Primitive neuroectodermal tumor of the prostate in a 58-year-old man: A case report

Tian DW et al. PNET of the prostate

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Abstract

BACKGROUND
Primitive neuroectodermal tumor (PNET), especially located in the prostate, is a rare tumor that mainly occurs in young men. Bladder and rectum invasion and distant metastasis are strongly associated with poor prognosis. Combination therapy, including radical surgery, adjuvant chemotherapy, and radiotherapy, is available. We present a case of prostatic PNET and a review of 17 cases identified in the literature.

CASE SUMMARY

A 58-year-old man was admitted complaining of dysuria for 2 years. Computed tomography and magnetic resonance imaging showed a large cystic-solid mass in the pelvic cavity compressing the surrounding bladder and rectum. The mass was iso- to hyperintense on T1-weighted imaging (WI) and heterogeneous hyperintense on T2WI. Cystic degeneration and necrosis were seen in the tumor, and solid tissues within the mass enhanced on contrast-enhanced scan. The patient underwent robot-assisted laparoscopic pelvic tumor resection. Histologically, the presence of many small round cells that were positive for expression of CD99, vimentin, and synaptophysin established the diagnosis of PNET in the prostate after surgery. The patient underwent
adjuvant chemotherapy. During 34 mo of follow-up the patient had no signs or symptoms of recurrence or residual disease.

CONCLUSION
We present the case of the oldest prostatic PNET patient, who has a good prognosis. This illustrates how older men with prostatic PNET may also benefit from combination therapy, like younger adults, and prolong survival. As always, PNET should be considered in the differential diagnosis of aggressive prostatic tumors in young men.

Key Words: Primitive neuroectodermal tumor; Prostate; Combination therapy; Magnetic resonance imaging; CD99; Case report


Core Tip: Prostatic primitive neuroectodermal tumors (PNETs) are usually malignant and occur in young men (median age 29 years; range: 20 to 58 years) with predominant complaints of dysuria, often with normal prostate specific antigen levels. Prostatic PNETs may invade adjacent organs, including bladder, rectum, and seminal vesicles, and are prone to distant metastasis. Forty-four percent of patients develop metastases, most commonly (75%) in the lung. CD99 is the most accepted immunohistochemical marker for prostatic PNET. Almost all patients receive chemotherapy. Despite combination therapy, including surgery, chemotherapy, and radiotherapy, the median survival of the patients remains 13 mo.
INTRODUCTION

Primitive neuroectodermal tumor (PNET) is an extremely rare neural crest tumor with poor prognosis that mainly affects children and adolescents. The clinical, morphological, and immunophenotypic characteristics of PNET are similar to Ewing’s sarcoma, and the two are thought to be related. Histologically, PNET is characterized by small round and oval cells. CD99, an antigen encoded by the Mic-2 gene, is present on the surfaces of most PNET cells, and therefore represents a useful diagnostic marker for PNET[1].

PNET is divided into central PNET and peripheral PNET according to its location. Peripheral PNETs have occurred in kidney, bladder, prostate, and adrenal, which images reveal an infiltrative mass with an ill-defined and necrotic region[2]. PNET of the prostate is extremely rare, with significant malignant potential. We here present the oldest reported prostatic PNET patient to date. Clinicopathological features of 18 cases reported since 2003, including ours, are listed in Table 1.

CASE PRESENTATION

Chief complaints

A 58-year-old man presented with a 2-year history of dysuria without obvious inducement.

History of present illness

The patient had dysuria without obvious cause accompanied by urinary hesitancy, which was progressively worsening. The pelvic ultrasound showed a cystic-solid mass. During 3 mo before admission, the patient had also presented with constipation and occasional pain.

History of past illness

The patient had no prior urologic history or significant medical history.
**Personal and family history**

There is no personal and family history.

**Physical examination**

The examination revealed a softly distended tympanitic abdomen with tenderness near the pubic symphysis.

**Laboratory examinations**

The serum prostate specific antigen (PSA) level was 0.82 ng/mL, the cytokeratin-19-fragment level was 6.79 ng/mL, and the other tumor markers including neuron specific enolase (NSE), alpha fetoprotein, carcinoembryonic antigen, and carbohydrate antigen 199, were all within normal ranges.

