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W J C C World Journal of Clinical Cases

Contents

Thrice Monthly Volume 10 Number 13 May 6, 2022

REVIEW

3969 COVID-19 and liver diseases, what we know so far Elnaggar M, Abomhya A, Elkhattib I, Dawoud N, Doshi R

MINIREVIEWS

3981 Amputation stump management: A narrative review

Choo YJ, Kim DH, Chang MC

ORIGINAL ARTICLE

Clinical and Translational Research

3989 Solute carrier family 2 members 1 and 2 as prognostic biomarkers in hepatocellular carcinoma associated with immune infiltration

Peng Q, Hao LY, Guo YL, Zhang ZQ, Ji JM, Xue Y, Liu YW, Lu JL, Li CG, Shi XL

Retrospective Cohort Study

4020 Role of clinical data and multidetector computed tomography findings in acute superior mesenteric artery embolism

Yang JS, Xu ZY, Chen FX, Wang MR, Cong RC, Fan XL, He BS, Xing W

Retrospective Study

Effect of calcium supplementation on severe hypocalcemia in patients with secondary 4033 hyperparathyroidism after total parathyroidectomy

Liu J, Fan XF, Yang M, Huang LP, Zhang L

4042 Comparison of clinical efficacy and postoperative inflammatory response between laparoscopic and open radical resection of colorectal cancer

He LH, Yang B, Su XQ, Zhou Y, Zhang Z

Three-dimensional echocardiographic assessment of left ventricular volume in different heart diseases 4050 using a fully automated quantification software

Pan CK, Zhao BW, Zhang XX, Pan M, Mao YK, Yang Y

Clinical effect of ultrasound-guided nerve block and dexmedetomidine anesthesia on lower extremity 4064 operative fracture reduction

Ao CB, Wu PL, Shao L, Yu JY, Wu WG

4072 Correlation between thrombopoietin and inflammatory factors, platelet indices, and thrombosis in patients with sepsis: A retrospective study

Xu WH, Mo LC, Shi MH, Rao H, Zhan XY, Yang M



Contents

Thrice Monthly Volume 10 Number 13 May 6, 2022

Observational Study

4084 High plasma CD40 ligand level is associated with more advanced stages and worse prognosis in colorectal cancer

Herold Z, Herold M, Herczeg G, Fodor A, Szasz AM, Dank M, Somogyi A

4097 Metabolic dysfunction is associated with steatosis but no other histologic features in nonalcoholic fatty liver disease

Dai YN, Xu CF, Pan HY, Huang HJ, Chen MJ, Li YM, Yu CH

Randomized Controlled Trial

4110 Effect of Xuebijing injection on myocardium during cardiopulmonary bypass: A prospective, randomized, double blind trial

Jin ZH, Zhao XQ, Sun HB, Zhu JL, Gao W

META-ANALYSIS

4119 Perioperative respiratory muscle training improves respiratory muscle strength and physical activity of patients receiving lung surgery: A meta-analysis

Yang MX, Wang J, Zhang X, Luo ZR, Yu PM

CASE REPORT

4131 Delayed diffuse lamellar keratitis after small-incision lenticule extraction related to immunoglobulin A nephropathy: A case report

Dan TT, Liu TX, Liao YL, Li ZZ

4137 Large vessel vasculitis with rare presentation of acute rhabdomyolysis: A case report and review of literature

Fu LJ, Hu SC, Zhang W, Ye LQ, Chen HB, Xiang XJ

- Primitive neuroectodermal tumor of the prostate in a 58-year-old man: A case report 4145 Tian DW, Wang XC, Zhang H, Tan Y
- 4153 Bilateral superficial cervical plexus block for parathyroidectomy during pregnancy: A case report Chung JY, Lee YS, Pyeon SY, Han SA, Huh H
- 4161 Primary myelofibrosis with thrombophilia as first symptom combined with thalassemia and Gilbert syndrome: A case report

Wufuer G, Wufuer K, Ba T, Cui T, Tao L, Fu L, Mao M, Duan MH

- 4171 Late contralateral recurrence of retinal detachment in incontinentia pigmenti: A case report Cai YR, Liang Y, Zhong X
- 4177 Pregnancy and delivery after augmentation cystoplasty: A case report and review of literature Ruan J, Zhang L, Duan MF, Luo DY
- 4185 Acute pancreatitis as a rare complication of gastrointestinal endoscopy: A case report Dai MG, Li LF, Cheng HY, Wang JB, Ye B, He FY



