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ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Kai Zhang, PhD, Professor, Department of Psychiatry, Chaohu Hospital of Anhui Medical University, Hefei 238000, Anhui Province, China. zhangkai@ahmu.edu.cn

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CASE REPORT

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

Da-Wei Tian, Xiao-Chun Wang, Hui Zhang, Yan Tan

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Da-Wei Tian, College of Medical Imaging, Shanxi Medical University, Taiyuan 030001, Shanxi Province, China

Xiao-Chun Wang, Hui Zhang, Yan Tan, Department of Radiology, The First Hospital of Shanxi Medical University, Taiyuan 030001, Shanxi Province, China

Corresponding author: Yan Tan, MD, Professor, Department of Radiology, The First Hospital of Shanxi Medical University, No. 85 Jiefang South Road, Taiyuan 030001, Shanxi Province, China. tanyan123456@sina.com

Abstract

BACKGROUND

Primitive neuroectodermal tumor (PNET), especially located in the prostate, is a rare tumor that mainly occurs in young men. Bladder or rectum invasion and distant metastasis are strongly associated with a 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 heterogeneously 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 the combination therapy, like younger adults, and achieve a long-term 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 the bladder, rectum, and seminal vesicles, and are prone to distant metastases. Forty-four percent of patients develop metastases, most commonly (75%) in the lung. CD99 is the most accepted immunohistochemical marker for prostatic PNETs. Almost all patients receive chemotherapy. Despite combination therapy, including surgery, chemotherapy, and radiotherapy, the median survival of the patients remains unsatisfactory at 13 mo.

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INTRODUCTION

Primitive neuroectodermal tumor (PNET) is an extremely rare neural crest tumor with a 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 surface 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 the kidney, bladder, prostate, and adrenal gland, often revealing an infiltrative mass with an ill-defined and necrotic region on imaging[2]. PNET of the prostate is extremely rare, with significant malignant potential. We here present the oldest prostatic PNET patient reported to date. Clinicopathological features of 18 cases reported since 2003, including ours, are reviewed.

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 was no personal or 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. However, prostate cancer could not be excluded considering the patient's age. 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 strongly staining small round 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. An 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 which adhesions to the 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 the 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 six 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 review 18 cases including ours and summarize 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[3-5]. In these 18 cases, ten (56%) had dysuria, six (33%) were accompanied with pelvic discomfort or pain, and three (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 a positive detection rate reaching 82%[6], the PSA values in all 18 patients with prostatic PNET were within normal limits (0 to 4 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 the bone (25%), liver (12.5%), and meninges (12.5%). Distant metastasis is known as the most unfavorable prognostic factor for Ewing's sarcoma[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 average size of the tumor was 8.5 cm (range: 2.6 to 14.4 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[8,9]. MRI generally shows the lesion

Table 1 Reported 18 cases of primitive neuroectodermal tumor in the prostate: Demographics and clinical features

