

# Primary adult primitive neuroectodermal tumor of the bladder

## A case report and literature review

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### Abstract

**Rationale:** A primary primitive neuroectodermal tumor (PNET) is a rare and highly malignant tumor that often occurs in the central nervous system of children and young adults. This tumor is rarely observed in the bladder.

**Patient concerns:** In this paper, we describe the case of a 64-year-old man with a PNET of the bladder. He experienced dull pain in the lower left abdomen for 5 months (without any obvious inducement), which gradually became aggravated and intolerable.

**Diagnoses:** Partial cystectomy was performed, and a PNET of the bladder, which is extremely rare, was confirmed.

**Interventions:** Following cystectomy, the patient's general postoperative state was poor and he could not tolerate chemotherapy. Thus, he was subjected to pelvic radiotherapy for 2 weeks.

**Outcomes:** His physical condition did not improve significantly after radiotherapy; however, we still plan to continue it. If the patient's physical condition improves, chemotherapy will be considered.

**Lessons:** Most cases of PNETs are intravesical or at least mainly endophytic. However, in this case, the mucosal layer was barely involved, and the tumor mainly grew out of the bladder, which is very rare. The present case provides reference for the diagnosis of PNET.

**Abbreviations:** CNS = central nervous system, CT = computed tomography, PNET = primitive neuroectodermal tumor, pPNET = peripheral primitive neuroectodermal tumor, RO = radical operation.

**Keywords:** adult, case report, neuroectodermal tumor, urinary bladder

## 1. Introduction

A primary primitive neuroectodermal tumor (PNET) is a rare and malignant neoplasm that belongs to the Ewing family of tumors. These tumors have a predilection for the central nervous system<sup>[1]</sup> of children and young adults; however, they may occasionally be

observed in other sites such as the chest wall,<sup>[2]</sup> head and neck,<sup>[3]</sup> kidneys,<sup>[4]</sup> adrenal glands,<sup>[5]</sup> female genital tract,<sup>[6]</sup> extremities, and scrotal sac.<sup>[7]</sup> A PNET occurring in the bladder is very rare; it develops more commonly in children and adolescents than in adults. This paper describes a rare case of a PNET in the bladder of an adult.

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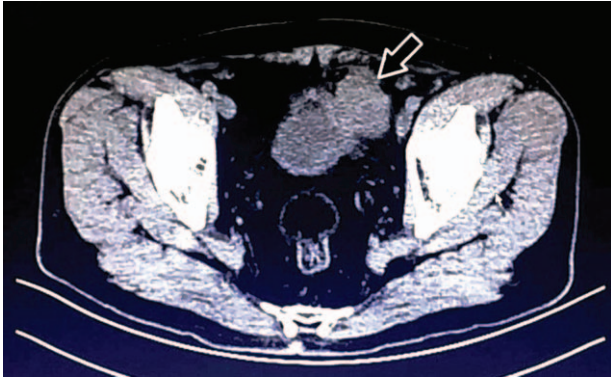
<http://dx.doi.org/10.1097/MD.0000000000021740>

## 2. Case report

A 64-year-old man (Han Chinese, company staff) presented with complaints of worsening dull pain (that developed 5 months before presentation) in the lower left abdomen. He had not sought any medical intervention before this. Complaints of fever, nausea, and vomiting were denied. He had no personal or family history of tumors. The pain gradually became aggravated and intolerable. While there was tenderness in the lower left abdomen, no rebound pain or muscle tension was observed.

No obvious abnormalities were found in the laboratory examinations. Abdominal computed tomography (CT) upon admission revealed that a pelvic tumor had developed in the left lateral wall of the bladder and measured about 6 × 5 cm (Fig. 1). No significant abnormality was found by cystoscopy. No tumor metastasis was detected by head CT, bone scan, abdominal ultrasonography, and lung radiography.

