CASE REPORT

IMAGING EVALUATION OF AN EXTREMELY RARE PRIMITIVE NEUROECTODERMAL TUMOR OF ADRENAL GLAND: AN INTERESTING CASE

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ABSTRACT

Primitive neuroectodermal tumor of adrenal gland is a rare malignant neoplasm. It is categorised under peripheral primitive neuroectodermal tumors (pPNET). They have aggressive course with very poor prognosis. A 10-year old male patient was being evaluated for left loin pain. Ultrasonography showed a large mass in left lumber region with heterogenous echotexture and increased vascularity on colour Doppler. Computed tomography showed the mass was arising from left suprarenal gland. PET-CT scan revealed the mass was metabolically active. Biopsy from that mass showed histopathological features consistent with primitive neuroectodermal tumor of adrenal origin.

Key words: Adrenal gland, Primitive neuroectodermal tumor, F^{18}-FDG , PET CT scan, Ewing sarcoma

Abbreviations: PNET = Primitive neuroectodermal tumor, PET = Positron Emission Tomography, CT= Computed Tomography, FDG= Fluorodeoxyglucose

Introduction

Primitive neuroectodermal tumors (PNET) are malignant neoplasms believed to be originated from neural crest cells. Most of the neuronal cells of these tumors appear undifferentiated and that is why they are called 'primitive'. Majority of them are found in the cerebellum and parts of central and sympathetic nervous systems. Peripheral PNET is less common and its occurrence is 1% of all sarcomas.[2] PNET of adrenal gland is even rarer. The tumor can occur at any age, although peak incidence is seen during adolescence and young adults. In general, PNET is an extremely aggressive neoplasm with a very poor prognosis, 5 year disease free survival rate being 45-55%.[1] The prognosis is relatively better in younger people. The tumor shows equal gender predisposition. The most common locations of peripheral PNETs are the thoracopulmonary region, the head and neck region and the retroperitoneal paravertebral soft tissues. 14% of all peripheral PNETs occur in the abdomen and pelvis, including the retroperitoneum.[1]

Case Report

A 10-year-old male child presented with abdominal pain for past 2 months. As he stated, initially the pain was intermittent but gradually became constant, dull aching and localised to left upper abdomen. He had associated history of weight loss. There was no history of hematuria, urinary tract infection, fever, headache, sweating or palpitation. On examination, the patient had stable vitals. Physical examination revealed tenderness over left hypochondrium and left lumber

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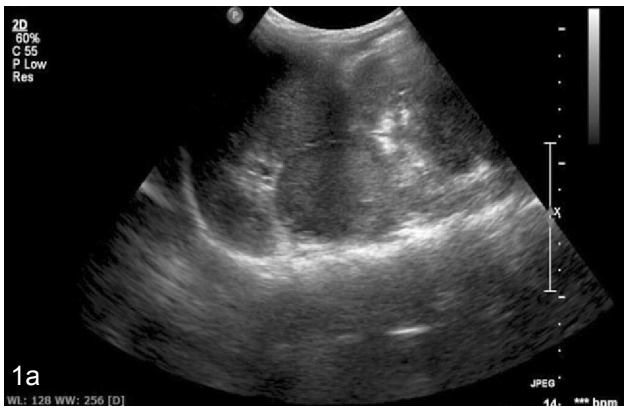
region on deep palpation. Other physical findings were unremarkable. The routine haematological tests were normal. Serum cortisol, dehydroepiandrosterone, testosterone, serum electrolytes, urinary metanephrine and nor-metanephrine levels were within normal limits. Ultrasonography revealed large mass (10.6 cm × 5.6 cm × 5 cm) in the left hypochondrium with heterogenous echotexture and increased vascularity on colour doppler. It could not be definitively opined whether it was of renal or suprarenal origin. Contrast enhanced computed tomography was performed which revealed an irregular, multiloculated, heterogenous mixed density enhancing lesion in left suprarenal region extending to left renal fossa, compressing and invading the part of left kidney; Absolute percentage wash (APW) of the mass was 9.6 that is less than 60. Features were consistent with malignant adrenal neoplasm. Also, multiple significantly enlarged necrotic retroperitoneal lymph nodes were noted with complete encasement of left renal vessels and abutting the aorta from right side. Biopsy was done from that mass and histopathological examination showed hypercellular tumor composed of small blue round cells with hyperchromatic nucleus, stippled chromatin and scanty cytoplasm arranged in sheets, trabeculae and cell nests within a fibrocollagenous stroma. Many cells showed spindling, occasional true and pseudorosettes were seen. Tumor was metabolically active. The optical microscopic features and immunohistochemistry were consistent with primitive neuroectodermal tumour of adrenal gland. A whole-body F^{18}-FDG (Fluorodeoxyglucose) PET-CT scan was done to confirm suprarenal gland as the primary site for the tumour and the status of metastasis. It showed that the suprarenal mass was metabolically active and