No.	Ref.	Age	Symptoms	PSA (ng/mL)	Size (cm)	Immunohistochemistry (positive)	Molecular studies	Treatment	Follow-up (mo)	Metastases
1	Colecchia *et al*[1], 2003	31	NA	2.06	7	CD99, vimentin, NSE, synaptophysin	EWS/FLI1 fusion	CT, RT, SR	NA	NA
2	Peyromaure *et al*[21], 2003	27	Dysuria and pelvic discomfort	NA	NA	CD99	t (11; 22) (q24; q12)	CT, SR, RT	2+	NA
3	Thete *et al* [10], 2007	26	Dysuria and pelvic discomfort	0.3	NA	CD99(Mic-2)	NA	NA	NA	NA
4	Kumar *et al* [16], 2008	25	Burning micturition and dysuria	0.88	6.7	CD99, vimentin, S100, NSE, synaptophysin	NA	CT	NA	NA
5	Funahashi *et al*[13], 2009	20	Gross hematuria and miction pain	0.7	10	CD99, NSE, CD56, MIB-1, p53	t (11; 22) (q24; q12)	SR	10+	Lung
6	Mohsin *et al* [14], 2011	29	Burning micturition and urinary retention	1.3	NA	CD99	NA	CT	4	Lung
7	Al Haddabi *et al*[4], 2012	24	Dysuria, constipation, back pain, and pelvic discomfort	0.7	10	CD99, Bcl2, CK19, AE1/AE3, CK, vimentin	Rearrangement of chromosome 22	CT	NA	No
8	Wu *et al*[5], 2013	29	Difficult defecation and anus distention	1.19	7.4	CD99, Bcl-2	NA	SR, CT	12+	Lung
9	Liao *et al* [17], 2015	49	Frequent urination, dysuria, and pelvic discomfort	NA	7.1	CD99, CD56, NSE, Ki-67	NA	CT, RT	24+	No
10	Shibuya *et al* [3], 2015	23	Dysuria and anal pain	NA	NA	MIC-2, cytokeratin, vimentin, N-CAM	Translocation at chromosome 22q12	CT	4	Bone, lung, meninge
11	Esch *et al* [11], 2016	33	Pelvic pain, dysuria, and urgency	NA	6	Cytokeratin	EWSR1-gene	SR	12+	No
12	Kord *et al*[8], 2018	38	Abdominal pain, constipation, pain with defecation, and hematuria	NA	14.4	CD99	EWSR1/FLI1 fusion	CT, SR	14	Lung, liver, peritoneum
13	Du *et al*[9], 2019	39	Notalgia and paraplegia	1.07	2.6	CD99, CD56, P63, vimentin	NA	RT, CT	17	Thoracic spine
14	Javanmard *et al*[22], 2019	37	Painless gross hematuria	1.07	8.6	CD99, vimentin, BCL2, Ki67	NA	SR, CT	16	Yes
15	Liu *et al*[23], 2020	40	Dysuria	NA	11.2	CD99, synaptophysin, CD56, vimentin	FLI1	SR, CT	14+	No
16	Teng *et al* [15], 2020	27	Dysuria and dyschezia	1.52	8.4	CD99, CD56, desmin, vimentin	NA	SR	5	Lung and peritoneum
17	da Ponte *et al* [12], 2021	29	Pelvic discomfort and dysuria	0.4	8.8	CD99/MIC-2, synapto-physin	EWS gene rearrangement	CT, SR	84+	No
18	Present case	58	Dysuria, constipation, and pain with defecation	0.82	10.8	CD99, vimentin, synapto-physin	NA	SR, CT	34+	No

NA: Not available; PSA: Prostate specific antigen; NSE: Neuron specific enolase; EWS: Ewing's sarcoma; N-CAM: Neural cell adhesion molecule; CT: Chemotherapy; RT: Radiotherapy; SR: Surgical resection.

to be hypointense on T1WI and iso- to hyperintense on T2WI, and contrast-enhanced T1WI shows heterogeneous enhancement[8,10-12]. MRI is sensitive to evaluate local tumor invasion. In nine reported cases, there was compression or involvement of the bladder; five of these had distant metastases[5,8,13-15]. There was compression or involvement of the rectum in six cases, two of which had metastases to distant sites[8,15]. Four tumors were in close association with seminal vesicles but without metastases[5,

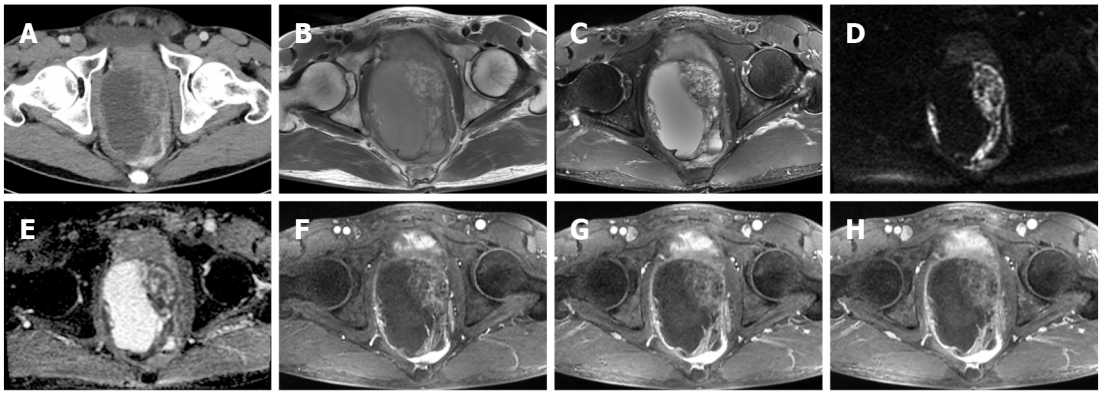

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Figure 1 Preoperative pelvic imaging. A: Contrast-enhanced computed tomography shows a large, cystic-solid mass in the pelvis; B and C: At magnetic resonance imaging (MRI), the lesion near the prostate is isointense to slightly hyperintense on T1-weighted imaging (WI), with heterogeneous intensity on T2WI; D and E: There is heterogeneous hyperintensity on diffusion-WI with opposing hypointensity on the apparent diffusion coefficient maps; F-H: The solid part is enhanced during the arterial phase on contrast-enhanced MRI, with persistent enhancement in the venous and delayed phases. No enhancement is seen in the cystic part.