A histopathological examination revealed that the tumor consisted of densely distributed, small-to-medium sized, similar round cells. The nucleus-cytoplasm ratio was high, and the chromatin had a fine texture. Nuclear division was observed frequently and was accompanied by massive coagulative necrosis. Homer-Wright rosettes (Fig. 2A, B) were observed



**Figure 1.** Pelvic computed tomography scan. The tumor is located on the left lateral wall of the bladder (arrow). It has the same density as the bladder wall, an unclear margin, and a size of about 6 × 5 cm. Its boundary with the surrounding tissues is unclear.

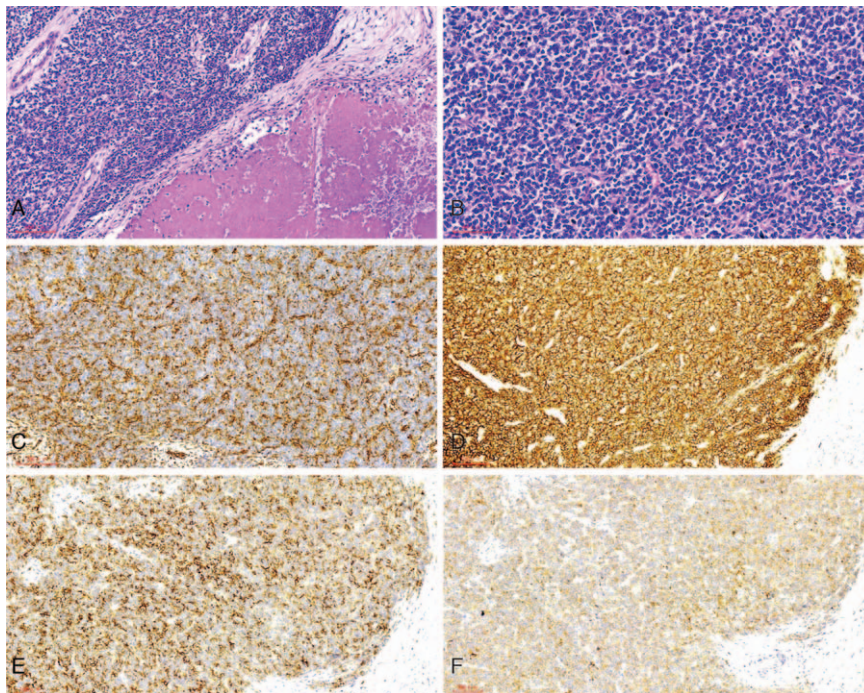
occasionally. Immunohistochemical examination revealed that the tumor cells expressed vimentin, CD99, synaptophysin, and CD56. The cells stained negative for CK (a broad-spectrum marker), P63, GATA3, NKX3.1, PSA, and S-100, and the Ki-67 proliferation index was nearly 50% (Fig. 2C–F). Fluorescence in situ hybridization detected the following gene mutations: *t*(11;22)(q24;Q12) chromosome translocation and *EWS-FL1* fusion gene expression (type 1 subtype). Thus, based on the results of the immunohistochemical examination and fluorescence in situ hybridization, a PNET of the bladder was diagnosed.

The patient underwent surgery. Intraoperative exploration revealed that the tumor had grown on the left wall of the bladder and was located close to the left pelvic wall. It had a hard, crispy texture and an unclear boundary. It was greyish white and red patches in color and had not become saturated with the bladder mucosa. The posterior wall of the bladder was separated from the peritoneum, and partial cystectomy was performed. The patient's general postoperative state was poor, and he could not tolerate chemotherapy. Presently, he has received 2 weeks of pelvic radiotherapy. His physical condition has not improved significantly and he is still unable to tolerate chemotherapy. We plan to continue radiotherapy; if his physical condition improves, chemotherapy will be considered.

The study was reviewed and approved by the Ethics Committee of the First Affiliated Hospital of China Medical University.

