

Primitive neuroectodermal tumor of the penile urethra

Ashishkumar Narsinhbhai Asari*, Bijal Kulkarni¹, T. B. Yuvaraja

Departments Uro-Oncology and Robotic Surgery and ¹Pathology, Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute, Mumbai, Maharashtra, India

*E-mail: asariashish@gmail.com

ABSTRACT

Primitive neuroectodermal tumor (PNET)/Ewing's sarcoma tumors are a group of highly malignant tumors composed of small, round cells showing neuroectodermal differentiation that commonly affects soft tissue and bone. PNET involving the genitourinary system is rare and PNET of the penile urethra is rarer still. It exhibits a highly aggressive biological behavior with poor prognosis. We report a case of a 27-year-old male presenting with penile swelling and difficulty in passing urine. Examination revealed a firm penile urethral mass. Pathological and immunohistochemical results of the specimen obtained from urethroscopic biopsy followed by total penectomy confirmed the diagnosis of PNET of the urethra. He received combination chemotherapy: ifosfamide and etoposide (IE) + vincristine, Adriamycin, and cyclophosphamide (VAC). In conclusion, PNET has to be considered in the differential diagnosis of a penile urethral mass in young patients.

INTRODUCTION

Primitive neuroectodermal tumors (PNETs) are a group of malignant round, small, blue cell tumors which are derived from primitive neuroectodermal cells.^[1] These tumors commonly affect the skeletal system, though it can originate in the visceral organs and soft tissues. They have similar features of primary Ewing's sarcoma, clinically and immunohistochemically, as well as cytogenetically.^[2] PNET typically occurs in the chest wall, limbs, and soft tissues and less frequently in genitourinary organs. The incidence of the malignant penile tumors is very low (0.5–5/100,000 cases), and PNET of the penis is even rarer.^[3] We report a case of PNET arising from the anterior urethra in a young adult.

CASE REPORT

A 27-year-old male presented with penile swelling and difficulty in passing urine for 2 months. Physical examination showed a 5 cm × 2 cm palpable firm mass

at the ventral aspect of the distal penis. Magnetic resonance imaging showed a 4.9 cm × 1.8 cm × 1.5 cm, well-defined lobulated mass lesion in the penile region involving the urethra and the corpus spongiosum, compressing the surrounding corpus cavernosum. It was hyperintense on T2-weighted imaging and hypointense on T1-weighted imaging with patchy irregular peripheral enhancement on contrast scan. The patient underwent a cystourethroscopy, which showed a pedunculated mass arising from the right half of bulbar and penile urethra almost obliterating the lumen. The biopsy revealed a small, round cell tumor. ¹⁸F-fluorodeoxyglucose whole-body positron emission tomography-computed tomography (PET-CT) scan [Figure 1a] showed hypermetabolic lesion involving the entire length of the penile urethra up to bulbous urethra with a predominance on the right side and no uptake in lymph nodes or distant organs.

After a discussion within the tumor board, the patient was offered total penectomy and perineal urethrostomy with

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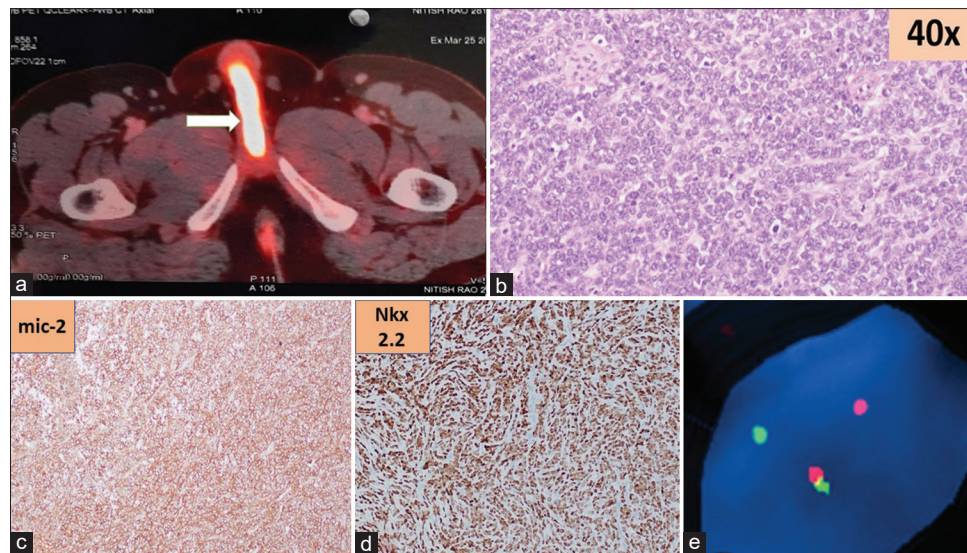