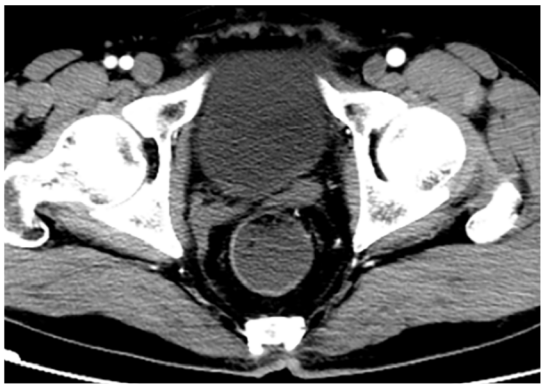

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Figure 2 Post-operative contrast-enhanced pelvic computed tomography. Imaging after the first cycle of chemotherapy at 2 mo postoperatively shows no obvious signs of residual tumor or recurrence.

8,16,17]. Additionally, there was one lesion that invaded the left ureter and bladder with bilateral hydroureteronephrosis[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% for NSE. Molecular analyses in eight 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 a 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 that we summarize, adjuvant or neoadjuvant chemotherapy was administered in all cases of prostatic PNET except for one case without detailed treatment strategy. In two cases in the literature, the patients underwent radical surgery combined with chemotherapy and radiotherapy[1,21]. Our patient and five others were treated by radical surgery combined with chemotherapy[5,8,12,22,23], four patients received chemotherapy alone

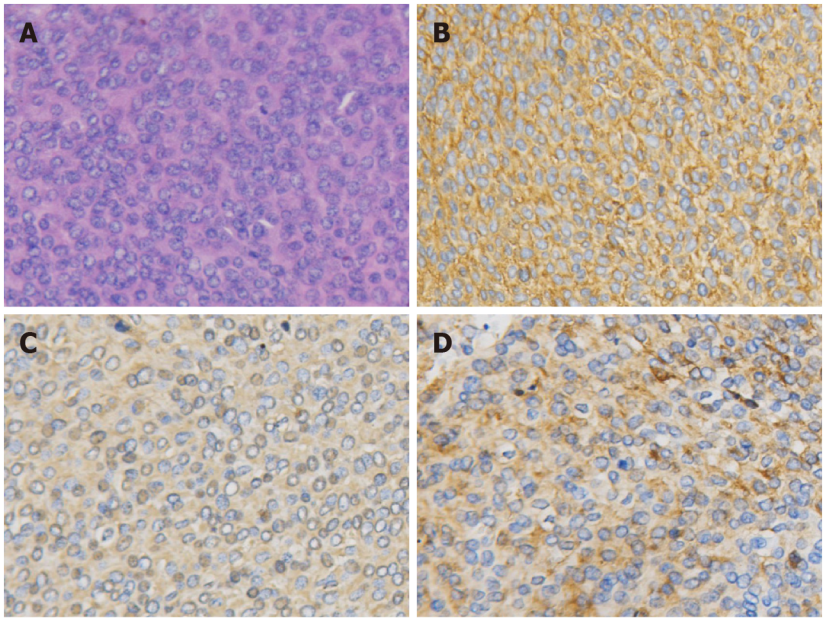

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Figure 3 Hematoxylin-eosin and immunohistochemical staining. A: Hematoxylin-eosin staining reveals small round cells arranged closely in a flaky pattern (× 200); B: Immunohistochemical staining of the small round cells for CD99 shows strong positivity for this marker (× 200); C and D: Immunohistochemical staining for vimentin and synaptophysin is positive (× 200).

[3,4,14,16], and in other cases, the 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 period: 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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FOOTNOTES

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ORCID number: Da-Wei Tian 0000-0002-1770-5627; Xiao-Chun Wang 0000-0002-3216-5710; Hui Zhang 0000-0002-0565-0411; Yan Tan 0000-0002-7529-9807.

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