Conton	World Journal of Clinical Cases
Conten	Thrice Monthly Volume 10 Number 13 May 6, 2022
4190	Paraneoplastic neurological syndrome with positive anti-Hu and anti-Yo antibodies: A case report
	Li ZC, Cai HB, Fan ZZ, Zhai XB, Ge ZM
4196	Primary pulmonary meningioma: A case report and review of the literature
	Zhang DB, Chen T
4207	Anesthesia of a patient with congenital cataract, facial dysmorphism, and neuropathy syndrome for posterior scoliosis: A case report
	Hudec J, Kosinova M, Prokopova T, Filipovic M, Repko M, Stourac P
4214	Extensive myocardial calcification in critically ill patients receiving extracorporeal membrane oxygenation: A case report
	Sui ML, Wu CJ, Yang YD, Xia DM, Xu TJ, Tang WB
4220	Trigeminal extracranial thermocoagulation along with patient-controlled analgesia with esketamine for refractory postherpetic neuralgia after herpes zoster ophthalmicus: A case report
	Tao JC, Huang B, Luo G, Zhang ZQ, Xin BY, Yao M
4226	Thrombotic pulmonary embolism of inferior vena cava during caesarean section: A case report and review of the literature
	Jiang L, Liang WX, Yan Y, Wang SP, Dai L, Chen DJ
4236	EchoNavigator virtual marker and Agilis NxT steerable introducer facilitate transseptal transcatheter closure of mitral paravalvular leak
	Hsu JC, Khoi CS, Huang SH, Chang YY, Chen SL, Wu YW
4242	Primary isolated central nervous system acute lymphoblastic leukemia with <i>BCR-ABL1</i> rearrangement: A case report
	Chen Y, Lu QY, Lu JY, Hong XL
4249	Coexistence of meningioma and other intracranial benign tumors in non-neurofibromatosis type 2 patients: A case report and review of literature
	Hu TH, Wang R, Wang HY, Song YF, Yu JH, Wang ZX, Duan YZ, Liu T, Han S
4264	Treatment of condylar osteophyte in temporomandibular joint osteoarthritis with muscle balance occlusal splint and long-term follow-up: A case report
	Lan KW, Chen JM, Jiang LL, Feng YF, Yan Y
4273	Hepatic perivascular epithelioid cell tumor: A case report
	Li YF, Wang L, Xie YJ
4280	Multiple stress fractures of unilateral femur: A case report
	Tang MT, Liu CF, Liu JL, Saijilafu, Wang Z
4288	Enigmatic rapid organization of subdural hematoma in a patient with epilepsy: A case report
	Lv HT, Zhang LY, Wang XT



•	World Journal of Clinical Cases
Conten	Thrice Monthly Volume 10 Number 13 May 6, 2022
4294	Spinal canal decompression for hypertrophic neuropathy of the cauda equina with chronic inflammatory demyelinating polyradiculoneuropathy: A case report
	Ye L, Yu W, Liang NZ, Sun Y, Duan LF
4301	Primary intracranial extraskeletal myxoid chondrosarcoma: A case report and review of literature
	Znu Z1, wung 1D, Li H1, wu AM
4314	Mass brain tissue lost after decompressive craniectomy: A case report
	Li GG, Zhang ZQ, Mi YH
	LETTER TO THE EDITOR
4321	Improving outcomes in geriatric surgery: Is there more to the equation?
	Goh SSN, Chia CL
4324	Capillary leak syndrome: A rare cause of acute respiratory distress syndrome

Juneja D, Kataria S

Contents

Thrice Monthly Volume 10 Number 13 May 6, 2022

ABOUT COVER

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The primary aim of World Journal of Clinical Cases (WJCC, World J Clin Cases) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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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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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.



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

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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



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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 <i>et al</i> [21], 2003	27	Dysuria and pelvic discomfort	NA	NA	CD99	t (11; 22) (q24; q12)	CT, SR, RT	2+	NA
3	Thete <i>et al</i> [<mark>10]</mark> , 2007	26	Dysuria and pelvic discomfort	0.3	NA	CD99(Mic-2)	NA	NA	NA	NA
4	Kumar <i>et al</i> [<mark>16</mark>], 2008	25	Burning micturition and dysuria	0.88	6.7	CD99, vimentin, S100, NSE, synaptophysin	NA	CT	NA	NA
5	Funahashi <i>et</i> al[<mark>13</mark>], 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 <i>et al</i> [14], 2011	29	Burning micturition and urinary retention	1.3	NA	CD99	NA	СТ	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	СТ	NA	No
8	Wu et al <mark>[5</mark>], 2013	29	Difficult defecation and anus distention	1.19	7.4	CD99, Bcl-2	NA	SR, CT	12+	Lung
9	Liao <i>et al</i> [<mark>17</mark>], 2015	49	Frequent urination, dysuria, and pelvic discomfort	NA	7.1	CD99, CD56, NSE, Ki-67	NA	CT, RT	24+	No
10	Shibuya <i>et al</i> [<mark>3</mark>], 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 <i>et al</i> [11], 2016	33	Pelvic pain, dysuria, and urgency	NA	6	Cytokeratin	EWSR1-gene	SR	12+	No
12	Kord <i>et al</i> [<mark>8</mark>], 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 <mark>[9]</mark> , 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 <i>et al</i> [<mark>23</mark>], 2020	40	Dysuria	NA	11.2	CD99, synaptophysin, CD56, vimentin	FLI1	SR, CT	14+	No
16	Teng <i>et al</i> [15], 2020	27	Dysuria and dyschezia	1.52	8.4	CD99, CD56, desmin, vimentin	NA	SR	5	Lung and peritoneum
17	da Ponte <i>et al</i> [<mark>12</mark>], 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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Tian DW et al. PNET of the prostate



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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 (x 200); B: Immunohistochemical staining of the small round cells for CD99 shows strong positivity for this marker (x 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 followup 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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