Case Report

Primitive neuroectodermal tumor/Ewing's sarcoma in adult uro-oncology: A case series from a developing country

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Abstract

Peripheral primitive neuroectodermal tumor/Ewing's sarcoma (PNET/EWS) is primarily a tumor of soft tissues and bones. Primary localization of PNET/EWS in genitourinary organs is rare. No data on this localization of PNET/EWS are available in literature from Pakistan. We searched our adult uro-oncology records from 1994 till date and identified all cases of adult genitourinary and adrenal PNET/EWS diagnosed on histology and immunohistochemistry. Their case records were reviewed to obtain data on demographics, presentation, pathologic features, management and outcome. Six cases were found; all were young and had aggressive disease at presentation. Four had renal PNET/EWS. One case each of prostate and adrenal PNET/EWS was seen. Surgery and chemotherapy formed the mainstay of management. Three patients (50%) died during treatment, two were lost to follow-up and one case with renal PNET/EWS showed good initial response to chemotherapy but was later on lost to follow-up. In conclusion, PNET/EWS should be considered in the differential diagnosis of genitourinary malignant tumors in young patients. These tumors are aggressive with poor outcome.

Key Words: Adrenal gland, kidney, primitive neuroectodermal tumor/Ewing's sarcoma, prostate, uro-oncology

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Received: 20.06.2010, **Accepted:** 05.10.2010

INTRODUCTION

Peripheral primitive neuroectodermal tumor/Ewing's sarcoma (PNET/EWS) is primarily a tumor of soft tissues and bones. The tumor can occur in both adults and children.[1] Genitourinary localization of this family of tumors is very rare.[2] The presentation is nonspecific and radiological findings non-characteristic.[2-10] Hence, accurate diagnosis is challenging and depends on histology and immunohistochemistry (IHC) with positivity of CD 99. The disease most often presents at advanced stage, and although management has improved, the outcome is poor.[2-10]

There is no detailed clinicopathologic study available on PNET/EWS in adult uro-oncology literature from Pakistan. We undertook this study to review our experience relating to the diagnosis, management and outcome of cases of genitourinary and adrenal PNET/EWS in our practice.

Access this article online

Quick Response Code:

Website: www.urologyannals.com

DOI: 10.4103/0974-7796.82180

CASE REPORTS

We searched our adult uro-oncology record from 1994 till date and identified cases of adult genitourinary and adrenal malignancies which were diagnosed as primary PNET/EWS of these organs on histology and IHC. Six cases were identified, four of kidney and one each of prostate and adrenal gland. Their case records were reviewed to obtain data on

demographics, presentation, pathologic features, management and outcome.

Herein, we report our experience with six cases of genitourinary and adrenal PNET/EWS in our practice.

Case 1 (Kidney PNET/EWS)

GM, a 26-year-old male, presented in the uro-oncology OPD with right-sided flank pain, hematuria, abdominal swelling and weight loss. Physical examination revealed palpable fixed non-tender mass in the right flank.

Ultrasonography (USG) of abdomen demonstrated huge, well-demarcated, complex mass measuring about 18×10 cm involving right kidney. Left kidney was normal. Computerized tomography (CT) scan confirmed a large vascular right renal mass with single metastatic nodule in left lung and abdominal lymphadenopathy [Figure 1]. Bone scan was negative.

