Case Report

Histopathological and immuno-histochemical characteristics of primary renal primitive neuroectodermal tumor

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ABSTRACT

We report a 32-year-old male who presented with huge (17x10.5x5 cm) right kidney with metastasis in the liver and retroperitoneal lymph nodes. Histological, detailed immunohistochemical studies and electron microscopic examinations were performed. Microscopy revealed small to intermediate sized cells with hyperchromatic nuclei, scanty cytoplasm, abundant mitosis with no pseudorossete formation. Immunohistochemical study revealed positive staining of the tumor cells for S100, neurofilaments, neuron specific enolase, vimentin and myoglobin. Primitive neuroectodermal tumors are rare malignant round cell tumors of the kidney. A correct diagnosis can be made on light microscopic features, and by immunohistochemically positive staining for more than one neural marker. This neoplasm should be differentiated from other renal neoplasms composed of small round cells.

Keywords: Extraskeletal Ewing's sarcomas, peripheral primitive neuroectodermal tumor, primitive neuroectodermal tumor of kidney.

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Historically it was Stout in 1918, who described a tumor of the ulnar nerve that formed rosettes and axons in tissue culture[1] and which, he called peripheral neuroepithelioma, but it was later more commonly designated as malignant peripheral primitive neuroectodermal tumor (PNET). In 1921 Ewing described a tumor of bone[2] which, became known as Ewing's sarcoma, and which subsequently was recognized to occur in extra-skeletal locations.[3,4] Cytogenetic evidence shows that PNETs and extra-skeletal Ewing's sarcoma (EES) share t(11:22) (q24:q12) chromosomal translocation and are closely related to each other.[4] However, later some workers have suggested that PNETs should be differentiated from EES on the basis of positivity for more than one neural marker or some other evidence of neuronal differentiation in the former, or both, and also as the latter has a better prognosis.[5] Correct diagnosis of these tumors is a challenge especially when the presentation is unusual. This study describes a case of PNET, which presented as a renal mass and discusses some of the problems faced in distinguishing these tumors from other small round cell tumors that also occur in the kidney.[6-9] Only 17 cases of renal PNETs have been recorded in the literature.[10-24]

Case Report. A 32-year-old male presented with a huge (17x10.5x5 cm) right kidney with metastasis in the retroperitoneal lymph nodes. The first clinical impression was of renal cell carcinoma. He underwent surgical radical excision with right unilateral nephrectomy and multiple retroperitoneal

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lymphadenectomies. Detailed histological, electron microscopic and immunohistochemical studies were performed on these specimens.

Pathological features. Grossly the kidney measured 17x10.5x5 cm with a dilated ureter measuring 5x1 cm with a smooth external surface containing multiple hemorrhagic foci. Cut surface of the kidney revealed infiltration by tan - white to gray tissue with multiple foci of hemorrhage and necrosis involving mainly the central portion of the kidney, measuring 8x6.5x3 cm. Microscopic examination revealed tumor cells infiltrating the medullary region of the kidney in the form of islands of small to intermediate sized cells with hyperchromatic nuclei, scanty cytoplasm, abundant mitosis, no cytoplasmic striations or glycogen and no pseudorossete formation **Figure 1**. Multiple areas of necrosis were seen. Focally the tumor showed areas of cortical invasion but no extension outside the Gerota's fascia. The kidney tissue adjacent to the tumor showed unremarkable glomeroli, (**Figure 2)** however there was a diffuse infiltration of mononuclear cell infiltrate in the cortex and medulla with the dilation of tubules containing proteinacious eosinophilic material.

Immunohistochemical features. The first panel of antibodies was performed including keratin, EMA, desmin, myoglobin, actin, S100, vimentin, LCA, B and T cell markers. The tumor cells stained positive with vimentin, S-100, neuron specific enolase, desmin and myoglobin. The differential diagnosis was small cell carcinoma, peripheral neuroectodermal tumor, extra skeletal Ewing's sarcoma, rhabdomyosarcoma and metastatic malignant melanoma. A 2nd panel of antibodies was performed including repeat of S-100, HMB 45, chromogranin, CD - 99 and neurofilaments. The tumor cells revealed positive stain with S-100 and focally with neurofilaments and CD-99, all other antibodies were negative. These features highly suggested the diagnosis of peripheral neuroectodermal tumor. A 3rd panel of antibodies was performed including S-100, chromogranin, neurofilaments, desmin, myoglobin and actin. The tumor cells showed positive stain for S-100, myoglobin, desmin (**Figure 3)** vimentin and focally positivity for neurofilaments. ***Electron microscopic features.*** The tumor cells showed autolysis with increased nuclear cytoplasmic ratio. The chromatin was primitive hetrochromatin, cytoplasm was sparse with few mitochondria and large number of free ribosome. No neurosecretory granules or striated thin or thick filaments were visualized.

