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Case Report

Primary angiosarcoma of the prostate: a case report and literature review

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Abstract: Primary sarcomas of the prostate are rare, accounting for about 0.1% of all prostatic malignancies. Prostate angiosarcoma is exceedingly rare with only sixteen cases reported in the literature to date. Seven out of the sixteen cases were followed by radiotherapy for prostate adenocarcinoma. Despite the rarity, it usually presents with no detectable serum prostate-specific antigen levels and poor prognosis, representing a diagnosis and treatment challenge. The present study reports a new case of primary prostate angiosarcoma without radiation exposure history, reviewing the clinical symptoms, morphologic changes, prognosis, and treatment of angiosarcomas of the prostate.

Keywords: Prostate, angiosarcoma, primary

Introduction

Primary sarcomas of the prostate are rare, accounting for about 0.1% of all prostatic malignancies [1]. Rhabdomyosarcomas are the most frequent sarcomas of the prostate, accounting for more than 75% of all cases, typically seen in children and young adults. Angiosarcomas are malignant tumors of endothelial origin, frequently presenting in the deep soft tissue of the extremities, skin, breasts, and occasionally in different organs. It is exceedingly rare in the prostate with only sixteen cases reported in the literature. Angiosarcomas have been associated with exposure to radiation and chemical agents such as thorium, arsenic, and vinyl chloride. Seven of the cases of prostate angiosarcomas, mentioned above, were related to radiotherapy [2-4]. This study reports a new case of primary prostate angiosarcoma without history of radiation exposure, reviewing the literature of primary and secondary angiosarcomas of the prostate.

Case report

This case was a 41-year-old man with progressive dysuria, urinary bifurcation, frequent urination, and increased number of defecations. Symptoms were relieved after treatment with a urinary catheter but repeated after removal of the catheter. Since that time, the patient had experienced persistent abdominal discomfort for about one year. Serum prostate-specific antigen level of the patient was 0.08 ng/mL. Rectal palpation revealed a marked enlarged prostate. A large mass involving the left transitional zone, peripheral zone of the prostate, left seminal vesicle, and bladder was seen on magnetic resonance imaging (MRI) (**Figure 1A**). Computed tomography (CT) scans showed no obvious abnormalities of the brain, chest, and abdomen organs.

Pathologic diagnosis of angiosarcoma was made, according to the transrectal prostatic core biopsy. Considering the size of the tumor, the patient received adjuvant chemotherapy, with four cycles of gemcitabine and paclitaxel, before the operation. However, the tumor was not sensitive to chemotherapy. One month later, he received radical cystoprostatectomy, bricker operation, and underwent radiotherapy.

The patient died six months after the operation with the tumor metastasizing to the brain and liver.

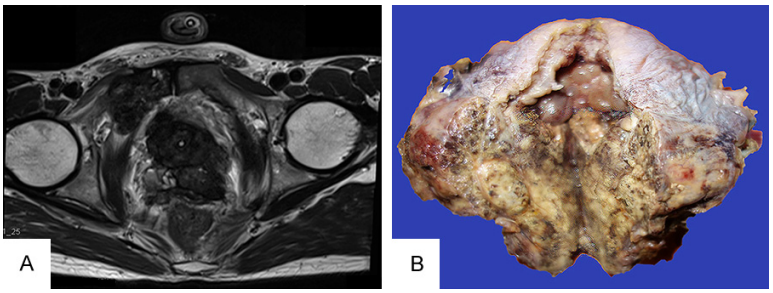

Figure 1. MRI revealed an ill-defined huge mass with low signal intensity of the prostatic origin on T2WI (A). Gross examination showed the tumor nearly replaced the whole prostate parenchyma and involved the bladder. The cut-off surface of the tumor was solid and gray with focally hemorrhage and necrosis (B).

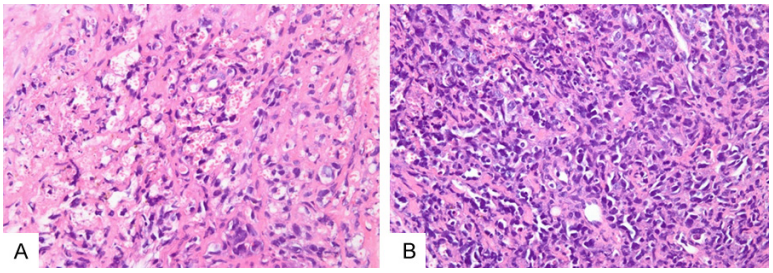

Figure 2. Histological features of the areas of well-formed anastomosing vessels formed by atypical endothelial cells (A) and areas of solid sheets without clear vasoformation (B). The tumor cells were spindle-shaped or polygonal with hyperchromatic nuclei and partial conspicuous nucleoli.