**Imaging examinations**

Contrast-enhanced computed tomography (CT) showed a mass between the bladder and rectum with cystic and necrotic components and heterogeneous enhancement (Figure 1A). Magnetic resonance imaging (MRI) of the pelvis confirmed a large cystic-solid mass measuring 10.7 cm × 10.8 cm × 8.1 cm near the prostate and compressing the rectum and bladder (Figure 1B-H). The lesion appeared isointense to slightly hyperintense on T1-weighted imaging (WI) and was heterogeneously hyperintense on T2WI. The solid portion of the tumor was hyperintense on diffusion-WI and correspondingly hypointense on the apparent diffusion coefficient maps. The mass showed prominent heterogeneous enhancement in the arterial phase and continuous enhancement in the venous and delayed phases. These findings initially suggested prostatic cystadenoma, and considering the patient's age, prostate cancer could not be excluded. At repeat CT examination 2 mo after surgery and the first cycle of chemotherapy there was no evidence of residual or recurrent tumor (Figure 2).

**FINAL DIAGNOSIS**
The final diagnosis was prostatic PNET with cystic degeneration. Histopathology of the surgical specimens showed small round strongly-staining cells (Figure 3A). Immunohistochemistry analysis showed strong positivity for CD99 and positivity for vimentin and synaptophysin (Figure 3B-D).

TREATMENT
The patient underwent robot-assisted laparoscopic resection. The insufflation needle was inserted from the edge of the umbilicus and a longitudinal incision of about 1 cm was made at 2 cm from the upper edge of the umbilicus. A large cystic-solid mass was observed in the rectum and bladder space, with adhesions to surrounding prostate and rectum. The neoplasm had a vascularized appearance. The cystic fluid was extracted with an aspirator and the tumor was removed gradually and completely. The resected cystic-solid tumor measured about 8 cm × 7 cm. Histological examination and immunohistochemical staining ultimately confirmed PNET. After surgery, the patient received adjuvant chemotherapy based on an alternating VEC (vincristine, etoposide, carboplatin) and IE (ifosfamide, etoposide) regimen. Chemotherapy was repeated every 3 wk for up to 6 cycles as tolerated.

OUTCOME AND FOLLOW-UP
There was complete remission of the tumor after radical surgery and chemotherapy. At the most recent follow-up visit (34 mo), the patient was alive and well, and there was no recurrence.

DISCUSSION
PNET is an extremely rare malignancy that is aggressive and has a poor prognosis[3]. In 2003, Colecchia et al[1] were the first to report PNET of the prostate, and besides the present case, only 17 cases of prostatic PNET have been reported to date. We reviewed 18 cases including ours and summarized the clinicopathological features in Table 1.
In the published cases, the patients were mainly young adults (median age 29 years; range: 20 to 58 years). Our 58-year-old patient is the oldest patient described thus far. Patients with prostatic PNET may present with dysuria, hematuria, pelvic discomfort, constipation, and hematochezia\cite{3-5}. In these 18 cases, 10 (56%) of the patients had dysuria, 6 (33%) accompanied with discomfort or pelvic pain, and 3 (17%) presented with hematuria. Prostatic PNET should be suspected when young men present with dysuria. Although PSA is an essential serum marker for the diagnosis of prostate cancer, with the positive detection rate reaching 82 percent\cite{6}, the PSA values in all 18 patients with prostatic PNET were within normal limits (0 to 4 \text{ng/mL}). Approximately 44% of patients had distant metastases, with the lung as the most common site, accounting for 75% of all metastases, followed by bone (25%), liver (12.5%), and meninges (12.5%). Distant metastasis is known as the most unfavorable prognostic factor for Ewing's sarcoma\cite{7}. Therefore, the search for metastasis must be emphasized in patients with prostatic PNET as the early detection of metastasis is crucial.

