ABSTRACT

We hereby report a rare case of primary primitive neuroectodermal tumour (PNET)/Ewing’s tumour of the urinary bladder. Primary PNETs of the bladder are very aggressive neoplasms. They are extremely rare and only 12, as on July 2014, have been reported in the literature. A young 22-year old male patient, agricultural labourer by occupation, presented with complaints of urinary obstruction and haematuria of 1-month duration. A provisional diagnosis of small round cell tumour was considered on examination of the biopsy specimen. Subsequently, the panel of immunohistochemical markers CD-99, NSE, LCA, Desmin and vimentin were performed and finally reported as urinary bladder – PNET/Ewing’s tumour – CD-99+.

Keywords: Hematuria, Small round cell tumor, IHC, Primitive neuroectodermal tumour, CD-99, Ewing’s tumour, Urinary bladder, Metastasis

INTRODUCTION

Primitive neuroectodermal tumours (PNET) are malignant small round blue-cell tumours, exhibiting a variable degree of neural differentiation[1]. They occur predominantly in bones soft tissue, brain, spinal cord and sympathetic nervous system. They occur commonly in children and young adults[2]. Very rarely, they occur in older patients and in other organs[3].

These tumours are closely related to Ewing’s sarcoma, having the same immunohistochemical profile and chromosomal abnormality: t(11; 22)(q12; q24).[4]

Tumour cells are positive for the MIC2 gene product (CD99) and neural markers such as neuron-specific enolase (NSE), S100 and synaptophysin[5–7].

Primitive neuroectodermal tumours of the urinary tract are rare, usually involve kidney[8] and prostate[9]. Involvement of the urinary bladder by PNET tumours are extremely rare[5].

These tumours are very aggressive, showing rapid local infiltration with wide spread metastasis[7,8].

The five-year survival rate varies from 60% to 90%, when treated with surgical resection and radio chemotherapy[8].

To the best of our knowledge, only 12 cases of primary PNET of the urinary bladder have been reported so far[10].

Our case is the 13th case to be reported.

CASE PRESENTATION

A young 22-year-old male patient, agricultural labourer by occupation, presented with complaints of difficulty during micturition and haematuria, since 1 month. He is a known smoker since 15 years.

O/E: A mass in supra-pubic region measuring about 10 x 10 cm, not mobile was palpable.
Investigations: Basic investigations including hematological, biochemical and serological tests were done and all were found to be within normal limits. The chest X-ray was normal.

Ultrasound abdomen and bladder showed bilateral hydro-uretero-nephrosis. Urinary bladder showed a well-defined heterogenous lesion of size 9.7 x 8.4 cm with few areas of cystic degeneration and calcific specks were noted within it. Bladder parenchyma was thinned out.

Contrast enhanced computerised tomography scan of abdomen and pelvis showed evidence of 9 x 6.7 cm, enhancing intra luminal mass arising from posterior and lateral wall of urinary bladder with necrotic areas and extending into right paravesical space.

No regional/para aortic lymphadenopathy was observed.

Impression: carcinoma urinary bladder with paravesical infiltration.

TURBT was done and biopsy bits were sent for histopathological examination.

Gross: tumour specimen consisted of grey-brown soft tissue bits altogether measuring 4cc. The entire tumour tissue was submitted for histopathological examination.

Microscopic examination: sections studied from TURBT specimen showed native bladder tissue lined focally by intact transitional epithelium showing stratification. The subepithelial tumour tissue is composed of diffuse sheets and few clusters consisting of predominantly monotonous population of cells. Individual cells are small round to oval shaped, characterised by having scanty cytoplasm with hyperchromatic nucleus. Mild pleomorphism was observed. Few cells showed vacuolated cytoplasm. Occasional mitotic activity noted. Peritheliomatous arrangement of tumour cells around blood vessels was also seen. Proliferated congested blood vessels were observed.

No evidence of necrosis/vascular emboli seen.

Provisional diagnosis: suggestive of small round cell tumour? Lymphoma? Embryonal RMS and? PNET was considered.

For definitive characterisation of tumour, histochemical special stain PAS and a panel of immunohistochemical markers were advised (Figure 1).

**Special stain:** PAS: positive.

**IHC results:**

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<tr>
<td>Cytokeratin</td>
<td>Negative</td>
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<td>LCA</td>
<td>Negative</td>
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<tr>
<td>Desmin</td>
<td>Negative</td>
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<tr>
<td>CD-99 (MIC2 gene)</td>
<td>Strongly positive</td>
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<tr>
<td>NSE</td>
<td>Positive</td>
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<td>Synaptophysin</td>
<td>Positive</td>
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Based on the histomorphology and correlating with PAS positivity and IHC profile, final diagnosis of PNET-urinary bladder was made.

**DISCUSSION**

PNET of the urinary bladder is extremely rare, aggressive masses with only 12 cases being previously reported, to the best of our knowledge[10].

Patients are of young age as in other small round-cell tumours[6,13,14]. The age of our patient noted was 22 years.

Histologically, PNET is a malignant small round cell tumour that exhibits a variable degree of neural differentiation, though most of them share predominantly lobular growth pattern[11].

For IHC analysis, the most useful neural markers are neuron specific enolase, S100 and synaptophysin, with staining detectable in up to 60% of the cases[5].

Further, the tumour cells show a strong expression of MIC2 protein (CD99)[6].

It has been suggested that the tumour must show rosettes and be positive for at least two of the neural markers, to be diagnosed as PNET[11].
Figure 1: (A–C) H&E shows nests, lobules, sheets and peritheliomatous arrangement of monotonous, undifferentiated primitive small round cells. (D, E) PAS: low-power view and high-power view – positivity of monotonous cells. (F, G) IHC–NSE: Scanner and low-power view – diffuse, intense positivity. (H, I) IHC: Desmin: low-power view and high-power view: negative. (J, K) IHC: Vimentin: Scanner and high-power view: negative. (L, M) IHC–LCA: low-power view and high-power view: negative. (N, O) IHC: CD99: scanner and high-power view: diffuse and dense cytoplasmic positivity in tumour cells.
As observed in most cases of PNET, showing positivity for neuron-specific enolase and MIC2 gene\[^{5,7,13,15}\], similar findings were observed in our case.

Other immunohistochemical markers such as cytokeratin, epithelial membrane antigen, desmin, vimentin, smooth muscle actin, and leucocyte common antigen were negative in our case, thereby excluding other differential diagnosis of small round cell tumours such as rhabdomyosarcoma and lymphoma. This observation is similar with the results as reported in other studies.

In cases that are difficult to diagnose, even with the use of immunohistochemical markers and if strongly suspecting PNET/Ewing’s tumour, then detection of EWSFL1 type I fusion will be the conclusive diagnostic modality.

Diagnosis of PNET, in our case, was established by histological and immunohistochemical marker-positive staining NSE and CD99.

Total cystectomy with adjuvant chemotherapy, consisting of vincristine, doxorubicin and cyclophosphamide, alternating with ifosamide and etoposide\[^{14}\] seems to provide long-term survival for PNET of the urinary bladder.

CONCLUSION

To conclude, we present the 13th known case of PNET of the urinary bladder. Diagnosis of this type of tumour especially signifies the role of immunohistochemistry and prompt therapy must be started as soon as possible in view of its highly malignant potential.

REFERENCES


Urinary Bladder: Primitive Neuroectodermal Tumour/Ewing’s Tumour – A Rare Case

