

Primitive neuroectodermal tumor with inferior vena cava thrombus: A rare case report

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ABSTRACT

Primitive neuroectodermal tumors (PNETs) are rare type of small cell, aggressive tumors, commonly seen in the central nervous system, and PNET of the kidney with inferior vena cava thrombus is an extremely uncommon presentation of this entity. There are no established distinctive signs or radiological characteristics for diagnosis, but a majority of cases report positivity for CD99 marker. The patients usually present in the advanced stages of the disease and require progressive techniques of immunohistochemical analysis and expertise of multidisciplinary team of physicians to arrive at a correct diagnosis and have a proper management. Although rare, these tumors should be considered in the differential diagnosis of all patients with large renal masses, especially in the younger population. We present a case of a 23-years-old female, with PNET of the left kidney, treated with radical nephrectomy and adjuvant chemotherapy.

Key words: *Inferior vena cava thrombus, Kidney tumor, Primitive neuroectodermal tumor*

Primitive neuroectodermal tumors (PNETs) are a group of tumors from the phenotypic spectrum of Ewing's family of tumors, originating from the neuroectoderm [1]. These are small-round cell, biologically aggressive and highly malignant tumors [1]. PNETs were originally defined in 1918 [2], but the first case of renal PNET was reported in 1975 [3] and very few cases of renal PNET with inferior vena cava (IVC) thrombus have been reported since [4]. Although there has been an increase in the reporting of this entity in the recent years due to improved immunohistochemistry and cytogenetic techniques of analysis, the prognosis remains poor, with the median disease-free survival of 5.0 months [4].

We report a case of renal PNET in a 23-year-old female from the left kidney, with thrombus extension into the IVC diagnosed by post-operative immunohistochemical analysis of the resected specimen.

CASE REPORT

A 23-year-old female presented with pain and a mass on the left side of the abdomen for 4 months. The pain was progressive in nature. There was no history of fever, dyspnea, nausea, vomiting, diarrhea, hematuria, or change in bowel/bladder habits. On examination, the patient was calm, conscious, and afebrile, with stable vitals. The abdomen was soft, non-tender, and not distended. A solid, firm, mobile mass was palpable in the left lumbar region,

about 20 cm × 15 cm, moving with respiration, non-ballotable, and non-tender. The mass had a smooth surface and the margins could not be properly delineated. Her other examinations were unremarkable.

The ultrasonography of the abdomen showed a large, retroperitoneal mass in the paraumbilical region, extending up to the left hypochondrium, with necrotic areas and calcifications, and increased vascularity on color Doppler. Computed tomography (CT) (Fig. 1) showed a heterogeneously enhancing, well-defined, lobulated mass, measuring 20.6 cm × 12.2 cm × 9.8 cm, in the left renal fossa, almost completely obliterating the left kidney, extending into the perinephric space, infiltrating the Gerota's fascia, and crossing the midline anterior-superiorly, invading the left adrenal gland as well as presence of a thrombus in the renal vein, extending into the IVC, up to the intrahepatic portion. Multiple tortuous vessels were observed in the periphery of the mass, extending centrally. Based on the age group of the patient and the characteristics of the tumor described, the presumptive diagnosis of renal cell carcinoma was established.

Renal angiography with embolization of the tumor was done, through left superficial femoral artery under local anesthesia. Aortic angiography showed the blood supply to the tumor arising from branches of left renal artery and three collaterals from the abdominal aorta below the renal artery, two from thoracic aorta, and one from superficial epigastric artery. Embolization of all the feeders was done by selective cannulation using 6F JR 3.5

and propagate microcatheter over whisper wire, using polyvinyl chloride particles of 250-355 nm diameter. Post-procedure all feeders were embolized and no complications were observed.

