

## Renal primitive neuroectodermal tumour in childhood: Case report and review of literature

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### Abstract

Primitive neuroectodermal tumour (PNET) is presumed to be of neural crest origin, mostly presenting as bone or soft tissue masses. It usually occurs in the trunk or axial skeleton; while renal PNET is considered an extremely rare tumour. We report a case of 11-year-old male who presented with right flank pain and gross hematuria after suffering blunt trauma. During investigations, he was found to have a large renal mass on computed tomography. He underwent a right radical nephrectomy where the pathology report showed PNET of the kidney. The patient received chemotherapy afterwards. Despite the chemotherapy, he had a local tumour recurrence 3 months after and continued to deteriorate and developed distant metastasis. Primitive neuroectodermal tumour of the kidney is a distinct and rare entity. It is very aggressive, with a poor survival despite combined modality treatment.

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### Case report

A previously healthy 11-year-old boy came to the emergency department complaining of right flank pain and gross hematuria for 1 week duration after suffering blunt trauma. He had no other associated symptoms. Physical examination revealed a palpable firm and large right upper quadrant mass. His hemoglobin and serum creatinine levels were normal.

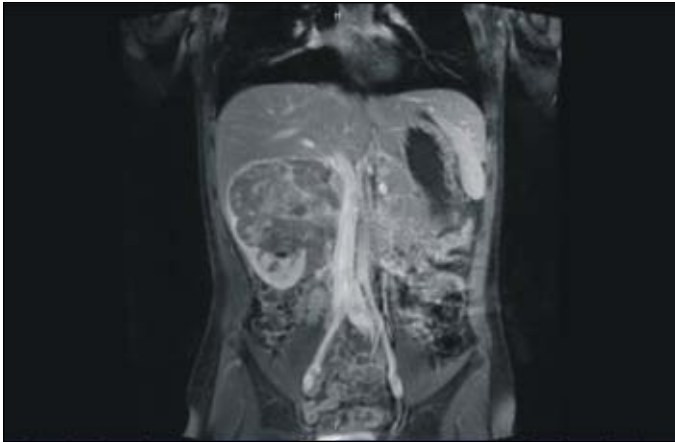
A computerized tomography (CT) scan of the abdomen demonstrated a large heterogeneous enhancing mass with areas of cystic degeneration noted involving the upper and mid regions of the right kidney. It measured 10 × 9 × 11 cm with areas of necrosis and hemorrhage and no lymphadenopathy (Fig. 1). Although necrosis and hemorrhage are pathological diagnosis, areas of high attenuation in pre-contrast CT might suggest hemorrhage, while after intravenous contrast non-enhanced areas may suggest necrosis. There was no evidence of renal vein or vena caval extension by magnetic resonance imaging (Fig. 2).

Chest CT and radionuclide bone scan showed no evidence of a metastatic disease. The patient was referred to the physicians in the pediatric oncology department and they agreed with our plan of performing a radical nephrectomy first. The patient then underwent a right radical nephrectomy and hilar lymph node dissection. There was only one grossly enlarged lymph node that was resected along with other areas of hilar fat. Grossly, the kidney weighed 700 g and measured 16 × 14 × 9 cm. On sectioning, there was a huge mass almost replacing the whole kidney, sparing only a rim of the kidney at the lower pole. Margins were negative and adrenal gland was unremarkable.

Microscopically, sections revealed neoplastic growth displayed in vaguely nodular pattern with intersecting thick fibrous septa. The neoplastic growth is composed of sheets of undifferentiated small blue cells with occasional Homer-Wright rosettes. These cells have basophilic chromatin and frequent mitosis. Also there are areas of spindle fibroblast-like cell proliferation. No glycogen globules were identified. There was marked hemorrhage and occasional necrotic foci encountered within the tumour. Vascular and perineural invasion were seen. One hilar lymph node showed reactive changes and was negative for malignancy. The adrenal gland was normal.

