Aegean Pathology Journal **2**, 49–53, 2005
Available on line at www.epd.org.tr/apj.php

Primitive neuroectodermal tumor of the kidney: A case report and review of the literature

Seyda Erdogan*, Canan Ersoz*, Gulfiliz Gonlusen*, Ahmet Tuganalp**
** Department of Pathology, Cukurova University Faculty of Medicine, Adana, Turkey*
*** Department of Urology, Adana SSK Hospital, Adana, Turkey*

Accepted for publication on 6 May 2005

Background: Primitive neuroectodermal tumors (PNETs) represent a family of neoplasms, presumed to be of neuroectodermal origin and mostly presenting as bone or soft tissue masses in the trunk or axial skeleton in adolescents and young adults.
Case: The patient was 32-year-old man. On gross examination, the tumor measured 16x14 cm in dimensions, with cystic areas and necrosis. Microscopically, the neoplasm was highly cellular consisting sheets of small-round-to-oval cells with irregular nuclei. Immunohistochemical stains were positive for vimentin and CD99. Microscopic and immunohistochemical findings were compatible with PNET.
Conclusion: Although rare, PNET must be included in the differential diagnosis of renal tumors especially in children and young adults. We present a case of renal PNET as an unusual case, discuss the differential diagnosis of small round-cell tumors in this location and review the literature.

Keywords: primitive neuroectodermal tumor, kidney

Introduction

Primitive neuroectodermal tumor (PNET) is thought to arise from primitive cells of neural crest and commonly involves the bone and soft tissue in adolescents.[1] It was first described by Stout in 1918.[2] Renal PNET is an extremely rare entity. It had been documented as isolated case reports.[1,3–17] There are only two series of renal PNET that was published by Parham[11] and Jimenez[12] in the literature. Here we report a rare case of renal PNET and review the literature.

Case report

A 32 year-old-man was admitted to a hospital with abdominal pain. Physical examination revealed a palpable mass in the right upper abdomen. Computerized tomography (CT) of the abdomen demonstrated a large tumor which was confined to the right renal paranchyma. The results of laboratory studies were within normal limits. Chest X-ray and bone scan showed no evidence of a metastatic disease. CT investigations ruled out any other primary tumor, except kidney. The patient underwent a right nephrectomy and was introduced to our hospital for further evaluation. Gross examination of the resected kidney showed extensive replacement of the renal paranchyma by grayish-yellow, 16 x 14 x 10 cm tumor with focal cystic areas and irregular areas of necrosis (Figure 1). Macroscopically, renal parenchyma, perirenal space and renal vein were invaded by tumor. Microscopically tumor consisted of small-sized, round-oval shaped cells with irregular nuclei and ill defined cytoplasmic borders. Poorly formed rosette-like structures were rarely observed (Figure 2). There were extensive areas of hemorrhage and necrosis. Paraffin-embedded preparation was stained immunohistochemically using streptavidin biotin

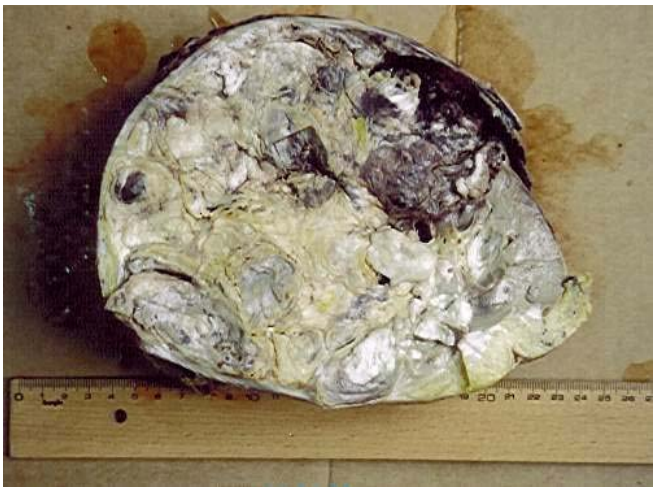

Figure 1. Gross appearance of the resected specimen showing extensive replacement of the kidney by necrotic tumor.