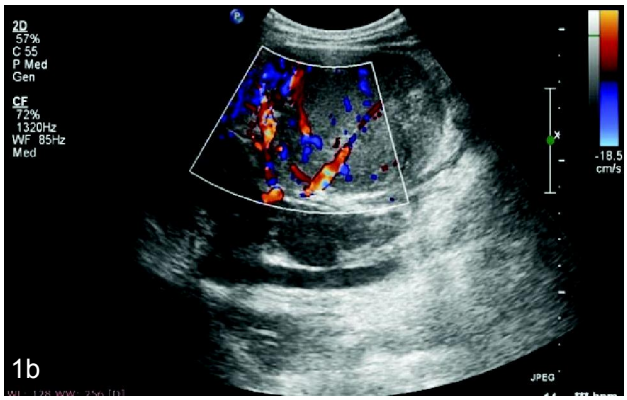


Figure 1: Ultrasonographical appearance of the mass in saggital section **(a)** 2D grayscale mode showing the mass between spleen and left kidney and **(b)** Colour doppler showing increased vascularity of the mass.

active metastatic involvement of left ilium was present. After retrospective review of literature, diag-nosis of adrenal PNET was obtained.

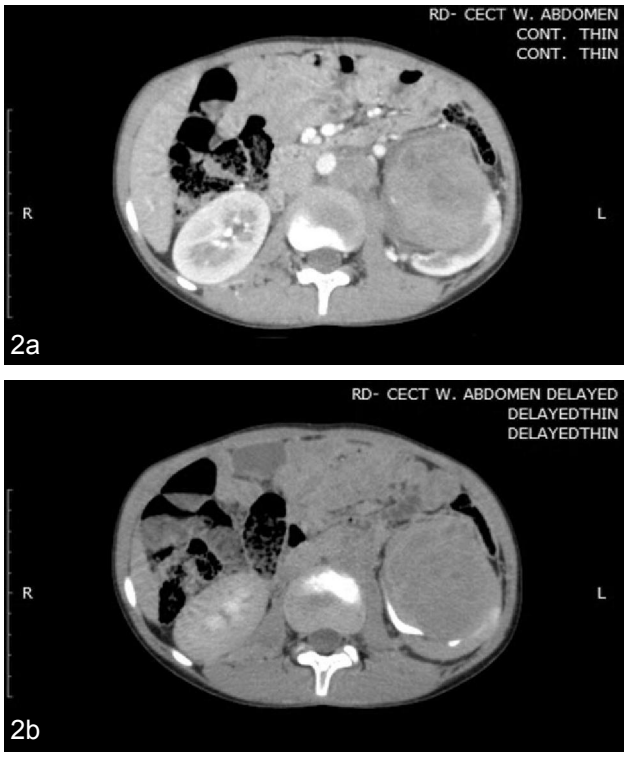


Figure 2: Contrast enhanced CT appearance of the left suprarenal mass showing enhancement **(a)** and washout in delayed scan **(b)**.

Discussion

In children, adrenocortical masses are most often non-functional benign lesions such as adenoma but

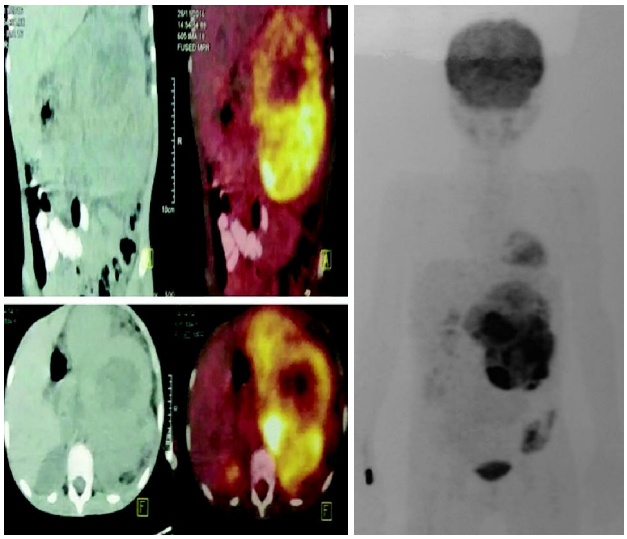


Figure 3(a): Appearance of the left suprarenal mass in PET-CT scan showing increased metabolic activity; **(b)** Whole body bone scan shows metastatic involvement of left ilium

can be functional with hormonal symptoms. Adrenal carcinoma is very rare and follow a bimodal distribution with one peak at 5 years and the other in 4th decade. These tumors are most often functional especially in children and often larger than 4 cm. Adrenal medullary tumors such as pheochromocytoma and neuroblastoma are more common in children. Majority of them are quite large, accompanied by increased catecholamines and/or abnormal uptake on metaiodobenzylguanidine (MIBG) scan.