Imaging examination is beneficial in diagnosis, clarifying the internal structure, and assessing local invasion and distant metastasis. In 14 cases, including ours, the size of the tumor was 8.5 \text{cm} (range: 2.6 to 14.4 \text{cm}). PNET of the prostate has been described as an ill-defined aggressive soft tissue mass with hemorrhage, necrosis, and cystic degeneration; as a multilobulated mass with heterogeneous enhancement; and as a mass replacing the prostate on CT and MRI\cite{8,9}. MRI generally shows the lesion to be hypointense on T1WI and iso- to hyperintense on T2WI, and contrast-enhanced TIWI shows heterogeneous enhancement\cite{8,10-12}. MRI is sensitive to evaluate local tumor invasion. In 9 reported cases, there was compression or involvement of the bladder; 5 of these had distant metastases\cite{8,13-15}. There was compression or involvement of the rectum in 6 cases, 2 of which had metastases to distant sites\cite{8,15}. Four tumors were in close association with seminal vesicles and were without metastases\cite{5,8,16,17}. Additionally, there was 1 lesion that invaded the left ureter and bladder with bilateral hydroureteronephrosis\cite{16}. In general, the imaging examination is useful to identify the
relationship with adjacent tissues and distant metastasis, but preoperative diagnosis based on imaging alone is challenging.

The final diagnosis of a PNET involving the prostate relies on histopathological features. Under the light microscope, PNET is a mass of undifferentiated small round cells, which are arranged closely in a flaky, lobulated, or nest-like pattern. The characteristic small round cells of PNET are reactive to anti-CD99 antibody (Mic-2), and more than 90% of PNETs have demonstrated a translocation between the long arms of chromosomes 11 and 22, and are positive for the EWS-FLI1 fusion gene[18]. The translocation can be confirmed by molecular techniques such as fluorescence in situ hybridization and reverse transcriptase polymerase chain reaction[4]. At present, the diagnosis scheme proposed by Schmidt et al[19] has been extensively adopted, including the presence of Homer-Wright rosettes and/or the expression of at least two neural markers. Among 18 cases of prostatic PNET, 89% were immunohistochemically positive for CD99, 44% for vimentin, 28% for synaptophysin, 28% for CD56, and 22% with NSE. Molecular analyses in 8 cases showed translocations of the chromosomes or EWSR1/FLI1 fusion. However, molecular techniques were not used to detect chromosomal translocations in our case. Identification of translocation may be crucial, as some translocation types are associated with poor prognosis.

Combinations of surgery, chemotherapy, and radiotherapy can form an effective treatment strategy for prostatic PNET. The commonly recommended chemotherapy drugs include vincristine, doxorubicin, cyclophosphamide, etoposide, and ifosfamide[18,20]. In the 18 cases we summarized, adjuvant or neoadjuvant chemotherapy was administered in all cases of prostatic PNET except for one case without detailed treatment strategy. In 2 cases in the literature, the patients underwent radical surgery combined with chemotherapy and radiotherapy[1,21]. Our patient and 5 others were treated with radical surgery combined with chemotherapy[5,6,12,22,23], 4 patients received chemotherapy alone[3,14,16], and in other cases, patients adopted single radical resection or chemoradiotherapy. Although standard treatment has not been established, a multimodal approach is recommended. Follow-up information was available for 13
patients and our case. In general, during an average follow-up period of approximately 18 mo (median 13 mo; range: 2 to 84 mo), patients with combination therapy had longer survival than patients with monotherapy.

CONCLUSION

PNET of the prostate shows aggressive biological behavior and is often overlooked in the differential diagnosis due to its rare occurrence. It should be considered in young men with the complaint of dysuria to contribute to early diagnosis. The appropriate therapeutic schedule is radical surgery as early as possible, and combined chemotherapy or radiotherapy, which could be helpful to improve prognosis. Further studies and longer-term follow-up await.
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<td>6</td>
<td>Zhi-Hong Wan, Jing Wang, Qing Zhao.</td>
<td>&quot;Acute myocardial infarction in a young man with ankylosing spondylitis: A case report&quot;, World Journal of Clinical Cases, 2021</td>
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<td>Kentaro Takanami. &quot;F-18 FDG PET/CT Findings in Two Patients With Hepatic Angiomyolipoma With and Without Intratumoral Hemorrhage :&quot;, Clinical Nuclear Medicine, 01/2010</td>
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<td>Imaging of Brain Tumors with Histological Correlations, 2011.</td>
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<td>Yoichi Katayama. &quot;Peripheral-type primitive neuroectodermal tumor arising in the tentorium : Case report&quot;, Journal of Neurosurgery, 01/1999</td>
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<td>Ning Xu, Mei-Shan Jin, Liang Chen, Chun-Xi Wang, Shou-Tian Sun, Ai-Ping Shi. &quot;Renal Primitive Malignant Tumor with Endocrine Activity&quot;, Medical Principles and Practice, 2013</td>
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