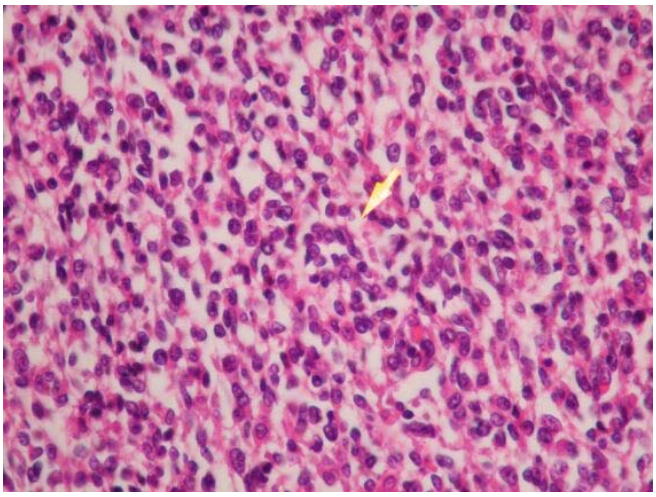

Figure 2. Microscopic view of tumor consisted of small cells with dark nuclei, ill-defined cytoplasmic border and poorly formed rosette like structures (arrow), H&E X 200.

system. Immunohistochemical stains were positive for vimentin and CD99 (MIC-2 gene product, 12E7) (cytoplasmic surface membrane staining) whereas negative for cytokeratin, LCA, desmin, S-100, Tdt (Terminal deoxynucleotidyl transferase), NSE, and synaptophysin (Figure 3). There was also focal positivity with chromogranin. Based upon the microscopic appearance and immunohistochemical features, the diagnosis of PNET of kidney was established. Unfortunately, we couldn't perform cytogenetic analysis. The pathologic stage of tumor was pT3b. Despite additional chemotherapy the patient died two months after the initial diagnosis.

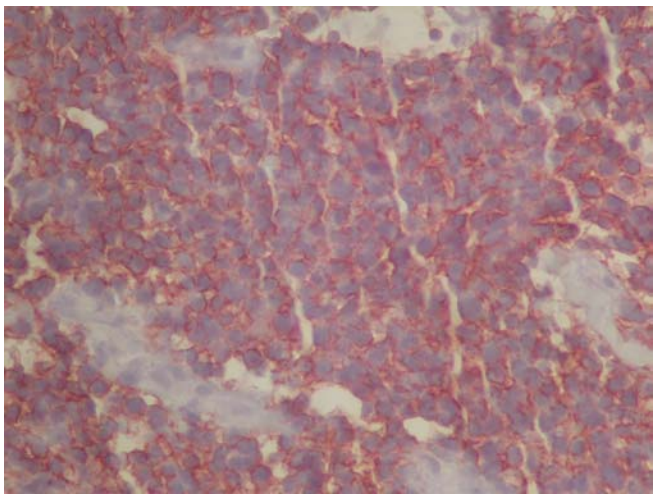

Figure 3. Tumor cells showing intense positive staining with CD 99, Immunohistochemistry X 400.

Discussion

The small cell tumors of the kidney are a heterogeneous group of neoplasms with overlapping morphologic features and different prognostic/therapeutic implications. This group of tumors usually include blasteme-predominant Wilms' tumor (WT), PNET, neuroblastoma, rhabdomyosarcoma, lymphoma and desmoplastic round cell tumor.[4–6] Among these, PNET of the kidney is a rare entity that classically occurs in children and young adults.[7–10]

Several theories have been proposed for a reasonable explanation for the genesis of PNETs which arise at peripheral sites.[5,11] One of them is the presence of aberrant neural crest cells in the kidney. Another explanation for genesis is arising from the neural ramifications of the celiac plexus that intervates the kidney.[5,11]

Renal PNET was first reported by Mor et al.[5] Between 1994-2004, approximately 40 renal PNET cases have been reported.[1–17] However, Parham et al. have reported a large series of malignant neuroepithelial tumors of the kidney including 79 cases considered to be PNET on the basis of histology and immunohistochemistry.[11] Recently, Jimenez et al. have cited additional 11 cases including 8 cases with follow-up information.[12] Among these, one patient was alive without evidence of disease with a survival of 64 months which seems to be the longest survival in the literature.[12] In other reports, survival time ranged from

Table 1. Review of the literature on primitive neuroectodermal tumor of the kidney.