PNET arising from the adrenal are extremely rare with very limited literature about them or their management. Though PNET occurs equally in both sexes, it is more common in younger age group.

In 1918, Stout first reported a 42-year-old man with ulnar nerve tumors and raised the concept of PNET.[3] After three years in 1921, Ewing reported a case of a 14-year-old boy with osteoclasia in the ulna and proposed the name 'Ewing sarcoma'.[4] Both of the tumors were derived from primitive neuroectoderma. To sub classify these tumors, the degree of neural differentiation are used which are evaluated by various microscopic modalities; for example, classic ES with minimal neuronal differentiation and ES/PNET, where translocation of t (11; 22) (q24; q12) involving the EWSR1 gene on chromosome 22 and the FLI-1 gene on chromosome 11 occur, yielding the EWL/FLI-1 fusion protein. Ewing sarcoma and PNET, both tumours show positivity for CD99 whereas only PNET shows positivity for NSE.[5] Though criteria are not well defined but most authors agree that positivity for atleast CD99 and Neuron Specific Enolase and presence of small blue cells arranged in nest and rosettes are required for diagnosis. In 1973 Hart and Earle defined a group of unspecialized small cell tumors as PNETs and raised the concept that these kind of tumors were all primitive derivates of neural crests originating from basal embryo cells in the primitive neural tube and belonged to the PNET family.[6] Later, in 1979, Askin et al. named PNETs in the thoracic cavity (PNETs in a special location) as 'Askin tumors'.[7] PNETs can be divided into two types: central and peripheral. Peripheral PNETs (pPNETs) originate outside the central nervous system. pPNET can occur in the trunk especially to the chest wall, limbs, paravertebral and retroperitoneal areas , parenchymal organs, such as kidneys, adrenal glands, spleen, pancreas, lungs, post-mediastinum, testicles, spermatic cords, bladder, prostate and rectum etc. It is a very rare disease. Case reports around the world are mostly based on small quantities of patients.

pPNET is very rare and found mostly in children and young adults and with equal gender predisposition. People of older age group has poorer prognosis.[5] The tumor can be solid or solid - cystic with no envelope. It grows invasively and may cause bleeding and necrosis. In CT scans, tumor sites appear as rough-bordered, diffusively growing unevenly enhancing masses.[8]

PNET in the adrenal gland is even rarer. It is a very aggressive neoplasm with a poor prognosis. Unlike most other adrenal tumors like chromaffinoma or adrenocortical carcinoma , PNET does not show any specific endocrinological change and those test results are usually negative.[8] As PNET shows no specific clinical changes, a combination of histopathological and immunohistochemical examinations and cytogenetic analysis are essential for its diagnosis.

Radiological features of pPNETs are non specific. However, most of the tumors are larger than 3 cm, may contain internal septations, intratumoral cysts, foci of calcifications, areas of hemorrhage and necrosis within the tumor. The tumors exhibit heterogenous enhancement in contrast enhanced CT scans and may show invasion to adjacent organs and vessels.[9] The diagnosis and differential diagnosis of PNET is

ultimately made by histopathological and immunohistochemical examinations. Under Light Microscope, PNET appears as many primary small diffusively distributed uniform round cells which may form lobulated structures. The cell has little cytoplasm, dark stained nucleus with high nucleoplasm. Tumor cells can form classical Homer - Wright rosette or other kind of rosettes. Areas of focal necrosis can also be seen. Immunohistochemical tests can provide valuable support to the definitive diagnosis of the tumor. P30/32MIC2 (now called as CD99 antigen) is the most important marker.[10] It is a cell surface glycoprotein coded by heterochromatin MIC2 genes located on X and Y sex chromosomes. Its biological function is not clearly known (probably related to the formation of the rosettes). CD99 is highly sensitive and specific, as its detection rate in PNET is as high as 100%. Other important markers are: neuron-specific enolase (NSE), S-100 Protein, neurofilaments, chromogranin A (CgA), vimentin synaptophysin (Syn), etc. They all help in diagnosis of PNET.