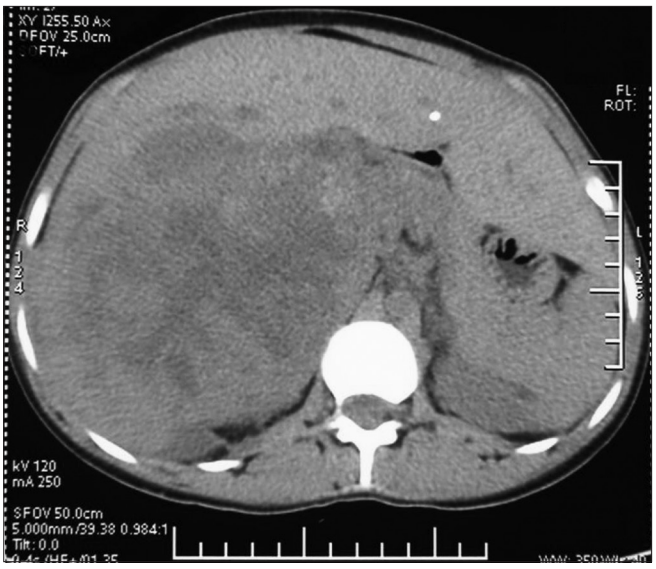

Figure 1: CT scan of abdomen showing a large heterogeneous right renal mass

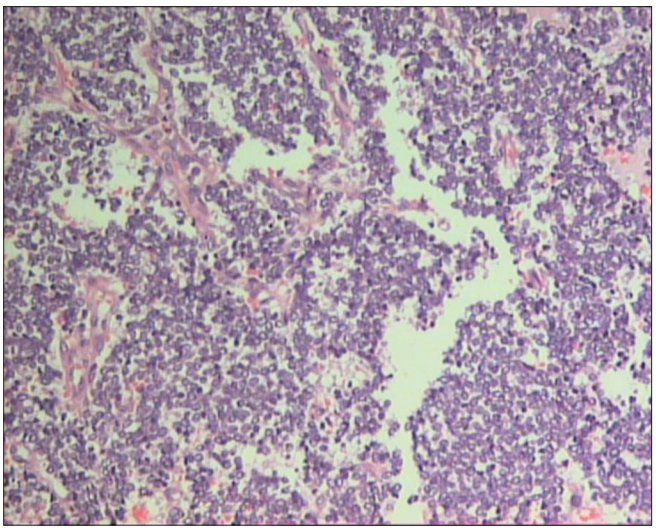

Figure 3: Light microscopy of the tumor shows sheets of small, uniform, round blue cell tumor, separated by delicate fibrovascular septae (H and E, ×200)

The patient underwent preoperative right renal arterial angioembolization followed by right radical nephrectomy. On macroscopic examination, nephrectomy specimen measured 20×13×10 cm in size. On cutting, the entire kidney was replaced by a predominantly solid, gray white, vaguely nodular growth. The tumor was infiltrating the renal pelvis and main renal vein at the hilum. Capsule was grossly intact [Figure 2]. Histological examination revealed sheets of small round cells with hyperchromatic round nuclei and scanty cytoplasm, an appearance consistent with small round blue cell tumor (SRBCT) [Figure 3]. IHC was positive for CD 99, consistent with PNET/EWS [Figure 4].

The patient received adjuvant chemotherapy (Vincristine,

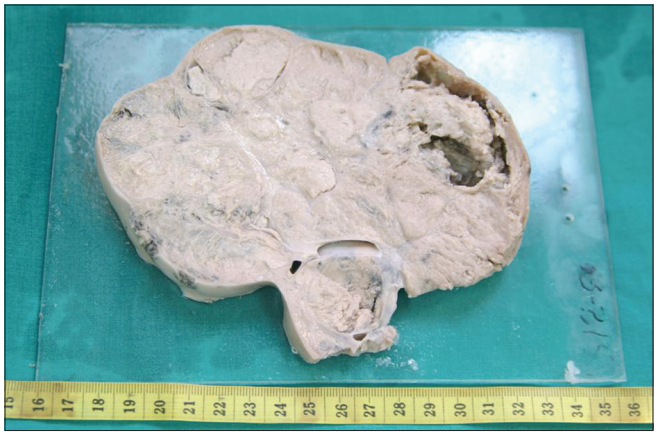

Figure 2: Gross appearance of right kidney completely replaced by solid, gray white, vaguely nodular growth

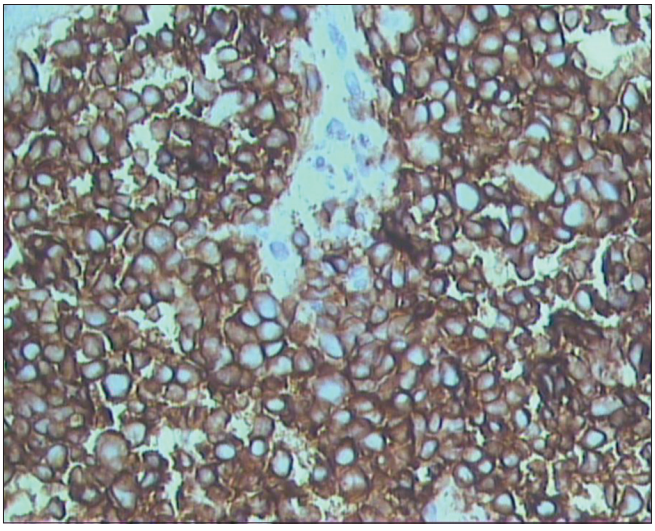

Figure 4: IHC staining showing diffuse membranous positivity of CD 99 in tumor cells (CD 99 antibody, ×200)

Doxorubicin, Cyclophosphamide and Dactinomycin). On the 10th day of fourth cycle of chemotherapy, he presented with high grade fever and loose motions. His total leukocyte count was low. General condition of the patient deteriorated and he died of complications of chemotherapy.

