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Case Report

Renal primitive neuroectodermal tumor in an adolescent: a case report and review of literature

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ABSTRACT

Renal primitive neuroectodermal tumor is a highly malignant neoplasm that commonly affects young adults and infrequently presented in children and adolescents. We report a case of a 14-year-old female child who presented with abdominal mass. PET-CT showed an FDG avid cystic lesion in the inter and lower polar regions of the right kidney, extending into the right renal fat and renal vein, with multiple FDG avid lesions in the axial and appendicular skeleton, suggesting renal mass with bony metastases. Biopsy confirmed the diagnosis of primitive neuroectodermal tumor of the kidney. The patient completed six cycles of chemotherapy with partial response and subsequently the patient defaulted and lost to follow-up. To emphasize the critical significance of renal PNET in the differential diagnosis of renal tumors in children.

Keywords: Primitive neuroectodermal tumor, Non-Wilms renal tumors, Small round blue cell tumors

INTRODUCTION

Primitive neuroectodermal tumors (PNETs) are neoplasms comprising small, round cells of neural crest origin, that arise either within the central nervous system (CNS) or in peripheral tissues. Peripherally located PNETs (pPNETs) are members of the Ewing's sarcoma family of tumors (EFTs).[1] First reported in 1994, Primary PNET of the kidney, is a rare and aggressive malignancy with a median presentation age of roughly 30 years.[2,3] It is uncommon in children below the age of 15 years, with only a few cases reported thus far.[4] Due to its rarity, renal PNET is usually not suspected and pose a challenge to distinguish this from other more prevalent kidney tumors.[2,5] In this report, we describe the case of a 14-year-old girl who presented with renal mass and was ultimately diagnosed with renal PNET.

CASE REPORT

A 14-year-old female child presented to our hospital with the complaints of pain in the bilateral thigh for the past one month. The pain was intermittent with occasional nocturnal pains disturbing sleep. The patient has been

treated in the past with oral analgesics with no significant improvement.

There were no complaints of fever, abdominal pain, and altered bowel habits. She did not have any significant past medical history. General examination was unremarkable. Local examination did not reveal any abnormality in the thigh region except for tenderness. Abdominal examination revealed a mass in the right iliac fossa. There were no dysmorphisms or external anomalies. Her complete blood count, renal and liver function tests were within normal limits. Magnetic resonance imaging of the lumbosacral spine was planned which showed multiple T2/STIR hyperintense lesions scattered in the lumbosacral vertebral bodies and posterior elements of L3 and L5.

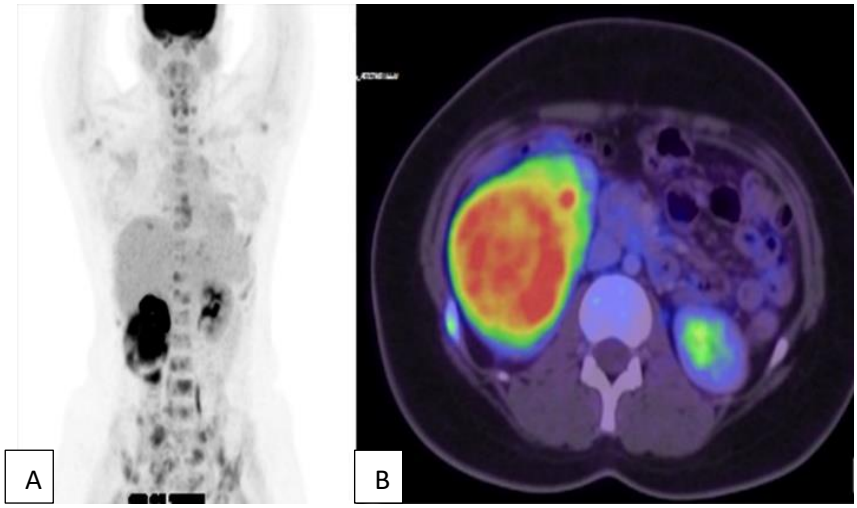

Figure 1: (A) PET-CT coronal view showing multiple FDG avid lesions in the lower pole of right kidney, axial and appendicular skeleton; (B) PET-CT axial view with FDG Avid mass lesion (11.6×7.5×7.1 cm; SUV max: 13.09) in the interpolar and lower pole of the right kidney.

