Peripheral primitive neuroectodermal tumor of the adrenal gland: A rare entity

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ABSTRACT
Peripheral primitive neuroectodermal tumor (PNET) is an uncommon tumor and the overall incidence is 1% of all sarcomas. PNET of the adrenal gland is an even rarer entity. A 37-year-old female was evaluated for an episode of loin pain. Ultrasonography showed a large heterogenous left adrenal mass with internal echogenic components. Computed tomography did not show any fat density within to suggest a myelolipoma. Biopsy suggested a poorly differentiated neoplasm with a possibility of PNET of the adrenal gland.

Key words: Adrenal, PNET, CD99

INTRODUCTION
Peripheral primitive neuroectodermal tumor (PNET) is an uncommon tumor and the overall incidence is 1% of all sarcomas.² PNET is so named because the majority of cells in the tumor are derived from the neuroectoderm but have not developed and differentiated in the way a normal neuron would, and so the cells appear “primitive.” This tumor can occur at any age, although the peak age incidence is during adolescence and young adulthood. In general, PNET is a very aggressive neoplasm with a poor prognosis, 5-year disease-free survival rate being 45%-55%.² The most common locations of peripheral PNETs are the thoracopulmonary region, the retroperitoneal paravertebral soft tissues, and the head and neck region. The incidence of peripheral PNET in the abdomen and pelvis, including the retroperitoneum, is about 14% of all peripheral PNETs.²

CASE REPORT
A 37-year-old female presented with an episode of dull aching pain in the left loin. There was no history of hematuria, calciuria, lower urinary tract symptoms (LUTS), headache, palpitation, excessive sweating, weight loss, jaundice, or fever with chills. Her pulse rate was 70/ min and blood pressure was 110/70 mm Hg. There was no palpable mass. Her serum cortisol (8 a.m., 4 p.m., and midnight), dehydroepiandrosterone (DHEAS), testosterone, electrolytes, urinary metanephrines, and normetanephrines were normal. Her 24 h urine cortisol was raised and low-dose dexamethasone test was positive. She was diagnosed to have Cushing's syndrome. Ultrasonography revealed an 8 × 7 cm large heterogenous left adrenal mass with internal echogenic components. Contrast-enhanced computed tomography (CECT) abdomen and pelvis also showed an 8 × 7 cm left adrenal mass with no fat density [Figure 1]. Left open radical nephrectomy, adrenalectomy, and spleenoraphy was done as the tumor seemed to infiltrate the kidney and was densely adhered to the spleen and the diaphragm. She had an uneventful postoperative recovery. She was given hydrocortisone during the operation which was gradually tapered in the postoperative period. Following excision of the mass, the 24 h urine cortisol level returned to normal.

Gross specimen showed a 12 × 10 × 8 cm left adrenal mass, infiltrating the left kidney. Cut section showed hemorrhagic and necrosed adrenal mass adherent to the kidney [Figure 2]. Microscopy showed a predominantly necrotic and hemorrhagic tumor with few viable areas composed of diffuse sheets of small to medium sized round cells with

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round to oval vesicular nuclei exhibiting mitoses up to 10-15/50 hpf and containing scant to moderate cytoplasm. The tumor cell nests infiltrated the thick fibrous capsule and extended into the pericapsular adipose tissue. There were foci of vascular invasion [Figure 3]. Immunohistological staining using CD 99 showed strong positivity [Figure 4]. There was weak positivity with FLI 1, in at least 50% of cells [Figure 5].

DISCUSSION

In 1918, Stout first reported a 42-year-old man with ulnar nerve tumors and raised the concept of PNET.[3] They are primitive derivates of neural crests which originated from basal embryo cells in the primitive neural tube.

Peripheral PNETs often arise in deep soft tissues. The tumor can be solid or solid-cystic with no capsule. It is a highly invasive tumor leading to bleeding and necrosis. Tumor sites are shown as rough-bordered, diffusely growing, and heterogeneously enhancing masses in computed tomography scans. Histopathological and immunohistochemical examination is essential for the diagnosis of PNET.

Immunohistochemical tests can provide valuable support to the definitive diagnosis of the tumor CD99 is highly specific and sensitive, as its detection rate in PNET is as high as 100%. Besides CD99, other markers of neural differentiation include: Neuron-specific enolase, S-100 protein, neurofilament protein, synaptophysin, chromogranin A, etc. They are all significant in the diagnosis of PNET.[4] The FLI-1 gene and FLI-1 protein are also well-known for their role in the pathogenesis of Ewing’s sarcoma and PNET. The majority of these tumors are characterized by the translocation t(11;22)(q24;q12), resulting in a fusion of the Ewing’s sarcoma (EWS) gene on chromosome 22 to the FLI-1 gene on chromosome 11. FLI-1 is a member of the ETS family of transcription factors.[5]

The rarity of this entity is documented by Zhang and
Li[6] who noted that only 16 cases had been reported as of 2010. Since adrenal PNET is a very rare clinical disease, an effective treatment protocol is yet to be established. Most patients have metastasis at presentation. Local control through surgery, radiotherapy or chemotherapy would not improve prognosis. Surgery is usually followed by adjuvant radiotherapy and chemotherapy. A recommended schedule is alternating use of the CAV protocol (cyclophosphamide: CTX; adriamycin: ADM; and vincristine: VCR) and the IE protocol (ifosfamide: IFO; and etoposide: ETO).[7]

REFERENCES

1. Maccioni F, Della Rocca C, Salvi PF, Manicone AM, Ascarelli A, Longo F, et al. Malignant peripheral neuroectodermal tumor (MPNET) of the kidney. Abdom Imaging 2000;25:103-6.
2. Jurgens H, Bier V, Harms D, Beck J, Brandeis W, Etspuler W, et al. Malignant peripheral neuroectodermal tumors: A retrospective analysis of 42 patients. Cancer 1988;61:349-57.
3. Stout AP. A tumor of the ulnar nerve. Proc NY Pathol Soc 1918;12:2-12.
4. Weidner N, Tjoe J. Immunohistochemical profile of monoclonal antibody O13: Antibody that recognizes glycoprotein p30/32MIC2 and is useful in diagnosing Ewing’s sarcoma and peripheral neuroepithelioma. Am J Surg Pathol 1994;18:486-94.
5. Rossi S, Orvieto E, Furlanetto A, Laurino L, Ninfo V, Dei Tos AP. Utility of the immunohistochemical detection of FLI-1 expression in round cell and vascular neoplasm using a monoclonal antibody. Mod Pathol 2004;17:547-2.
6. Zhang Y, Li H. Primitive Neuroectodermal tumors of adrenal gland. Jpn J Clin Oncol 2010;40:800-4.
7. Granowetter L, Womer R, Devidas M, Krailo M, Wang C, Bernstein M, et al. Dose-intensified compared with standard chemotherapy for nonmetastatic Ewing sarcoma family of tumors: A Children’s Oncology Group Study. J Clin Oncol 2009;27:2536-41.