### 3. Discussion

PNETs originate from neural crest cells<sup>[7]</sup> and can be classified into central PNETs and peripheral PNETs (pPNETs). Most patients with PNETs have a young age at onset. However, according to the 9 cases of bladder PNETs (Table 1) currently available in the literature,<sup>[8–16]</sup> this type of PNET is predominant in middle-aged and elderly individuals, with an average onset age of 53.5 years; in 60% of the cases, including the present one (6/10), the patients were older than 60 years. This type of bladder tumor is often overlooked by clinicians, because the patient's age and tumor site show inconsistencies with the onset characteristics of PNETs.



**Figure 2.** HE staining and immunohistochemical staining. A: Small, round tumor cells are distributed in a patchy form; they have a similar cell size and morphology, little cytoplasm that stains light, deeply stained nuclei, easily visible mitotic figures, and large areas of local necrosis (HE staining; magnification: ×100). B: At high magnification, the tumor cells are seen to form Homer-Wright rosettes (HE staining; magnification: ×200). C: Immunohistochemistry shows that it is a vimentin-positive diffuse-type lesion (magnification: ×100). D: Immunohistochemistry shows a diffuse-type lesion with strong CD99 positivity (magnification: ×100). E: Immunohistochemistry shows a CD56-positive diffuse-type lesion (magnification: ×100). F: Immunohistochemistry shows a synaptophysin-positive diffuse-type lesion (magnification: ×100). HE = Hematoxylin and eosin.

**Table 1**  
**Characteristics of 10 cases of primitive neuroectodermal tumors of the bladder.**

Author	Year of publication	Age/sex	Symptoms	Growth pattern	Direct infiltration	Distant organ metastasis	Treatment	Status after the last follow-up
Banerjee et al <sup>[9]</sup>	1997	21/M	Microscopic hematuria and dysuria	Endophytic	-	-	OP, chemotherapy (vincristine, adriamycin, and cyclophosphamide)	Alive, NED after 18 mo of follow-up
Desai <sup>[10]</sup>	1998	38/F	Gross hematuria	Endophytic and exophytic	+	-	OP	NA
Colechia et al <sup>[11]</sup>	2002	61/F	NA	Exophytic	+	-	NA	NA
Krüger et al <sup>[12]</sup>	2003	81/M	Lymphedema of the lower extremities, fatigue, and urge incontinence	Endophytic and exophytic	+	-	OP (palliative)	DOD, 2 wk postoperatively
Ellinger et al <sup>[13]</sup>	2006	72/M	Gross hematuria and oliguria	Mainly endophytic, partly exophytic	+	-	OP (palliative)	NA, discharged in a poor general condition 2 mo postoperatively
Lopez-Beltran et al <sup>[14]</sup>	2006	21/F	Frequency, dysuria, and gross hematuria	Endophytic	-	-	OP, chemotherapy (adjuvant systemic chemotherapy followed by maintenance with imatinib)	Alive, NED after 3 yr of follow-up
Zheng et al <sup>[15]</sup>	2011	74/M	Frequency, dysuria, and gross hematuria	Endophytic and exophytic	+	-	OP (palliative) and chemotherapy (epirubicin, vincristine, and cyclophosphamide)	DOD, 4 mo after diagnosis
Okada et al <sup>[16]</sup>	2011	65/M	Gross hematuria and dysuria	Endophytic	+	+	OP and chemotherapy (cisplatin and etoposide, or docetaxel and dexmethasone)	Died of acute superior mesenteric artery thrombosis 22 mo postoperatively
Tonyali et al <sup>[17]</sup>	2016	38/F	Gross hematuria	Endophytic	-	-	OP and chemotherapy (vincristine, doxorubicin, cyclophosphamide, and mesna alternating with courses of etoposide, ifosfamide, and mesna)	Alive, NED after 14 mo of follow-up
Present case	2019	64/M	Abdominal pain and urination	Only exophytic	+	-	OP (palliative) and radiotherapy	Alive after 6 wk of OP

+ = Positive, - = Negative, DOD = dead of disease, F = Female, M = Male, NA = not available, NED = no evidence of disease, OP = operation.