Case 2 (Kidney PNET/EWS)

MA, a 25-year-old male, presented with hematuria and left flank pain. On physical examination, he had a left-sided, hard, somewhat fixed mass in the left flank. USG showed a large left renal mass. Right kidney and bladder were unremarkable. CT scan revealed a left renal mass with involvement of renal vein and also liver and lung metastasis.

A palliative nephrectomy was done. On macroscopic examination, the kidney measured 15×11×8 cm. On sectioning, the entire kidney parenchyma was replaced by a solid, vaguely nodular, gray white tumor with small areas of hemorrhage and necrosis. The tumor was seen infiltrating through the capsule into perinephric fat and main renal vein. Histology and IHC were consistent with PNET/EWS.

Adjuvant chemotherapy was planned but general condition of the patient deteriorated and his disease progressed and he died 2 months later.

Case 3 (Kidney PNET/EWS)

DL, a 30-year-old female, presented with the main complaint of abdominal swelling. On physical examination, she was anemic and there was a large mass in the right flank, almost crossing the midline. USG confirmed huge right renal mass. CT scan abdomen revealed a huge malignant mass measuring about 18×12 cm in size with involvement of vertebral bodies. Bone scans were positive for metastasis.

Open biopsy of the mass was performed which revealed PNET/EWS. A palliative chemotherapy was started with Doxorubicin and after one cycle the patient left against medical advice.

Case 4 (Kidney PNET/EWS)

MH, a 34-year-old male, presented with hematuria and right flank mass. On physical examination, he was anemic and there was a hard mass palpable in the right flank. USG revealed right renal mass occupying whole of the kidney with multiple metastases in liver. CT scan revealed a large neoplastic mass replacing almost the whole right kidney. There were multiple metastatic deposits in liver and lungs.

A palliative nephrectomy was performed. On macroscopic examination, the kidney measured 17×10×9 cm. On sectioning, entire kidney tissue was replaced by solid, gray white tumor. The tumor was reaching the raw areas on medial aspect of the kidney. Main renal vein was not involved. Microscopy and IHC results were consistent with PNET/EWS. This patient had massive bleeding peroperatively and remained on ventilator support for 2 weeks and expired on 14th postoperative day.

Case 5 (Prostate PNET/EWS)

HA, a 29-year-old male, presented with burning micturation of 4 months duration followed by acute retention of urine which was relieved by Foley's catheterization at another hospital. Physical examination revealed a palpable mass in suprapubic region. Digital rectal examination showed large hard mass in the prostate. Serum prostate specific antigen (PSA) was 1.3 ng/ml. USG revealed bilateral normal kidneys, adequate filling of the bladder with no abnormality and prostate appearing enlarged with heterogeneous texture with dense calcifications. Transrectal ultrasound (TRUS) revealed hugely enlarged prostate with a volume of 235 ml with cystic areas and calcification; vascularity was increased. Left seminal vesicle appeared bulky. CT scan of abdomen and chest showed mass lesion arising from pelvis involving prostate and bladder with suspicion of fatty infiltration. Lymphadenopathy was noted in left perirectal region with left-sided pleural and pulmonary metastasis. Magnetic resonance imaging (MRI) pelvis confirmed the findings of CT scan.

TRUS guided biopsy was performed, which revealed a malignant round blue cell tumor. IHC showed CD 99 positivity, consistent with PNET/EWS of prostate. Chemotherapy was planned and first line of treatment was given with Vincristine and Doxorubicin, which was later changed to second line chemotherapy with Docetaxel and Gemzar due to non-tolerance of primary drugs. The patient showed no response with second line chemotherapy, and was put on third line chemotherapy with Ifosphamide. Over the succeeding 4 months, his disease progressed and the patient left against medical advice.