A panel of immunohistochemical markers was performed which included neuron-specific enolase (NSE), synaptophysin, macrophage inhibitory cytokine (MIC-2), Wilms' tumour and P53. The tumour cells were positive for MIC2, NSE and synaptophysin, while they were negative for the rest of the markers.

The patient was seen by the pediatric oncology team before discharge and scheduled to receive multi-agent chemotherapy. During his 3-month follow-up, he complained of abdominal pain and lower limb swelling. A CT scan was repeated and revealed a local tumour recurrence. Although a biopsy of the mass was not taken, he continued to receive chemotherapy. Despite this, he deteriorated and developed distant metastasis.



**Fig. 1.** A computed tomography scan of the abdomen and pelvis showing large, heterogeneous and enhancing right renal mass



**Fig. 2.** A magnetic resonance imaging of the abdomen and pelvis, which shows the patent's inferior vena cava with no evidence of thrombosis.

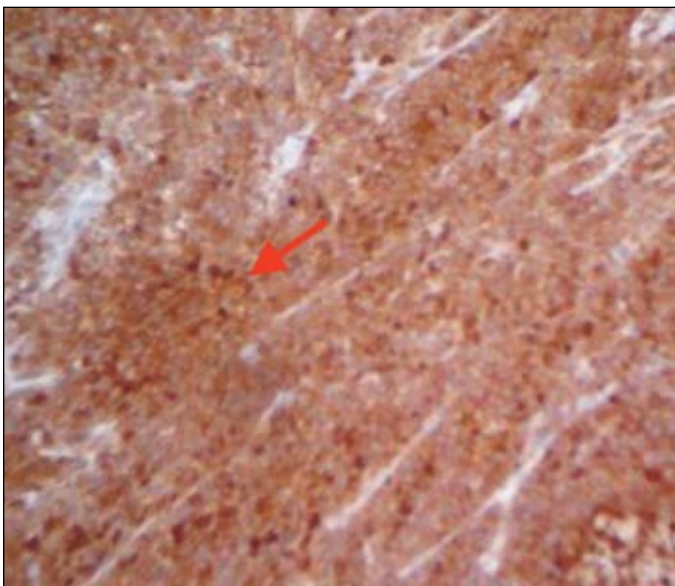
### Discussion

Primitive neuroectodermal tumour is a malignant small cell neoplasm of neural crest origin. It was first described by Arthur Pourdy Stout in 1918, where it occurred in the ulnar nerve.<sup>1</sup> It is a very rare tumour representing about 1% of all sarcomas.<sup>2</sup> It can occur in the trunk, extremities, brain, spinal cord and sympathetic nervous system, as well as peripheral tissues, like the chest wall (Askin's tumour),<sup>3</sup> paraspinal region and, less commonly, the genitourinary tract.<sup>4</sup> In 1921, Ewing described this tumour in the bone, which became known as Ewing's sarcoma.<sup>5</sup> Renal PNET was first reported by Mor and colleagues.<sup>6</sup> There are only 4 reported series of renal PNET, which includes articles by Parham and colleagues,<sup>7</sup> Jimenez and colleagues,<sup>8</sup> Carlos and colleagues<sup>9</sup> and Yuvaraja and colleagues.<sup>10</sup>