The patient was taken up for radical left nephrectomy and removal of IVC thrombus under deep hypothermic circulatory arrest (Fig. 2), under which the temperature of the body is lowered to 18°C on a heart-lung machine and the body tissue (especially brain) can withstand no blood circulation for 40 min duration, ensuring a bloodless field to undertake operations on major vessels. The entire involved kidney along with the tumor, and the IVC thrombus was removed completely. A few mesenteric lymph nodes were also resected. Following the surgery, the patient had an uneventful recovery, was extubated after 12 h, and ambulated on the 1st post-operative day.

The resected specimen along with the lymph nodes was sent for immunohistochemical analysis. The report described a brown mass measuring 26 cm × 15 cm × 9.5 cm, weighing 4 kg, with nodular external surface, solid-white cut surface with cystic and necrotic areas (Fig. 3a). Histology examination of the specimen showed small tumor cells arranged in Homer-Wright rosettes with hyperchromatic nuclei, scanty cytoplasm, and many apoptotic bodies (Fig. 3b). Immunostain analysis demonstrated diffuse membranous positivity for CD99. Reevaluation of the patient was done based on this report of the excised mass, and the diagnosis of renal PNET was established, as a Stage IV, T₄N₁M₀.

Post-operative CT scan of the patient showed no residual mass in the left renal bed or IVC thrombus. The oncology team advised the patient to undergo adjuvant chemotherapy as per the vincristine, doxorubicin, and dexamethasone regimen for 4-6 cycles, over 6 months from an outside center, as radiotherapy treatment was not available in authors' hospital at the time. The patient was discharged on the 7th post-operative day in a stable condition, with a healthy wound and good saturation on room air. At 1-month follow-up, the patient was doing well, saturating 96% on room air, with healthy wounds. At the latest follow-up, the patient was due to start the chemotherapy in 2-week duration.

DISCUSSION

PNETs, along with Ewings's sarcoma (ES) and asking tumors form ES/PNET family of tumors [5], are usually referred to interchangeably in the literature. When the first case of PNET was described by Stout in 1918 [2], they were thought to arise directly from nerves; however, more recently, the origin of renal PNETs has been postulated to be from the adrenergic fibers that invest in the renal tissue from celiac plexus or the neural crest cells that migrate to the kidney and undergo tumor genesis later in life [6]. Although these tumors are more common in the first two decades of life, with an incidence of 2.9 per million annually in this population [7], cases have been reported in all age groups [8]. Peripheral PNETs more commonly arise in the chest wall and paraspinal regions [9] and are very rarely seen in other soft tissues such as kidneys.

This tumor, when arising in the kidneys, presents with the symptoms of hematuria, bulky renal mass, and abdominal or flank pain, with one-third of the patients having renal vein or

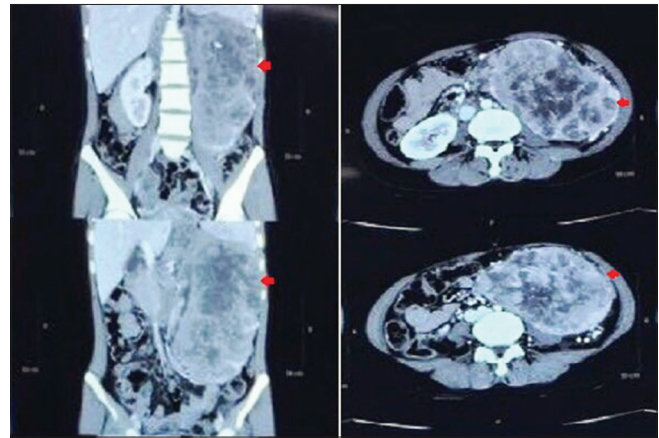


Figure 1: Pre-operative computed tomography scan of the patient, the red arrows showing the tumor growth of the left kidney