Figure 1: (a) Fluorodeoxyglucose positron emission tomography–computed tomography images showing lesion (arrow) involving anterior urethra along with corpus spongiosum; histopathology slides show (b) poorly differentiated small, round cells with scanty cytoplasm without nuclear molding and many mitotic figures; (c) Immunohistochemistry staining with strong mic-2 expression; (d) Nkx2.2 strong diffuse nuclear staining; and (e) fluorescence *in situ* hybridization for EWSR1 gene rearrangement shows an interphase cell showing 1 fusion, 1 green, and 1 orange signal

adjuvant chemotherapy. Groin lymph node dissection was not performed as there was no evidence to support its role. Histopathological examination of total penectomy specimen showed [Figure 1b] sheets of small, round, blue cells with scanty cytoplasm without any nuclear molding, few tumor rosettes, and many mitotic figures. On immunohistochemistry (IHC, Figure 1c and d), cells expressed vimentin, Fli1, NKX 2.2, and mic-2. They were immunonegative for CK, EMA, CK7, CK20, p63, Gata3, chromogranin A, synaptophysin, CD56, Melan-A, HMB45, and S-100p. The fluorescence *in situ* hybridization (FISH) analysis showed a rearrangement of the EWSR1 gene locus in 96% of the tumor cells [Figure 1e; done with ZytoLight SPEC EWSR1 Dual Color Breakapart Probe Kit, analyzed on an Olympus BX51 fluorescent microscope using Applied Spectral Imaging Software]. The tumor was seen as a submucosal periurethral polypoidal mass infiltrating the corpus spongiosum. The margins of resection were free. Based on these findings, the diagnosis of PNET of the penile urethra was made. Postoperatively, the patient received 5 cycles of adjuvant chemotherapy (Injection etoposide 180 mg days 1, 2, 3, 4, and 5 and injection ifosfamide 3000 mg days 1, 2, 3, 4, and 5) and 3 cycles of VAC. This treatment was completed without dose modifications on the scheduled days. Follow-up studies including clinical examination and PET-CT scan were normal at 6th and 12th months. The patient is currently disease free at 12 months.

DISCUSSION

PNET is a neuroectodermal tissue derived small, round cell tumor that belongs to the Ewing's sarcoma family of tumors. Ewing's sarcoma primarily occurs in bones and uncommonly in soft tissues.^[1] It occurs away from the vital

organs. PNET rarely occurs in the genitourinary system and the involvement of urethra is even rarer. PNET of the penis was first reported in 1999 by Toh *et al.*^[4] Most of the literature about PNET of the penis shows that glans and shaft of the penis are commonly affected.^[5] In our case, it was primarily involving the anterior urethra.

The diagnosis of PNET is through biopsy. Histologically, the PNET appears as small, round cellular tumor composed in sheets. In the IHC analysis of PNET, mic-2 and NKX 2.2 are the most sensitive indicators. However, in the recent era, the PNET can be confirmed by molecular testing such as FISH or reverse transcription polymerase chain reaction for Ewing's sarcoma (EWS) translocations.^[6]

The overall prognosis of urethral PNET is poor as it is highly aggressive with a tendency of local recurrence and remote metastases to organs such as lung and liver. Multimodal therapy, including aggressive surgery, intensive chemotherapy, and adjuvant radiotherapy, is necessary for local tumor control and to prevent metastasis. The standard chemotherapy regimen involves cyclophosphamide, Adriamycin, and vincristine (CAV) alternated with ifosfamide and etoposide (IE). Brachytherapy serves as a palliative therapeutic option to prevent or delay tumor metastasis.

Hu *et al.*^[6] reported a case in 2016 from China of a 49-year-old male diagnosed with PNET of the posterior urethra, who was given chemotherapy using CAV and IE after he refused surgery in order to preserve sexual function. The patient developed local disease recurrence and metastasis to the brain and died from respiratory failure. This is the only case that has been reported of PNET involving posterior urethra.

Our patient presented with urinary symptoms and had a urethral tumor in the anterior urethra. This is the first case of PNET anterior urethra described according to our knowledge. The patient underwent a total penectomy and perineal urethrostomy and received CAV + IE chemotherapy. The patient tolerated chemotherapy well with mild-to-moderate side effects and closely followed for 1 year with no evidence of tumor recurrence. The patient is currently on regular follow-up and longer follow-up is required to know the disease status.

CONCLUSION

In adolescents and young adults with a urethral mass, a diagnosis of urethral PNET should be considered. Surgical intervention should be considered as the first choice in definitive therapy. Further research is required in this locally aggressive disease to improve prognosis and survival.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not

be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

REFERENCES

1. Kumar V, Khurana N, Rathi AK, Malhotra A, Sharma K, Abhishek A, *et al.* Primitive neuroectodermal tumor of prostate. *Indian J Pathol Microbiol* 2008;51:386-8.
2. Lopez-Beltran A, Pérez-Seoane C, Montironi R, Hernández-Iglesias T, Mackintosh C, de Alava E. Primary primitive neuroectodermal tumour of the urinary bladder: A clinico-pathological study emphasising immunohistochemical, ultrastructural and molecular analyses. *J Clin Pathol* 2006;59:775-8.
3. Lowentritt B, Parsons JK, Argani P, Gearhart JP. Pediatric epithelioid sarcoma of the penis. *J Urol* 2004;172:296-7.
4. Toh KL, Tan PH, Cheng WS. Primary extraskelatal Ewing's sarcoma of the external genitalia. *J Urol* 1999;162:159-60.
5. Huang W, Liu Z, Chen R, Wang T, Lan R, Liu J. Peripheral primitive neuroectodermal tumor (pPNET) of the penis: A case report and literature review. *Int Surg* 2015;100:1340-5.
6. Hu X, Che X, Xiao J, Wang Z, Zhu H. Primitive neuroectodermal tumor of the posterior urethral: A case report and literature review. *Int J Clin Exp Med* 2016;9:18650-4.

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