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Case Report

RENAL PRIMITIVE NEUROECTODERMAL TUMOR (RPNET) IN CHILDREN

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Abstract:

Renal primitive neuroectodermal tumor (rPNET) as a member of Ewing's sarcoma family is extremely rare and usually occurs in children and young adults. Most literature about rPNET was isolated case reports.

Here we described a case of renal PNET in a 7-year-old girl who presented at our Paediatric Surgery Department of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh with fever, left flank pain and mass Ultrasonogram (USG) and Computer tomography (CT) scan revealed a huge mass in the left kidney. The patient underwent left radical nephrectomy with neoadjuvent chemotherapy on April,2016. Histopathology and immunohistochemistry (IHC) confirmed the diagnosis of PNET. She did not receive adjuvant chemotherapy, as advised. She had a local tumor recurrence 3 months after the surgery and continued to deteriorate but not developed distant metastasis. She again received 2-cycle of chemotherapy but size did not decrease. So re-do surgery was performed on 10.01.2017 and send to paediatric haemato-oncology department of BSMMU for further management.

rPNET is rare and presents aggressive clinical behavior and worse prognosis. We expect that further awareness and study of this rare tumor can be had by presenting our case.

Key Words: Renal, PNET, IHC

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Introduction:

Extracranial primitive neuroectodermal tumors (PNET) are described as small round cell, malignant tumors that have the neural crest regarded as the most likely progenitor and that arise from outside the central nervous system.[1] Other terms used for PNET are peripheral neuroepithelioma, adult neuroblastoma, and Askin tumor; the latter involving the chest wall and lung. These tumors are part of the Ewing's sarcoma family of tumors.[2] The peak incidence of PNET occurs within the second decade of life. Recent studies, however, have described cases of PNET within an age range of newborn patients to 14-year old patients and for a median of 1 year of age in a population of 26 patients.[2, 3] The primary site for PNET is frequently the thorax, either in the intrathoracic or chest-wall areas.[3] Other less frequent primary sites are pelvis, retroperitoneum, limbs, neck, and the paraspinal region.[4] There are few cases of PNET of the kidney reported in the literature. Moreover, this study have described PNET of the kidney as a rare entity.[5, 6]

PNET has been diagnosed by morphology, immunohistochemistry (IHC) or molecular techniques.[7] PNET can be confounded with sarcomas and neuroblastomas negative for urinary

catecholamine due to the histopathologic, immunohistochemical, and cytogenetic similarities found in Ewing's sarcomas.[8]

Patients are managed aggressively with surgery, chemotherapy with or without adjuvant radiotherapy. A commonly employed regimen includes combination chemotherapy with vincristine, adriamycin, cyclophosphamide (VAC) with alternating ifosfamide and etoposide (IE).[9]

Renal PNETs present as very clinically aggressive tumors.[10-13] Cases of local recurrence and metastasis have been shown to comprise more than 50% of the clinical presentations in this cancer,[14] with the most common sites of metastasis shown to be the lymph nodes, lungs, and liver.[12] In 2001 a review of 25 cases of renal PNET, the mean patient survival was approximately 10 months.[11] Other work has shown the overall 5-year disease-free survival rate for peripheral PNETs to be between 45% and 55%.[12]

Here we report a case of Renal PNET in a 7-year-old female

Case presentation:

Isha, a 7-year old girl was admitted in our Paediatric Surgery Department Of BSMMU on 6th April,2016 with the complaints of low grade fever, dull aching left flank pain and gradually increasing left flank mass for about one year. She had no history of haematuria and jaundice but anorexic. In addition, patient also complained of weight loss of 5kg during this period Child was negative for family history of neoplasia.

On physical examination, patient was found anaemic, her body core temperature was about 38^0C and weight was 14.5 kg.

There was mild tender ill defined lump in left lumber region, size was about (12cm x 9.5cm).

We carried out laboratory and X-ray of chest examination. Her Hb%-6.4gm/dl, serum bilirubin-0.5mg/dl, serum creatinine- 0.64mg/dl, urine R/M/E- no RBC, urinary VMA- 6 I.U and X-ray of chest-normal.