Ninety percent (9/10) of the cases of adult bladder PNETs reported endophytic growth; 4 of these were accompanied by an exophytic growth. Under such conditions, the lesion can be located preoperatively by cystoscopy, and pathological examination can help make a definite diagnosis. The tumor in the present case showed a purely exophytic growth. No significant abnormality was found by cystoscopy. Intraoperatively, the bladder mucosal layer was found to be smooth, and no tumor definitely involving the mucosal layer was found. Therefore, it was not possible to locate the lesion or make a definite diagnosis on the basis of cystoscopic findings. pPNETs originate from the neural crest cells outside the central nervous system.<sup>[17]</sup> In this case, the PNET grew in the bladder and barely involved the mucosal layer, because of the presence of neural crest cells in the bladder submucosa or muscular layer. Therefore, preoperative ultrasonography or CT was necessary. These modalities can avoid a missed diagnosis and can help in determining the anatomical relationship between the tumor and its surrounding tissues and whether there were enlarged lymph nodes around it, thus providing a basis for the formulation of treatment plans. In recent years, percutaneous fine-needle puncture guided by ultrasonography or CT has been applied frequently, which is helpful for making an early diagnosis of a PNET.

Generally, the prognosis of PNETs is poor<sup>[15]</sup>; the prognosis for adults is worse than that for minors.<sup>[18]</sup> The survival rates of patients with a pPNET or central PNET are roughly equivalent.<sup>[19]</sup> The prognosis of PNETs in the head and neck is better than that in other parts of the body. Tumors with a soluble *EWS-FLII* gene have a better prognosis than those with less soluble genes. In 8 cases of adult bladder PNET reported before, the frequency of localized infiltration and growth was more (7/8) than that of remote metastasis (1/8). Patients with local infiltration can rarely undergo a radical operation (RO); hence, they can only undergo palliative surgery, which is associated with a poor prognosis. Therefore, the presence of local infiltration is a sign of poor prognosis in cases of adult bladder PNET. The only reported case of multiple metastases occurred 8 months postoperatively. The patient died after 22 months from acute superior mesenteric artery thrombosis. Because of the small sample size and a short follow-up in some cases, it is not possible to make a comprehensive and objective evaluation of the prognostic factors of PNETs of the bladder.

Currently, surgery is the main treatment for PNETs, and it should be performed in patients who can tolerate it.<sup>[8,9,11–16]</sup> The prognosis of patients whose tumors can be completely removed (complete RO) is better than that of those who undergo palliative surgery.<sup>[8–16]</sup> Postoperative chemotherapy is the conventional treatment for adult bladder PNETs; vincristine, adriamycin, cyclophosphamide, epirubicin, cisplatin, etoposide, docetaxel, dexamethasone, doxorubicin, and mesna have been used as chemotherapeutic agents in such cases.<sup>[8,12–16]</sup> The symptoms in most patients were relieved to varying degrees after chemotherapy. Radiotherapy has been also used for local disease control in pPNETs,<sup>[20,21]</sup> and it is applicable to patients who have not undergone complete RO. The patient herein had a poor postoperative condition and could not tolerate the side effects of chemotherapy. Therefore, pelvic radiotherapy was chosen. After radiotherapy, the patient's abdominal pain, mental status, and strength improved slightly, but he could still only barely tolerate chemotherapy. Because of the short follow-up, the efficacy of radiotherapy for bladder PNETs needs further investigation.

## 4. Conclusion

Usually, PNETs are intravesical or at least mainly endophytic. However, the mucosal layer was barely involved occasionally, and the tumor mainly grew out of the bladder. This case provides reference for the diagnosis of PNET in the future.

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