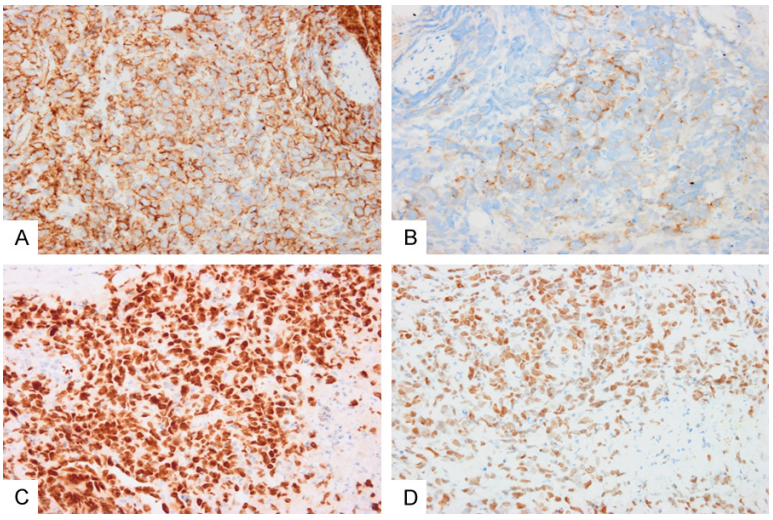

Figure 3. Immunohistochemically, the tumor cells were diffusely or focally positive for CD31 (A), CD34 (B), ERG (C) and Fli-1 (D).

Immunohistochemistry

Routine 4-μm sections were prepared from formalin-fixed and paraffin-embedded (FFPE) tissue blocks on 3-aminopropyltriethoxysilane-treated glass slides. Antigen retrieval was achieved by boiling the sections in 0.01 mol/L citrate buffer (pH 6.0) in a high-pressure cooker for 3 minutes. Envision kit (Dako Cytomation, Glostrup, Denmark) was used for immunohistochemical staining, according to manufacturer protocol.

Primary antibodies with the following dilutions were used for immunohistochemistry: CD31 (1:50; Dako Cytomation), CD34 (1:100; Dako Cytomation), CD99 (1:100; Dako Cytomation), CgA (1:100; Zymed, San Francisco, CA, USA), Desmin (1:100; Dako Cytomation), epithelial membrane antigen (EMA, 1:100; Dako Cytomation), ERG (1:400; Zymed), Fli1 (1:100; Zymed), myogenin (1:50; Zymed), pancytokeratin (PCK, 1:100; Zymed), P63 (1:50; Dako Cytomation), and S-100 (1:100; Zymed).

Results

Grossly, a huge lobulating prostate with the whole bladder was obtained from radical cystoprostatectomy. The prostate measured 7.5 cm × 6.0 cm × 6.0 cm, with a huge mass nearly completely replacing the whole prostate and invasion of the bladder. The cut-off surface of the tumor was solid and gray. Hemorrhaging and necrosis were seen focally (**Figure 1B**).

Microscopically, the tumor displayed a wide range of morphological appearances, ranging from areas of well-formed anastomosing vessels to solid sheets without clear vasoformation. Vasoformative areas consisted of ramifying channels lined by atypical endothe-

lial cells forming intraluminal buds. Solid areas were composed of high-grade spindle and epithelioid cells. The tumor cells were pleomorphic, varying from elongated and spindle-shaped to large and plump with abundant amphophilic to lightly eosinophilic cytoplasm, hyperchromatic nuclei, and prominent nucleoli. Mitoses were fairly frequent and some were atypical. Coagulative necrosis was easy to see in the tumor area (**Figure 2A**, **2B**).

According to immunohistochemistry, tumor cells were diffusely positive for CD31, CD34, ERG, and Fli-1 (**Figure 3A-D**) and negative for PCK, EMA, P63, CD99, S-100, Desmin, myogenin, and CgA.

Final diagnosis was primary angiosarcoma of the prostate.

Discussion

Angiosarcoma is particularly rare and comprises only 2% of all soft tissue sarcomas. Angiosarcomas of the prostate have been very rarely reported. Peak incidence has been noted between 40-50 and 70-80 years [5], with a median age of 57.5 years (range 19 to 79 years), summarized from cases reported.

Symptoms of prostate angiosarcomas are described in **Table 1**. Patients can present with symptoms of dysuria, hematuria, pelvic pain, and other lower urinary tract symptoms. Upon physical examination, the prostate is enlarged, firm, tender, or unremarkable [2, 5]. Because serum PSA levels are almost at the normal level, diagnosis of prostate sarcoma is usually established with ultrasound guided biopsy or transurethral resection.

Abnormal, pleomorphic, and malignant endothelial cells are the hallmarks of angiosarcoma. The most useful morphological characteristics leading to the diagnosis of angiosarcoma are the presence of blood-filled spaces of variable sizes and shapes lined by atypical cells. In poorly differentiated tumors, areas of hemorrhaging and necrosis among the continuous sheets of malignant endothelium cells can mimic poorly differentiated carcinoma or malignant melanoma. Therefore, an appropriate immunohistochemical panel of stains is necessarily to make the correct diagnosis. Angiosarcomas typically express endothelial markers, including CD34, CD31, factor VIII, ERG, and Fli-1. Individual studies have shown nuclear staining for c-Myc protein representing high-levels of c-Myc gene amplification in over half of post-radiation angiosarcomas [4].