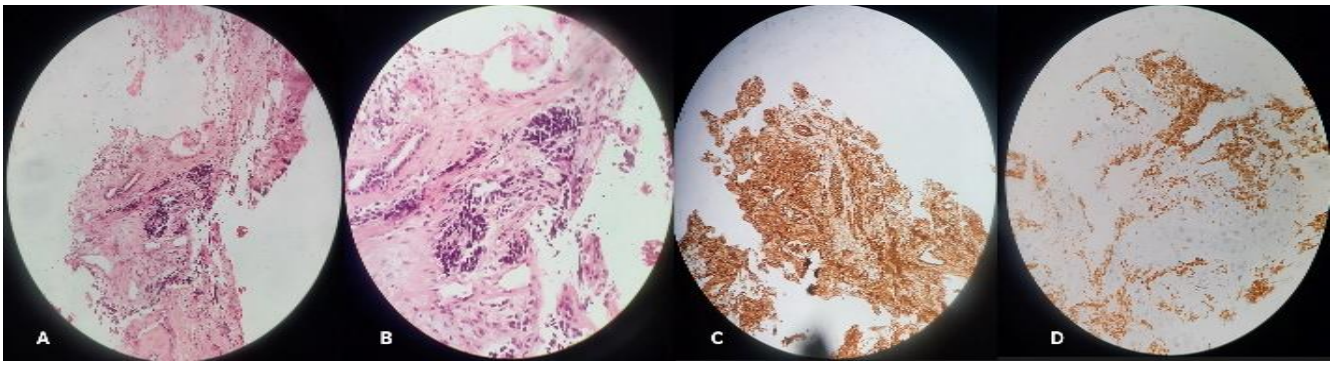

Figure 2: Histopathology of renal mass (A) H&E 10× view showing tissue infiltration with round blue cell; (B) H&E 20× view with round to oval cells with hyperchromatic nuclei; (C) vimentin positive staining; (D) NKX2.2 positive staining.

Additionally, large demarcated heterogenous space occupying lesion with cystic areas was visualized in the lower pole of the kidney. This was suggestive of renal malignancy with vertebral deposits, so a fluorodeoxyglucose (FDG)-positron emission tomography (PET) was planned to identify further metastases. PET showed FDG avid cystic lesion of 11.6 x 7.5 x 7.1 cm, (SUV max 13.09) in the interpolar and lower pole of the right kidney extending into the right renal fat and renal vein along with multiple FDG avid lesions in the axial and appendicular skeleton (Figure 1). Serum alpha-fetoprotein, serum uric acid, serum beta-human chorionic gonadotropin, serum lactate dehydrogenase and urine vanillylmandelic acid were normal. Ultrasound guided biopsy from renal mass showed infiltration of tissue with round to oval tumor cells with hyperchromatic nuclei and scanty cytoplasm. Immunohistochemistry showed the tumor cells stained positive for vimentin and NKX2.2, confirming the diagnosis of primitive neuroectodermal tumor of kidney (Figure 2). After counselling the family regarding the aggressive nature of disease and treatment options, the patient was started on chemotherapy. The patient completed six cycles of chemotherapy with partial response, after which the patient was lost-to-follow-up.

DISCUSSION

Pediatric renal tumors comprise approximately 6-7% of solid neoplasms in children, with Wilms tumor being the most prevalent, accounting for approximately 80%-90% of all pediatric renal tumors.[6] Non-Wilms renal tumors (NWRT) in pediatric cases represent a small proportion, with primitive neuroectodermal tumor of the kidney being a particularly rare entity, constituting less than 5% of renal tumors.[2,6] Other Non-Wilms renal tumors include renal-cell carcinoma (RCC), clear-cell sarcoma of the kidney (CCSK), congenital mesoblastic nephroma (CMN), malignant rhabdoid tumor of kidney (MRTK), cystic nephroma (CN), renal angiomyolipoma (RAML), inflammatory myofibroblastic tumor (IMT), ossifying renal tumor of infancy (ORTI), renal medullary carcinoma and metanephric tumors.[6-8] A study conducted by the Children's Cancer and Leukemia Group in the United Kingdom from 1991-2008 indicated that only 3% of patients (n=2) had primitive neuroectodermal tumors of all renal tumors between the ages of 10-16 years (n=67).[9] In a recent retrospective study of Non-Wilms renal tumors in China (2008-2019), renal primitive neuroectodermal tumors accounted for only 1.4% (n=2) of the total NWRT cases (N=139).[6] Similarly, Children accounted for 11% (n=4) of the total cohort (n=30) in a large retrospective cohort study of Ewings sarcoma family of tumors (ESFT) in MD Anderson cancer centre from 1990-2013.[2] While approximately 100 cases of renal PNET have been reported worldwide, only a few cases have been reported from India.[4,10] Renal PNET primarily affects young adults, with a median age of 30 (8-69).[2,6] Symptoms are highly non-specific making it difficult to differentiate from other renal malignancies and benign conditions with similar presentation. Common symptoms of renal PNET include abdominal pain and hematuria, with some cases presenting systemic symptoms such as fever or weight loss.[2,6] Unusual cases have been reported where patients presented with radiating flank pain (mimicking renal colic) and shortness of breath respectively.[1]