Discussion. Only 17 cases of primary renal primitive neuroectodermal tumor (PNET) have been described in the literature.[10-24] The patient's ages ranged in literature from 4 to 61 years; the majority were in the 2nd and 3rd decades of life. In our case,

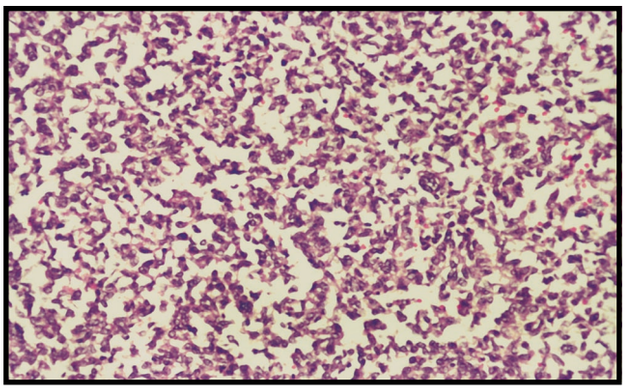

Figure 1 - Hematoxylin and eosin x 200 view of the tumor cells showing small to intermediate sized cells with hyperchromatic nuclei and scanty cytoplasm.

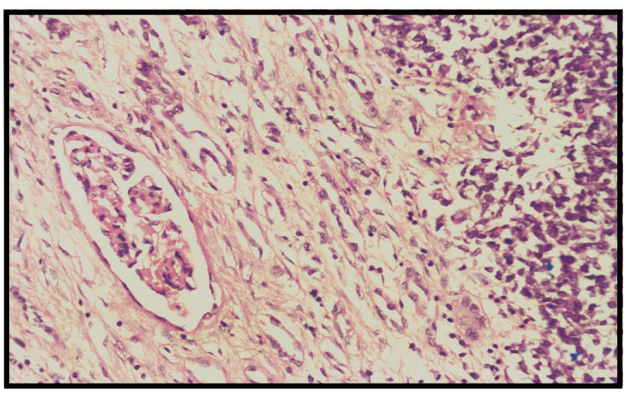

Figure 2 - Hematoxylin and eosin x 200 view showing the tumor cells invading the renal cortex.

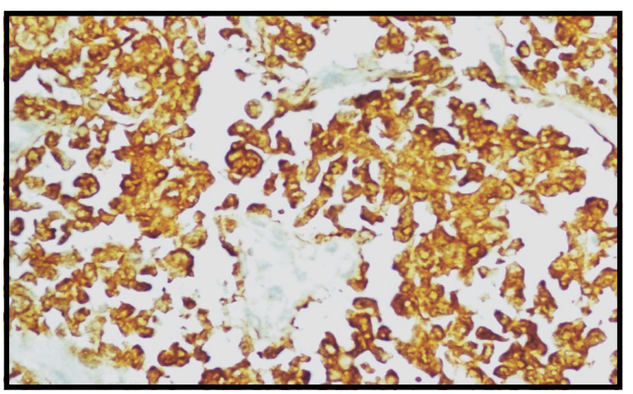

Figure 3 - Tumor cells are positive with myoglobin staining as well as desmin, S100, neurofilaments and vimentin.

age of the patient was 32 years. Initial signs and symptoms were nonspecific and similar to those of other renal mass lesions. Renal PNETs tend to be large at diagnosis and may entirely replace the underlying renal parenchyma. The reported sizes have ranged from 4 cm to 24 cm (mean, 16 cm).[10-15,17-19,22,23] The size of the tumor in our case was at midline of the described range measuring 8x6.5x3 cm. Invasion into adjacent tissues by the tumor, including perinephric adipose tissue, renal vein, or inferior vena cava have been reported in literature.[13-16] In our case the tumor was confined to the kidney with evidence of cortical invasion but not beyond Gerota's fascia. The gross descriptions of PNETs are all reported as tan-white to gray containing areas of hemorrhage, necrosis, and cystic degeneration.

At the microscopic level, these tumors resemble PNETs found elsewhere and consist of sheets of monotonous cells with scanty cytoplasm traversed by thin, fibrous bands. Perivascular pseudorosettes are often reported,[16-20] but true rosettes are unusual. Primitive neuroectodermal tumors mostly express positivity for vimentin, NSE, S-100 and variable positivity for neurofilaments. Two cases reported in the literature have shown positivity for desmin and no case,[16,17] so far, has shown positivity for myoglobin. Our case expressed positivity for both desmin and myoglobin. Expression of the MIC-2 (or CD 99) gene product (p30/32) as determined by immunohistochemistry using the 013 or HBA71 antibody, is of great assistance in diagnosing PNET, and it was also mildly positive in our case.[10,11,16,21,23]

One must bear in mind that lymphoblastic lymphoma and, occasionally, other neoplasms react with HBA71 and 013.[12,13] The majority of PNETs show positive results with antibodies to vimentin and neuron-specific enolase, while minorities are positive with S-100 protein and cytokeratin.[10,16,17] Electron microscopy demonstrates primitive cells with interdigitating cell processes containing a few dense-core granules and microtubules. Cytogenetic studies can be extremely useful in confirming the diagnosis of PNET at this site,[24] including reverse transcription polymerase chain reaction and fluorescence in-situ hybridization (FISH), which allow confirmation of the PNET/Ewing sarcoma specific t(11:22) and t(21:22).[24]

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