Previous radiation exposure is a high risk factor for angiosarcomas [1, 2]. Oncogenic effects of ionizing radiation and prolonged cellular stimulation during repair of tissue damage, resulting from radiation induced ischemic changes, play an important role in development of angiosarcoma [6]. Seven out of the sixteen prostate angiosarcomas reported had a history of radiation therapy, supporting the relationship of angiosarcomas and radiation exposure. The present case, however, was primary angiosarcoma of the prostate without any history of exposure to radiation and chemical agents.

Adult prostate sarcoma carries a very poor prognosis [7]. Angiosarcoma of the prostate can metastasize to lymph nodes, lungs, spleen, liver, and other organs. Most patients die of disease within a year after diagnosis (**Table 1**). As the present case indicated, the tumor was unsensitive to chemotherapy and the patient died of brain and liver metastasis 6 months after radical cystoprostatectomy.

Treatment for prostate angiosarcoma remains a challenge. Radical surgery with complete resection is the optimal choice for localized prostate angiosarcoma. Although complete resection with wide margins is recommended, clean margins sometimes can be difficult to achieve because of diffused tissue invasion, tumor size, and relationship to adjacent organs. Radiation therapy is generally avoided, given the epidemiological association between radiation and angiosarcoma. Adjuvant chemotherapy has shown benefits over unimodal therapeutic strategy [3]. However, the role of adjuvant chemotherapy to reduce the risk of metastasis in sarcomas has been controversial due to the lack of prospective clinical trials [5]. Novel vascular-targeting agents, such as bevacizumab, angiopoietin 1/2, PDGF, and endoglin, have been evaluated but the effects of these agents seems to be limited [8].

Acknowledgements

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Table 1. Angiosarcomas of prostates reported in the literature

Case	Publication year	Author	Patient age (years)	History of RT	Symptoms	Immunophenotype	Treatment	Clinical outcome
1.	1963	Shapira	NM	NM	NM	NM	NM	NM
2	1986	Smith	60	NM	LUTS	Factor VIII (+)	Radical cystoprostatectomy	Dead, 6 months
3	1986	Smith	42	NM	Pain	Factor VIII (+)	Radical cystoprostatectomy + chemotherapy	Alive, 24 months
4	1989	Wick	63	NM	NM	Vimentin (+), Keratin (-), EMA (-), PSA (-)	Radical prostatectomy + radiotherapy	Alive, 15 months
5	1990	Chan	35	NM	Pain + Hematuria + LUTS	Factor VIII (+), vimentin (+)	NM	Dead, 5 weeks
6	1992	Russo	NM	NM	NM	NM	NM	NM
7	2000	Luque Barona	78	NM	NM	NM	Surgery (no further details)	Dead, 9 months
8	2001	Oliva Encina	31	NM	LUTS	Factor VIII (+), CD31 (+)	Radical prostatectomy + chemotherapy + radiation therapy	Alive, 36 months
9	2003	Chan dan	77	Ext. RT	Hematuria + LUTS	Factor VIII (+), CD34 (+)	TURP	Dead, 4 Days after TURP
10	2006	Lee	19	NM	Hematuria + LUTS	CD31 (+), CD34 (+)	Radical cystoprostatectomy	Alive, 16 months
11	2009	Guo	NM	Ext. RT	Hematuria + perineal pain	CD31 (+), CD34 (+)	PE	Dead, 2 months
12	2012	Humphrey	67	Ext. RT	LUTS	NM	TURP + PE	NM
13	2012	Khaliq	73	Ext. RT + Brachytherapy	Hematuria + LUTS	VIII (+), CD31 (+)	PE + chemotherapy	Dead, Several months (no further details)
14	2014	Campschroer	69	Brachytherapy	LUTS + perineal pain	CD31 (+), CD34 (+), factor VIII (+), PSA (-)	None	Dead, 4 months
15	2015	Gupta	71	Brachytherapy	Hematuria + LUTS	Fli-1 (+), CD31 (+), CD34 (+)	Chemotherapy	NM
16	2016	Wang	79	RT	Hematuria + LUTS	CD31 (+), CD34 (+), ERG (+), Fli-1 (+), c-Myc (+)	Radical cystoprostatectomy	Alive, 20 months
17	The present study	Liu	41	No	LUTS	CD31 (+), CD34 (+), ERG (+), Fli-1 (+)	Radical cystoprostatectomy + chemotherapy	Dead, 6 months

Ext. RT, external radiotherapy; LUTS, lower urinary tract symptoms; NM, not mentioned; PE, pelvic exenteration; TURP, transurethral resection of the prostate.

Disclosure of conflict of interest

None.

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