Metastasis occurs in approximately 40-65% of newly diagnosed renal PNET patients, with the lungs and bones being the most common sites such as our own case with bone metastases. Other sites of metastasis include the liver, bone marrow, and leptomeninges.[2,6] The high incidence of metastatic disease is indicative of the aggressive nature of this tumor and in some cases, partly due to late presentation of symptoms.[2] Localized disease has a 5-year survival rate of 70%, while metastatic disease has a 5-year survival rate of 40%.[5] The differential diagnosis of renal PNET is complex and challenging due to overlapping morphological and immunohistochemical features among the different entities. It is important to distinguish PNET from other small blue cell tumors that can arise in the kidney, such as blastemal-predominant Wilms tumor, neuroblastoma, rhabdomyosarcoma, lymphoblastic lymphoma, small cell neuroendocrine carcinoma, desmoplastic small blue cell tumor, small-cell osteosarcoma, and synovial sarcoma. All of them have frequent overlapping morphological features. Thus, making an extensive immunohistochemistry (IHC) panel is frequently necessary to establish a definitive diagnosis.[1,10,11] The diagnosis of renal PNET relies heavily on histopathologic and IHC findings.[9,10] The light microscopic examination of the tumor shows primitive looking small round cells with high nuclear and cytoplasm ratio in nests and rosettes diffusely infiltrating the renal parenchyma.[5,12] An appropriate IHC panel subsequently plays a crucial role in distinguishing renal PNET from other small round cell tumors.[5] PNET are often positive for CD99 (MIC-2 gene product), FLI-1 in most of the cases. Some cases also stain positive NSE (neuron specific enolase), vimentin and synaptophysin.[5,12] Although the positive expression of CD99 is a strong clue to diagnosis of PNET, it is not specific for PNET among round cell tumors.[11] Therefore, confirmation of diagnosis is achieved through RT-PCR/Immunophenotypic studies, which demonstrate the presence of the molecular marker EWS-FLI chromosomal translocation. This diagnostic method is positive in 95% of PNET cases and is primarily employed in cases of unusual morphology.[12]

The diagnosis of primary renal PNET is also made challenging due to the non-distinctive radiological features. However, few imaging features have been described in literature that aid in distinguishing PNET from other lesions, such as Wilms tumor and renal cell carcinoma. They include: presence of multiple irregular septum like structures, presence of multifocal and diffuse necrosis, bulky disease with endophytic infiltrative growth pattern, weak enhancement with contrast, fewer foci of calcifications, and high rate of renal vein thrombosis and distant metastasis.[2,5,10] The treatment methods for renal PNET includes a combination of surgery, chemotherapy, and radiation. Surgical options include nephrectomy with cavotomy in cases of renal vein involvement.[10] The current recommendation for chemotherapy includes VDC (vincristine, doxorubicin, cyclophosphamide) in alternation with IE (ifosphamide, etoposide).[6] Radiation therapy is useful in treating patients with non-resectable margins or positive margins/residual disease.[5,12] Despite aggressive treatment with all the modalities and high dose chemotherapy with autologous stem cell rescue, the prognosis remains poor for metastatic disease with 45-55% overall 5-year survival rates.[5] Notably, a study by Aghili et al found that renal PNET in younger patients (even with distant and regional metastases) have better prognosis when compared to its older counterpart.[12]

CONCLUSION

Renal PNETs represent a rare and aggressive subset of pediatric renal tumors, often challenging to diagnose due to their nonspecific presentation and overlapping features with other renal malignancies. This case highlights the importance of considering renal PNET in the differential

diagnosis of renal masses, particularly in young patients presenting with atypical symptoms. Early recognition and prompt initiation of treatment are crucial for improving patient outcomes.

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