Ultrasonography and Contrast-enhanced tomography scan of the abdomen showed large lobulated well defined heterogeneously enhancing mixed density mass lesion having calcifications measuring about 13.5x9.8x9.5cm was noted involving the left kidney sparing lower pole. The mass causing compression and displacement of stomach, bowel loop, pancreas and vascular structures towards the right side. No metastatic foci noted in opposite kidney and other abdominal organs. No abdominal lymphadenopathy or ascites were noted (Fig.-A).

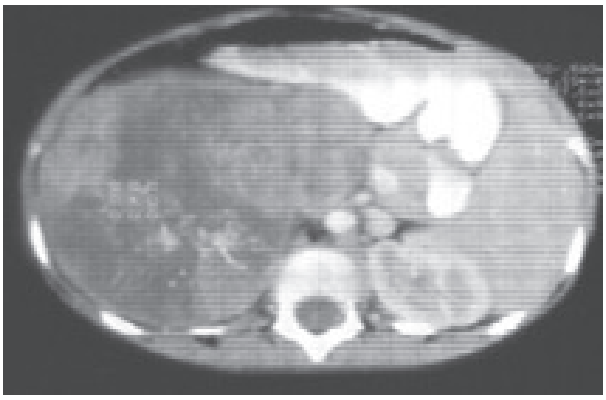

Fig.-A: *and Contrast-enhanced tomography scan of the abdomen showed large lobulated well defined heterogeneously enhancing mixed density mass lesion having calcifications measuring about 13.5x9.8x9.5cm was noted involving the left kidney sparing lower pole. The mass causing compression and displacement of stomach, bowel loop, pancreas and vascular structures towards the right side. No metastatic foci noted in opposite kidney and other abdominal organs.*

Our patient was received four cycle of neoajuvent therapy but the tumor mass not decreased in size.Then she submitted to surgical procedure of left radical nephrectomy with resection of one large hilar lymph node on 12/04/2016 and all resected tissues send for histopathology. The tumor presented the macroscopic features of a Wilms tumor.

The microscopic examination revealed that the tumor was composed of monotonous round cells with hyperchromatic round nucleus. The interspersed small dark cells indicating pyknosis of the tumor cells could form rosette-like structures (Figure B). The cytoplasm of the tumor cells was scanty, but, the rim of clear cytoplasm and discrete cell membranes were often apparent without extensive degenerative changes. Renal vein margin, Perinephric fat margin and ureteral margin were free. Venous and Lymphatic invasion were indeterminate.

Rosette

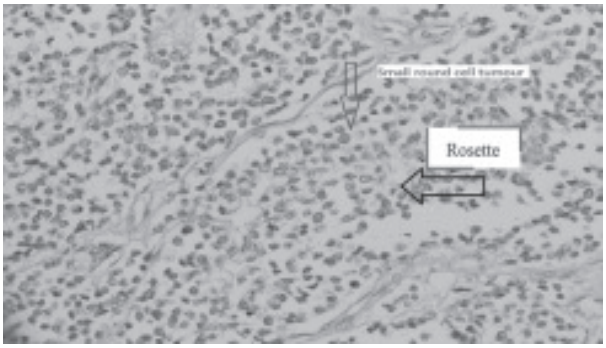

Fig:B- *showed HE of rPNET. The rosette-like structures formed by the small monotonous round cells*

Most importantly, immunohistochemical staining indicated the positive expression of CD99 and neuron-specific enolase (NSE) and negative of CD56, Chromogranin A, Synaptophysin, WT 1, Pancytokeratin(AE 1/AE 3),Myogenin in the tumor cells which supported the diagnosis of rPNET (Figure –C.1,C.2, C.3, C.4, C.5, C.6,C.7).

