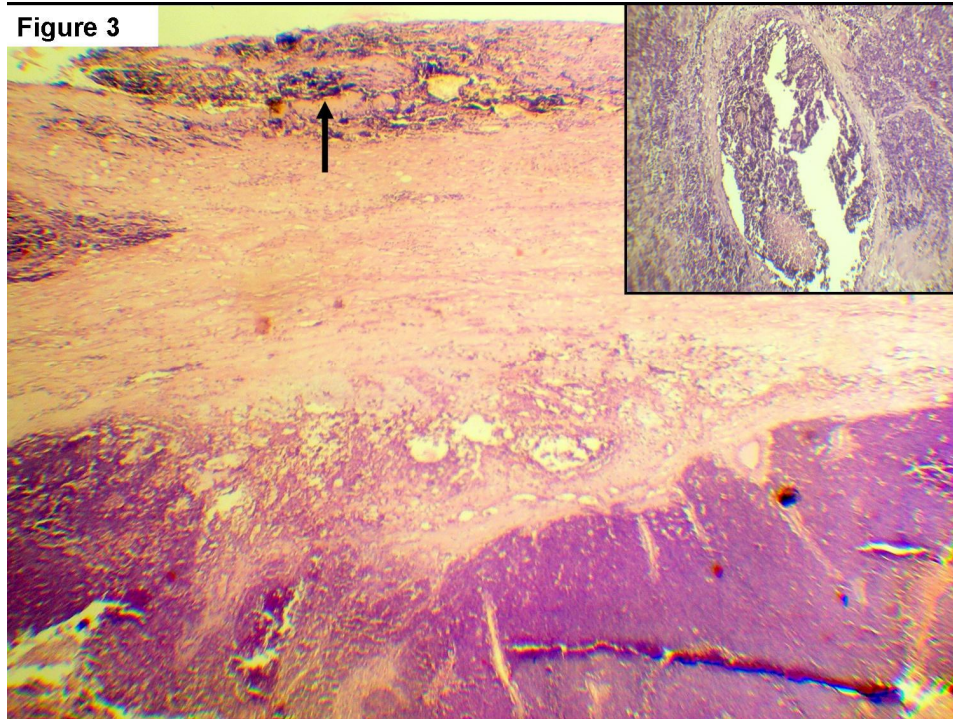


Fig. 3 - Microphotograph showing the tumor cells with involvement of perirenal fat (arrow) (Hematoxylin and eosin stain, X100 magnification) Inset shows the involved renal vein (X400 H&E stain)