Author	Number of cases	Age/sex	Metastase	Outcome
Mor et al.(5)	1	61/M	None	Died after 6 months
Chan et al.(13)	1	22/M	None	Died after 10 months
Mentzel at al.(9)	1	24/M	Lung	Died shortly after surgery
Kurihara et al.(14)	1	25/F	Vena cava inferior	Died after 2 months
Horiguchietal.(15)	1	27/M	Lymph node	Died after 3 months
Guputa et al.(16)	2	35/F, 42/M	None	Died after 60 and 14 months respectively
Furman et al.(7)	1	21/F	Lymph node	Died after 5 months
Takeuchi et al.(6)	1	22/M	Lung	Died after 4 months
Rodriguez et al.(1)	4	18/M, 20/M, 4/F, 14/M	Lung, lymph node, bone, liver	Died after 14 months, 4 months, 1 month, 3 weeks
Herman et al.(3)	1	17/not stated	Not stated	Not stated
Sheaff et al.(17)	1	56/F	None	Died after 5 months
Marley et al(4)	1	17/F	None	Died after 1 year
Kuroda et al.(9)	1	28/M	None	Alive without disease
Gonlusen et al.(8)	1	23/F	Local recurrence	Died after 1 month
Parham et al.(11)	79	Median 20 years	Follow-up was available in 14 patients.Of these 4 died of metastatic disease 7 to 35 months after diagnosis. 10 were alive. But it is not clear which, if any of these were PNET among the large series of 146 malignat neuroepithelial tumors of kidney.	
Jimenez et al.(12)	11	69/F, 33/F, 41/M, 32/F, 25/M, 11/M, 31/M, 29/M, 21/F, 27/F, 50/M	5 cases with lung, bone, pleura, liver lymph node metastasis, 1 with recurrence, 2 cases had no metastasis, not stated in 3 cases. 5 of them died after 6 to 26 months, 3 were not stated, 3 were alive without disease.	
Segura et al.(10)	1	38/M	Lung, liver, bone	Died of disease
Present case	1	32/M	Liver, recurrence	Died of disease

1 to 24 months with distinctively poor prognosis among patients with distant metastases at diagnosis[5-7,13–15,17] The most common metastatic sites were lymph nodes, lung, liver and bone.[1,6,7,15] Most of these previously reported cases have occurred in young male adults.[4–6,9–11,13,15] All of the cited cases exhibited the similar histologic features with small cells arranged in cords, nests or clusters with or without rosettes and pseudorosettes. A summary of cases cited in the literature appears in Table 1.

All other small round cell tumors of the kidney must be included in the differential diagnosis of renal PNET.[1–17] Immunohistochemically CD99, NSE and vimentin are expressed by PNET cells. S-100 protein,

synaptophysin, neurofilament protein, CD57 and chromogranin show variable reactivity. CD99 positivity is an universal feature of PNET. However, cannot be used as an absolute marker to separate it from small cell carcinomas. Malignant lymphoma especially lymphoblastic lymphoma also reveals positive staining with CD99; therefore LCA and Tdt should be performed as well. The distinction from Wilms' tumor of blastemic type may be difficult since these blastemic elements may occasionally be positive for CD99.[4–11] Jimenez et al. examined the expression of two recently described nuclear protein FL-1 and WT-1 in renal PNET. They noted FL-1 expression in 63% of PNET, but none in any of the Wilms' tumors. However they did not observe expression of WT-1 in renal PNET but in 78% of Wilms' tumors.[12] According to these findings, they pointed out that an immunohistochemical panel that includes antibodies to CD99, FL-1 and WT-1 maybe valuable in the differential diagnosis.[12] It is showed that renal PNET shows no reactivity for WT-1 gene product and can be use to exclude blastemic type Wilms tumor.

Several recent cytogenetic analyses of PNET have demonstrated a reciprocal translocation t(11;22)(q24;q12). This translocation which appears to be unique to the PNET and Ewing's sarcoma (ES), occurs in approximately 90% of these neoplasms.[4,6,7,9] Despite their genetic and antigenic similarity, most authors recognize PNET and extraskelatal ES as separate entities. Distinction is based primarily on the more neural differention of PNET.[7]

Renal PNETs are frequently aggressive and almost 30% of all newly diagnosed cases present with distant metastases. Surgical intervation, intensive chemotherapeutic drugs and radiation therapy are the best choices for the management.[8,11]

The features of our case strongly support the diagnosis of PNET of the kidney based on histopathological and immunohistochemical examinations. Histologically, the present case exhibited features of the so-called small round cell tumor. The neoplasm arose in a young male adult, was largely confined to the kidney and reacted positively with antibody to CD99. Negative staining with LCA and Tdt excluded Non-Hodgkin lymphomas especially lymphoblastic lymphoma. Focal areas of neural differentiation and positive reaction with antibody to chromogranin tend to favor PNET over ES. Immunohistochemically positive reaction with CD99 and negative reaction with cytokeratin, desmin, NSE and synaptophysin widely helped to differentiate most other small cell tumors like renal carcinoid, neuroblastoma and small cell carcinoma. In spite of an aggressive combined treatment (surgery and chemotherapy), the patient developed liver metastases and died from tumor progression after 2 months.