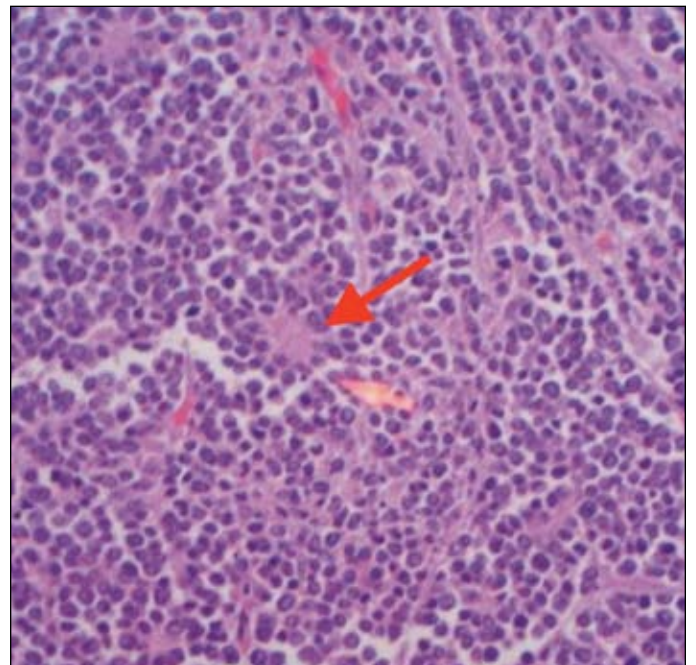
Renal PNET is extremely rare with fewer than 50 cases in the English literature. Renal PNET is a highly aggressive malignant neoplasm and is more aggressive than PNET arising from other sites.<sup>11</sup>

PNET also occurs in children and adolescents. The age range for this condition is from 4 to 61 years.<sup>7</sup> To our knowledge, our case is the fourth reported case in the pediatric age group; most of the reported cases occur with patients in their second or third decades of life.<sup>12,13</sup> The male to female ratio is about 3:1. The presenting symptoms and clinical signs are non-specific and similar to those of other renal tumours.<sup>14-18</sup>

The diagnosis of renal PNET is made usually postoperatively, based on histopathology and the panel of immunohistochemical stains.<sup>19</sup> Differential diagnosis includes



**Fig. 3.** Small blue cells with occasional Homer-Wright rosettes.



**Fig. 4.** Tumour cells were positive for immunohistochemical marker MIC2.

Wilms' tumour, neuroblastoma, clear cell carcinoma and lymphoma. Radiographic features of renal PNET are non-specific and are usually presented as a huge renal mass with or without calcification.<sup>20</sup> Histologically, PNET consists of sheets and nests of primitive small round blue cells and presence of Homer-Wright rosettes (Fig. 3, Fig. 4).<sup>21</sup> Immunohistochemical staining is crucial in the diagnosis. Renal PNET is positive for MIC2 in more than 90% to 95% of the cases. Other helpful markers are neuron-specific enolase and vimentin, synaptophysin and S100 protein.<sup>20-25</sup>

Furthermore, cytogenetic studies showed that renal PNET is consistently associated with translocation of the long arms of chromosome 11 and 22, t(11:22) (q24;q12) in more than 90% of the tumours; it is also characteristic of PNET and Ewing's sarcoma. Fluorescence in-situ hybridization (FISH) allows confirmation of the PNET/Ewing sarcoma specific t(11:22) and t(21:22).<sup>26</sup> Unfortunately, cytogenetic studies was not performed in our case because it is not available.<sup>24</sup>

Renal PNET is a highly aggressive tumour and almost 50% of patient present with distant metastases, most commonly to regional lymph nodes, lungs and liver. It has a high tendency toward early local recurrence after treatment. The survival rate is poor and most patients die within 1 year of the diagnosis; although, in some of the previous reports, the 5-year disease-free survival rate was 45% to 55%.<sup>2-18</sup>

Since PNET biologically behaves like Ewing's sarcoma, it should be treated with a combination of radical nephrectomy and chemotherapy, which includes vincristine, doxorubicin, cyclophosphamide, etoposide and ifosfamide.<sup>27</sup> In cases where there is an incomplete resection or positive margin or recurrence of the tumour, radiation is recommended. However, further studies are needed to find the appropriate treatment protocol.

## Conclusion

Primitive neuroectodermal tumour of the kidney is a distinct entity. It is very aggressive with a poor survival, despite combined modality treatment. Although PNET is rare, we should be aware of its presence. Cytogenetic studies and immunohistochemistry for CD99 are very helpful in the diagnosis of renal PNET.

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