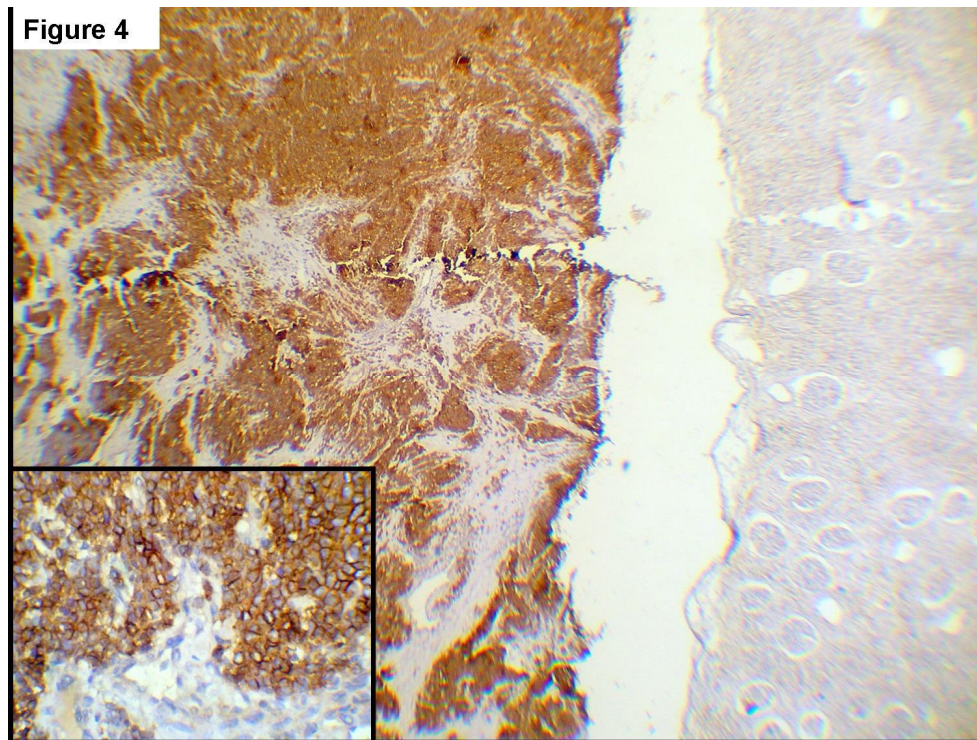


Fig. 4 - Immunohistochemistry showing diffuse membrane positivity of tumor cells for CD99 (X100 magnification). Inset shows a higher magnification (X400)

Discussion

Primary PNET of kidney are rare neoplasms with only about 50 cases reported in the medical literature, although it is difficult to estimate the exact number since often it has not been clearly differentiated from Ewing's Sarcoma (1). Largely believed to be of neural origin, the exact histogenesis and relation of ES/PNET was debatable issue for long time. With the advent of immunohistochemistry, cytogenetic and molecular genetic techniques common cytogenetic abnormality t (11, 22)(q24;q12) has been proved. Renal PNET/ES show similar translocation. Most of the cases were found among young adults. The initial sign and symptoms are similar to those of other renal tumors. PNET carries a poor prognosis, with a high tendency to recur locally and to metastasize to regional lymph nodes, lungs, liver, as well as bones at an early stage of the disease (4). The mean survival rate is only 10% (5). Jimenez *et al* published an analysis of 11 cases of Primary Ewing's sarcoma/PNET of the kidney with a mean age of 18-49 years and mean follow up of 28 months (range 6-64 months) which showed 4 lung and pleural metastases, 1 bone metastases, liver metastases, 2 local recurrences and 5 deaths from disease (3). In a large series reported by Cuesta *et al* (5) which included 26 patients and another series of 16 patients by Thyavihally *et al* (6), PNET is highly aggressive neoplasm and it should be differentiated from a variety of other primary renal neoplasms. The differential diagnosis includes extra-osseous Ewing's sarcoma, rhabdomyosarcoma, Wilm's tumor, carcinoid, neuroblastoma, clear cell sarcoma of the kidney, lymphoma, the small cell variant of osteosarcoma, desmoplastic small round cell tumor and nephroblastoma (7). Microscopically, this tumor is composed of loose cohesive sheets of small to medium sized monomorphic cells with round nuclei and scant cytoplasm. The presence of Homer-Wright type of rosettes are scarce or less well defined in extraskelatal ES while their presence clinch the diagnosis in favor of

PNET. Diffuse strong membrane positivity for CD-99 (a MIC-2 gene product) and negative staining for cytokeratin, vimentin, and chromogranin are helpful in confirmation of the diagnosis. Renal PNET should be included in the differential diagnosis of any rapidly enlarging mass presenting with local infiltration and clinical aggressive behavior. Demonstration of the reciprocal translocation of chromosomes t (11, 22) (q24;q12) is a very useful tool in the diagnosis of PNET (8). Exact diagnosis has clinical consequences because polychemotherapy and high dose chemotherapy may lead to dramatic tumor reduction even complete remission (9, 10). Most of the cases of renal PNET have poor response to standard treatment of combined surgical resection, postoperative irradiation, and chemotherapy. The present case, however, responded well to chemotherapy with no evidence of recurrence or metastasis at 6-month follow-up. The fact that there was no lymph node involvement appears to be a very important favorable prognostic factor in our case.

Acknowledgements

The authors declare that there is no conflict of interests.

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