In conclusion, renal PNET is a rare neoplasm and should be differentiated from the other small cell tumors of the kidney. Immunohistochemistry for CD99 and if possible cytogenetic studies should be performed in all cases where PNET is considered.

References

1. Rodriguez C, Marina N, Fletcher B, Parham D, Bodner S, Meyer W. Is primitive neuroectodermal tumor of the kidney a distinct entity? Cancer 1997; 79: 2243-2250.
2. Stout AP. A tumor of the ulnar nerve. Proc of the NY Pathol Soc 1918; 18: 2-12.
3. Herman T, McAlister W, Dehner L. Peripheral primitive neuroectodermal tumor: report of a case arising in the kidney. Pediatr Radiol 1997; 27: 620-621.
4. Marley E, Liapis H, Humphrey P, Nadler R, Siegel C, Zhu X, Brandt J, Dehner L. Primitive neuroectodermal tumor of the kidney-another enigma: a pathologic, immunohistochemical and molecular diagnostic study. Am J Surg Pathol 1997; 21: 354-359.
5. Mor Y, Nass D, Raviv G, Neumann Y, Nativ O, Goldwasser B. Med Pediatr Oncol 1994; 23: 437-440.
6. Takeuchi T, Iwasaki H, Ohjimi Y, Kaneko Y, Ishiguro M, Fujita C, Miura Y, Hiratsuka Y, Sakamoto K, Kikuchi M. Renal primitive neuroectodermal tumor: an immunohistochemical and cytogenetic analysis. Pathol Int 1996; 46: 292-297.
7. Furman J, Murphy W, Jelsma P, Garzotto M, Marsh R. Primary primitive neuroectodermal tumor of the kidney. Am J Clin Pathol 1996; 106: 339-344.
8. Gonlusen G, Ergin M, Paydas S, Bolat F. Primitive neuroectodermal tumor of the kidney: A rare entity. Int Urol Nephrol 2001; 33: 449-451.
9. Kuroda M, Urano M, Abe M, Mizoguchi Y, Horibe Y, Murakami M, Tashiro K, Kasahara M. Primary primitive neuroectodermal tumor of the kidney. Pathol Int 2000; 50: 967-972.
10. Segura A, Perez J, Reynes G, Yuste A. Letter to the editor: primitive neuroectodermal kidney tumor. Med Pediatr Oncol 2002; 38: 145.
11. Parham D, Roloson G, Feely M, Green D, Bridge J, Beckwith B. Primary malignant neuroepithelial tumors of the kidney. Am J Surg Pathol 2001; 25: 133-146.
12. Jimenez R, Folpe A, Lapham R, Ro J, O'Shea P, Weiss S, Amin M. Primary Ewing's sarcoma/primitive neuroectodermal tumor of the kidney. Am J Surg Pathol 2002; 26: 320-327.
13. Chan YF, Liewellyn H. Intrarenal primitive neuroectodermal tumor. Br J Urol 1994; 73: 326-327.

14. Kurihara K, Mizuseki K, Oka A, Shishido S, Manbe M. A case of renal primitive neuroectodermal tumor. Jpn J Clin Urol 1994; 48: 855-858.
15. Horiguchi Y, Nakashima J, Ishi T, Hata J, Tazaki H. Primitive neuroectodermal tumor of the retroperitoneal cavity. Urology 1994; 44: 127-129.
16. Gupta NP, Sirgh BP, Raina V, Gupta SD. Primitive neuroectodermal kidney tumor. Two case reports and review of the literature. J Urol 1995; 153: 1890-1892.
17. Sheaff M, McCannus A, Scheimberg I, Paris A, Shipley J, Baithun S. Primitive neuroectodermal tumor of the kidney confirmed by fluorescence insitu hybridization. Am J Surg Pathol 1997; 21: 461-468.