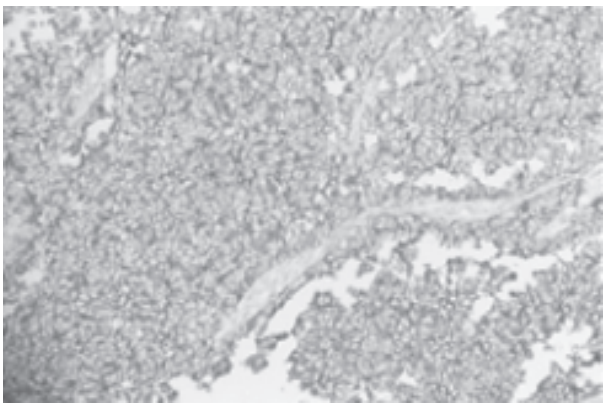

Fig. C.1: *positive expression of CD99*

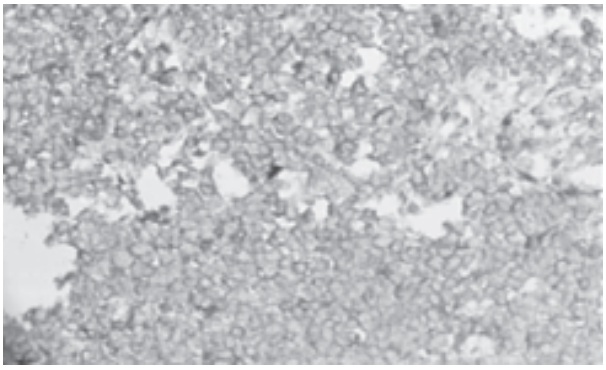

Fig. C.2: *positive expression of NSE*

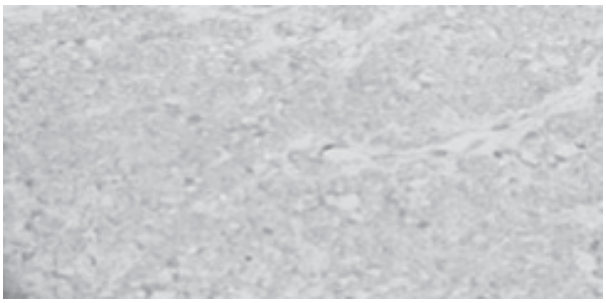

Fig. C.3*: negative expression of WT-1*

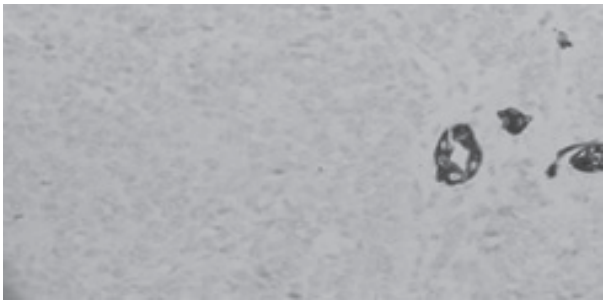

Fig. C.4: *negative expression of Pancytokeratin*

Fig. C.5: *negative expression of Chromogranin A*

Fig. C.6: *negative expression of Myogenin*

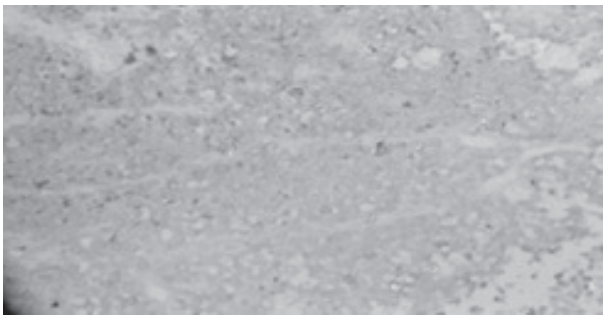

Fig. C.7: *negative expression of Synaptophysin*

After operation Bone marrow report showed uninvolved marrow and normal bone scinigraphy.

Patient was send to paediatric haemato-oncology department of BSMMU for further management .But she did not receive adjuvant chemotherapy , as advised. She had a local tumor recurrence 3 months after the surgery and continued to deteriorate.

At that time USG, CT scan, PET-CT scan and Bone marrow scan were performed. All these report showed no metastatic lesion, but dumble shaped mixed echogenic area noted in left paravertebral region.One measuring about 6.86x2.9cm and another one 5.39x2.86cm.

She again received 2-cycle of chemotherapy but size did not decrease. So re-do surgery was performed on 10.01.2017 and after wound healing , the patient was referred to paediatric haemato-oncology department of BSMMU for further management.

Unfortunately due to financial burden patient did not receive chemotherapy. On follow up after three month she developed local and distant metastasis and now she is on palliative care.