Case 6 (Adrenal PNET/EWS)

BM, a 20-year-old female, presented with right flank pain, anorexia, and weight loss. Physical examination revealed palpable mass in the right flank. Other systems were unremarkable. Laboratory studies were within normal limits. CT scan of the abdomen and chest demonstrated a malignant, large, heterogeneous supra renal mass with pulmonary metastases and malignant ascites with neoplastic implants.

Adrenal hormones including urinary vanillyl mandelic acid (VMA) and early morning cortisol were within normal limits. Trucut biopsy was performed which revealed SRBCT. IHC features were consistent with PNET/EWS. Neo-adjuvant chemotherapy including Vincristine, Doxorubicin,

Cyclophosphamide and Dactinomycin was started. She showed a good initial clinical response and was advised follow-up but unfortunately she did not turn up.

DISCUSSION

All our cases of renal PNET/EWS were young adults of age ranging from 25 to 34 years. Similar age incidence has been reported by all previous investigators,[4,5] with very few cases reported in old age.[6]

Although there is no gender predisposition for renal PNET/EWS,[3] our series showed male predominance with male to female ratio of 3:1. Similar male predominance was seen in the series of 10 patients of renal PNET reported by Lee *et al*.[8] This most probably is due to small number of cases and not the true reflection of gender predisposition. In concordance with the reported aggressive behavior of this tumor, all our cases presented at an advanced stage. All had distant metastasis which included metastases to liver, lungs and bones. Other investigators have also reported high rates (50–60%) of distant metastases at the time of presentation.[5]

Diagnosis of renal PNET/EWS is often challenging. Although radiological features may be suggestive, biopsy with IHC is required to confirm the diagnosis.[8] It is interesting to note that PNET was not considered in the radiological differential diagnosis in any of the six cases in this series. Although the imaging features of peripheral PNET are nonspecific, these tumors should be considered in the differential diagnosis when one encounters a large retroperitoneal mass with aggressive characteristics.[8]

Optimal management of this tumor is still not known. Current strategies include radical surgery combined with chemotherapy and radiotherapy but the results are poor.[4-7] We operated upon three cases of renal PNET/EWS as suspected cases of renal cell carcinoma (RCC), and PNET/EWS was not considered in the differential diagnosis before surgery. Had PNET/EWS been diagnosed before nephrectomy, we could have offered a neo-adjuvant chemotherapy with Vincristine, Doxorubicin and Cyclophosphamide, which is indicated in PNET/EWS.[4] One patient underwent an open biopsy because she was risky for surgical intervention. This patient was treated with Doxorubicin as neo-adjuvant treatment but after one cycle the patient left against medical advice.

PNET/EWS in prostate is also a rare occurrence, and to the best of our knowledge, only three cases have been reported in literature till date.[9] Our case presented at an advanced stage in a young male. Thete *et al*. also reported a case of prostatic PNET in a young male of 26 years.[9] We treated this patient with systemic chemotherapy with Vincristine, Cyclophosphamide and Doxorubicin as first line treatment; but as there was no response, so he was shifted to second line chemotherapy with Docetaxel and later shifted to Ifosfamide but no clinical response was achieved and the patient later left against medical advice.

Adrenal PNET/EWS is also a very rare occurrence and only occasional case reports are found in the literature.[10] In our practice, a young female had advanced adrenal PNET/EWS with a good clinical response with neo-adjuvant chemotherapy. She, however, was soon lost to follow-up.

This case series sheds light on many aspects of this highly aggressive tumor in the perspective of a developing country. The patients present at an advanced stage with very large primary tumors and often metastasis at the time of presentation. These tumors are often not considered in the clinical or radiological differential diagnosis before surgery. Despite multimodal therapy, the mortality rate is high, which is most likely related to the aforementioned factors. However, one finding unique to our series is a high rate of non-compliance to chemotherapy. Three out of six patients were lost to follow-up during the chemotherapy. This high rate of non-compliance is most probably due to the ignorance and socioeconomic issues of the patients and their families.

CONCLUSION

PNET/EWS is an often overlooked differential diagnosis in urologic malignancies due to its rare occurrence. We suggest that PNET/EWS should be included in the differential diagnosis of genitourinary tumors in young patients with advanced malignancy.

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How to cite this article: Mohsin R, Hashmi A, Mubarak M, Sultan G, Shehzad A, Qayum A, *et al*. Primitive neuroectodermal tumor/Ewing's sarcoma in adult uro-oncology: A case series from a developing country. Urol Ann 2011;3:103-7.

Source of Support: Nil, **Conflict of Interest:** None.