The gold standard for diagnosis of PNETs is the translocation showed by molecular techniques as FISH to detect the rearrangement of the EWSR1 gene.[11] Some other kidney cell-derived round cell tumors for example small cell carcinoma, myxoid liposarcoma or small round cell desmoplastic tumor can also express EWSR1 translocation, thereby making it difficult to differentiate from PNETs.[5,11-14] Some other tumors such as Wilms tumor, neuroblastoma, malignant lymphoma, synovial sarcoma exhibit morphological similarity with PNETS and can make the diagnosis harder due to rarity of PNETs.[5] Adrenal PNETs should also be differentiated from some other adrenal pathlogies including pheochromocytoma, neuroblastoma and adrenocortical cancer.[5,11-14]

The rarity of this entity is documented by Zhang and Li[8] who showed that only 16 cases had been reported as of 2010. As adrenal PNET is a very rare disease, there has not been an elaborate and effective treatment protocol. Most PNET patients exhibit metastasis by the time the tumor is diagnosed. Even the local site is controlled through surgery or chemoradiation, the prognosis will still be poor. The tumor is highly invasive and metastasizable. So it is very difficult to achieve total clearance and the tumor usually has recurrence. Some of the tumors show high sensitivity to radiotherapy and chemotherapy. So the surgery is usually followed by adjuvant radio - and/or chemotherapy to achieve clearance of tumor as far as possible. Minimal invasive approach like laparoscopic adrenalectomy has been proven to be safe and feasible with benifits of minimal pain and short recovery time. It is considered to be Gold standard by a growing number of authors. Robotic assistance has the potential of improved visualisation and enhanced dissection capability due to enhanced degrees of freedom of the instruments but with a precaution that the tumor may rupture which may lead to further need for chemoradiation. The chemotherapy protocol of PNET can be derived from that of Ewing sarcoma as they share the same origin. In majority of the cases, CAV protocol (cyclophosphamide: CTX; adriamycin: ADM; and vincristine: VCR) is used alternating with the IE protocol (Ifosfamide: IFO; and etoposide: ETO). However, it is only effective for the first few courses.[8]

Conclusion

PNET is a very aggressive disease with very short history and high mortality rate. The tumor is highly diffusive so it invariably shows local recurrence and distant metastasis. As the disease is very rare it is not usually considered in the differential diagnoses of an adrenal mass. However it should be suspected whenever the patient presents with large nonfuntional adrenal mass because early diagnosis is important to ensure early surgical resection followed by appropriate chemoradiation.

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 N Y Soc Pathol 1918; **12:** 2-12.

4. Ewing J. Diffuse endothelioma of bone. Proc N Y Soc Pathol 1921; **21:** 17-24.

5. Delattre O, Zucman J, Melot T, Garau XS, Zucker JM, Lenoir GM, Ambros PF, Sheer D, Turc-Carel C, Triche TJ, et al. The Ewing family of tumors - a subgroup of small-round-cell tumors defined by specific chimeric transcripts. N Engl J Med 1994; **331(5):** 294-9.

6. Hart MN, Earle KM. Primitive neuroectodermal tumors of the brain in children. Cancer 1973; **32:** 890-7.

7. Askin FB, Rosai J, Sibley RK, Dehner LP, McAlister WH. Malignant small cell tumor of the thoracopulmonary region in childhood: a distinctive clinicopathologic entity of uncertain histogenesis. Cancer 1979; **43:** 2438-51.

8. Zhang Y, Li H. Primitive Neuroectodermal tumours of adrenal gland. Jpn J Clin Oncol. 2010; **40:** 800-04.

9. Kim M, Kim B, Park C, Song S, Lee E, Park N, et al. Radiologic Findings of Peripheral Primitive Neuroectodermal Tumour Arising in the Retroperitoneum. American Journal of Roentgenology. 2006; **186(4):** 1125-32.

10. 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.

11. Etani T, Naiki T, Ando R, Iida K, Naiki-Ito A, Takahashi S, Kobayashi D, Kawai N, Tozawa K, Yasui T, Kohri K. A case of renal primitive neuroectodermal tumor confirmed by fluorescence in situ hybridization. Case Rep Oncol 2015; **8(1):** 205-11.

12. Carvajal R, Meyers P. Ewing's sarcoma and primitive neuroectodermal family of tumors. Hematol Oncol Clin North Am 2005; **19(3):** 501-25.

13. Kumar S, Govinda V, Singh SK, Singh J. Bilateral adrenal PNET: a rare presentation. J Clin Diagn Res 2016; **10(9):** XD01-02.

14. Sarver AE, Sarver AL, Thayanithy V, Subramanian S. Identification, by systematic RNA sequencing, of novel candidate biomarkers and therapeutic targets in human soft tissue tumors. Lab Invest 2015; **95(9):** 1077-88.