Discussion:

PNET covers one percent of all sarcomas.[15] It is a malignant small round cell tumor of neural crest origin, first described in the ulnar nerve by Arthur Pourdy Stout in 1918.[16] Commonly, PNETs arise in the ribs and paraspinal areas; involvement of skin, soft tissue, lungs, kidney, and retroperitoneum is rare. rPNET first described by Mor *et al*. in 1975 is a very rare and aggressive malignant tumor.[17] Till now, around 100 cases have been reported worldwide, with very few from India.[18]

The clinical features of PNET of kidney may be nonspecific like vague pain and lump in the loin and irregular fever, weight loss, and occasional hematuria. In our series, this case had similar presentations without haematuria.

Renal PNET commonly affects young adults, though the age range is 4 - 61 years in reported cases. It more commonly affects males, with a male to female ratio of 3:1.[18] The imaging characteristics of renal PNET are also nonspecific and overlap with those of other renal tumors, such as renal cell carcinoma, Wilm's tumor, neuroblastoma, lymphoma, desmoplastic small round cell tumor.[19] Most cases of renal PNET are diagnosed on resected specimens, based on histopathology and immunohistochemistry.[7]

Our case was a female child of 7 years old. She was also diagnosed on resected specimen based on histopathology and immunohistochemistry.

These tumors are composed of primitive appearing round cells with a high nucleo-cytoplasmic ratio. Perivascular pseudo-rosettes are usually identified; Homer-Wright rosettes are less frequently seen. A commonly appreciated feature on electron microscopy is aggregates of cytoplasmic glycogen granules though sometimes polar processes, microtubules or neurosecretory granules are seen, suggesting a neuronal differentiation.[19] Tumor cells express CD99 (MIC2) and FLI-1 with variable positivity for neuroendocrine markers including NSE, synaptophysin, and CG. WT1, a marker for Wilms' tumor, is not expressed in PNET. A combination of markers is generally helpful in arriving at the correct diagnosis. Eighty to ninety five percent of the cases show t(11;22) (q24;q12) while the remaining ones often display an EWS/Ets-related gene (ERG) mutation.[20]

Cytogenetic studies could not be performed in our case because of non-availability.

As the tumor is highly aggressive, it is often diagnosed in advanced stage when it has already involved perinephric fat, hilar lymphnodes, renal veins, and inferior vena cava. In more advanced stages, the tumor involves liver, spleen, peritoneum, and lungs. The 5-year disease-free survival rate is around 45–55% in well-confined cases, whereas cases with advanced stage at presentation have a median relapse-free survival of only 2 years.[21]

Patients are generally treated with a multi-modality approach; radical nephrectomy with combination of chemotherapy with drugs including vincristine, doxorubicin, cyclophosphamide, etoposide and ifosfamide. Adjuvant radiation is given in patients with incomplete resection, positive resection margins, or recurrence.[22]

Despite aggressive therapy, the overall cure rate of renal PNET is only 20%.[23] Geetha and his colleagues showed in their study that 7 cases had underwent radical nephrectomy. After surgery two received adjuvent chemotherapy only, one received radiation therapy only and three received both chemotherapy and radiotherapy. One patient was lost of follow up after surgery and not received chemotherapy or radiotherapy. Four patients were alive beyond 1 year,

and one is alive in remission at 15 months. The survival of their patient group ranged from 6 months to 18 months.[24]

In our study patients came without distant metastasis at presentation.After sugery patient did not receive adjuvant chemotherapy. As a result she developed local and distant metastasis within three months after redo operation and now she is on palliative care .

Conclusion:

Renal PNET is a distinct and rare entity, typically affecting young adults. This tumor is very aggressive with a low survival rate, even with multimodality treatment. Although the incidence of renal PNET in children is low, oncologists and pathologists need to be aware of this tumor and every attempt should be made to differentiate it from other more common tumors as it carries very poor prognosis. Morphology alone can only suggest PNET as an important differential of small round cell tumors; ancillary techniques and immunohistochemistry for CD99 with or without a molecular test are vital to establish a correct diagnosis.

We expect that further awareness and study of this rare tumor can be helpful by presenting our case.

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