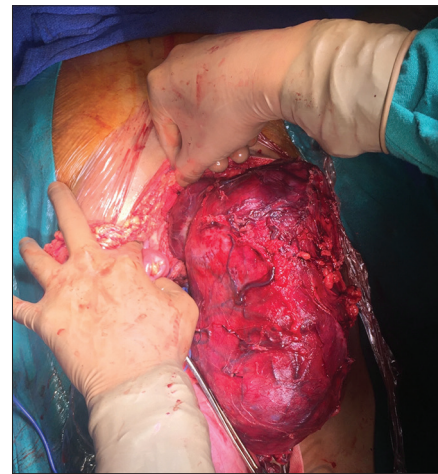


Figure 2: Intraoperative view

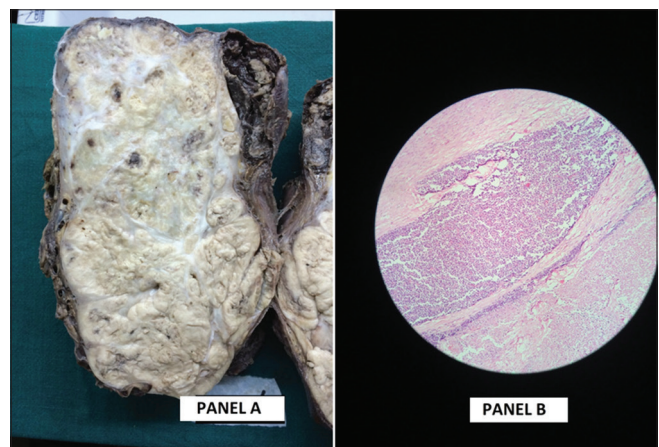


Figure 3: (a) Gross specimen, cut section. (b) Microscopic view of the specimen

IVC thrombus at the time of diagnosis [4]. Grossly, these tumors may range from 3.3 to 18 cm in size, characterized with areas of necrosis and hemorrhage [4,10]. On light microscopy, these tumors appear as monotonous collection of small, round, darkly stained cells, and electron microscopy reveals neurosecretory granules with microtubules and filaments [7], with cells arranged in Flexner-Wintersteiner rosettes having well-defined central

Lumina or as Homer-Wright rosettes with fibrillary cores [6]. The most commonly expressed immunohistochemistry markers are the proteins encoded by MIC2 gene, commonly CD99, O13 [8,11], with CD99 found to be positive in more than 90% of ES/PNET and Friend leukemia virus integration-1 (FLI-1) and antibody to FLI-1 seen in majority of cases [12]. Vimentin and neuron-specific enolase have also been found positive in more than 80% of cases [11].

Due to rarity of this entity, there is no standardized protocol of treatment but surgical excision of the primary tumor is undertaken for a majority of these patients. Neoadjuvant or adjuvant chemotherapy is given with multidrug therapy, commonly consisting of doxorubicin, vincristine, cyclophosphamide, ifosfamide, and etoposide [13]. Role of radiation therapy is not completely established but may be used for targeted treatment of positive lymph nodes following surgery [10]. Median overall survival of these patients has been estimated at 26.5 months [4].

This was a 23-year-old female, presenting with pain abdomen and a bulky abdomen mass arising on the left side of a few months duration, without any complaints of hematuria. According to the pre-operative CT, the tumor was a large mass, replacing the entire left kidney, invading the left adrenal mass, and crossing the midline. The histomorphology of the excised mass showed Homer-Wright rosettes and immunostain positivity for CD99. After undergoing surgical excision with thrombectomy, the post-operative CT scan of this patient did not show evidence of any residual disease, and the patient was subsequently advised chemotherapy for the metastatic disease.

CONCLUSION

The renal PNET with IVC thrombus is an extremely rare entity, presenting in advanced stages of the disease, posing a diagnostic challenge to the treating team of physicians, and having a dismal prognosis for the patient. Advanced techniques of immunohistochemical analysis along with high degree of suspicion and expertise of the physician are required to arrive at the correct diagnosis. Multidisciplinary team of physicians, in a tertiary care center, is required for the adequate approach to management of the patient, as correct diagnosis and timely

intervention can be highly valuable for a better prognosis of the patient.

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