Primary Ewing sarcoma of the kidney in an adult and a child: Solving a diagnostic challenge

Dear Sir,

Primary renal Ewing sarcoma (PNET) is a rare tumor that can pose a significant diagnostic challenge to both the pathologist and the radiologist. It is a highly aggressive neoplasm, often metastasizing to lymph nodes and viscera and is associated with a poor outcome. The median survival of these patients is 40 months with 5 year survival being 36% after metastasis has occurred.[1] While an early diagnosis is of paramount importance in these patients, ironically, this entity is rarely diagnosed correctly pre-operative by radiology alone. However, even morphologic diagnosis is not always easy, owing to its morphologic and immunohistochemical overlap with other primary renal tumors, both in adult and pediatric groups. Here we present two cases of primary renal PNET. To the best of our knowledge, case 2 is the youngest case of renal PNET reported in literature.

CASE 1

A 36-year-old lady presenting with hematuria was found to have a non-homogenously enhancing mass measuring 8.2 × 7 × 6.8 cm involving middle and lower parts of the left kidney on CT. An 8.3 × 7 cm tumor found in the nephrectomy specimen. Microscopically the tumor was composed of sheets of small blue round cells with high N: C ratio and scant cytoplasm. Numerous Homer Wright rosettes and perivascular pseudorosettes were identified. Several mitotic figures, large areas of necrosis and hemorrhage were present. No epithelial or stromal elements were identified [Figure 1a-c]. On IHC, the tumour cells showed strong nuclear positivity for FLI-1, and strong and diffuse membranous staining for CD99. Synaptophysin showed focal positivity; but EMA, Bcl2, LCA, EMA and NSE were completely negative in the tumor cells [Figure 1d].

Considering the radiographic, morphologic, and immunohistochemical findings, a final diagnosis of primary renal PNET was offered. RT-PCR performed paraffin embedded tumor tissue revealed the presence of the EWS-FLI1 fusion protein. The patient was put on chemotherapy and she is doing well till date, one year post surgery, without any recurrence or metastasis.

CASE 2

An 18 month old boy baby was brought with a large, rapidly growing lump in the left flank. A heterogeneously enhancing lesion measuring 9.5 × 7.1 cm, arising from the antero-medial aspect of the left kidney was found on CT [Figure 2a]. A preliminary diagnosis of Wilms tumor was suggested by the radiologists. A large partially necrotic mass of 9.8 × 7.2 cm was found in the nephrectomy specimen. Microscopically, patternless sheets of small blue round cells were noted, along with the malignant cells dissecting through the kidney parenchyma at multiple places. A few scattered rosettes were also seen [Figure 2b-c]. No mesenchymal, tubular, or glomerular elements were detected after extensive sampling. The adrenal gland was found to be uninvolved by the tumor. IHC panel revealed strong nuclear FLI-1 expression, strong membranous positivity for CD99, and focal positivity for PGP9.5. Again, WT-1, EMA, bcl2, LCA, CD56, and NSE were completely negative [Figure 2d]. Based on histology and IHC, a diagnosis of primary PNET of the kidney was made and the patient was put on chemotherapy. Eventually, he developed bone and lymph nodal metastasis and succumbed to the disease 3 months after surgery.

Ewing sarcoma and PNET are considered to belong to the common histologic spectrum of Ewing family of tumors, all of which share some degree of neuroectodermal differentiation and translocations involving the EWS gene and members of the ETS family of genes, the commonest being t (11;22)(q24;q12)(EWS/FLI-1).[2] The presence of this entity was first described in the kidneys in 1975, and primary renal PNET has been addressed in only a few small case series since then.[1,3,4] The mean age of presentation is 26 years, while the youngest patient reported so far was 3-years-old at the time of diagnosis.[5] Here, we report a case where the patient was 18 month old at diagnosis, while the other case is that of a 36-year-old lady.
The primary challenge in the diagnosis of this entity is its morphologic similarity with other small blue round cell tumors. In an adult patient, the main differential diagnoses are non-Hodgkin lymphoma, monophasic synovial sarcoma, small cell carcinoma, and desmoplastic small round cell tumor. In pediatric population, one must first rule out blastema predominant Wilms tumor, intra-renal neuroblastoma followed by primary renal rhabdomyosarcoma and anaplastic sarcoma.

Blastema predominant Wilms tumor tends to have round to oval cells, often showing a nodular arrangement, which was lacking in our case. Stromal elements were also completely absent. A combination of IHC markers such as CD99, WT-1 and FLI-1 can help in diagnosis, with FLI1 being the most specific. Strong positivity for CD99, combined with lack of positivity for chromogranin, synaptophysin or NB84 can help rule out neuroblastoma. Lymphoma cells in the kidneys tend to dissect through the interstitium, somewhat preserving the parenchymal structures. In our cases, the possibility of lymphoma was excluded, on the basis of extensive presence of rosettes, coupled with absence of immunostaining for LCA. Although CD99 positivity can be there in both PNET and monophasic synovial sarcoma, bcl2 and TLE-1 positivity along with EMA positivity can be a useful clue to establish the diagnosis of synovial sarcoma. Desmoplastic small round cell tumor, also CD99 positive in select cases, has a characteristic desmoplastic stroma, dot like positivity for vimentin and positivity for EMA and WT1.

Here we take the opportunity to describe two cases of renal PNET, one belonging to the usual age group, and the other is the youngest patient reported in literature so far. While immunohistochemistry and molecular analysis can greatly assist in making an accurate diagnosis for timely management, we do recommend a judicial and careful interpretation of immunohistochemical studies, to avoid misinterpretation of overlapping patterns found in many of its mimics.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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