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Prostate angiosarcoma: a case report and literature review

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Abstract

Angiosarcomas are a relatively rare histological subtype of sarcomas and represent <1% of all sarcomas. Prostate angiosarcoma is extremely rare and displays remarkable clinical and pathological heterogeneity. Despite the rarity, it usually presents with dysuria, hematuria, or pelvic pain and represents a treatment challenge. Only nine cases have been reported in the literature, and we report the 10th case of prostate angiosarcoma and the first case of prostate angiosarcoma with recurrent adenocarcinoma.

Keywords

Prostate angiosarcoma; Urinary frequency; Hematuria; Radiation therapy

Case report

A 73-year-old man with a history of hypertension, prostate adenocarcinoma, and smoking presented with chronic urinary frequency, nocturia, and urgency for almost 1 year. Eight years ago, the patient was diagnosed with prostate adenocarcinoma (PSA 11.5 ng/ml and Gleason score 3 + 3 = 6) involving both lobes of the prostate gland (Fig. 1a). Rectal examination and transrectal ultrasound were negative for clinical extracapsular extension

(clinical stage T1c). Staging workup was negative for metastatic disease. The patient received external beam radiation therapy with brachytherapy boost. A follow-up PSA level done at 1 year after radiation therapy was 1.2 ng/ml. After treatment, the patient developed chronic urinary frequency and urgency that were treated with doxazosin and oxybutynin.

Eight years after the treatment for his prostate adenocarcinoma, with a PSA of 0.6 ng/mL, the patient had chronic urinary frequency and urgency. A cystoscopy with transurethral incision of the prostate revealed a small prostate with severe chronic radiation changes in the prostatic urethra. Tissue samples from the incision showed proliferating vascular channels lined by atypical and malignant-appearing endothelial cells consistent with high-grade angiosarcoma (Fig. 1b). The tumor cells stained positive for factor VIII (Fig. 1c) and CD31 (Fig. 1d). Staging workup with a bone scan and CT chest/abdomen/pelvis was negative for metastases. The patient underwent pelvic exenteration and was found to have bladder and seminal vesicle involvement by direct tumor extension. At cystoprostatectomy, the tumor was present at the urethral margin and the left anterolateral pelvic sidewall. Six out of nine pelvic lymph nodes were positive for metastatic prostatic adenocarcinoma (but not angiosarcoma) with extranodal extension. Due to the positive margins, the patient was offered re-exploration surgery; however, he declined and opted for chemotherapy. Post-surgical evaluation with a CT abdomen/pelvis was unremarkable except for the surgical changes consistent with pelvic exenteration. The patient's blood work was significant for elevated alkaline phosphatase at 241 IU/l (42–121 IU/l) and a creatinine of 1.7 mg/dl (0.5–1.2 mg/dl). PSA was <0.1 ng/ml. MRI of the thoracic and lumbosacral spine showed no evidence of metastases.

Poor functional status was a major limitation to start the patient on standard sarcoma treatment involving ifosfamide, doxorubicin, or paclitaxel. Therefore, the patient was treated with experimental oral thalidomide for prostate angiosarcoma and managed expectantly for metastatic adenocarcinoma (by monitoring PSA). Two months after starting thalidomide, the patient had an episode of seizure. A head CT without contrast was negative for any acute changes. However, a CT of the chest/abdomen/pelvis revealed a pulmonary nodule, a hypodense lesion in liver, and a low-density mass in left kidney. These lesions were new and assumed to be metastatic sarcoma. Diagnostic biopsy was postponed due to patient's worsening performance status. The patient died 2 weeks later after opting for comfort care.

Discussion

Angiosarcoma is a type of soft tissue sarcoma that develops from the endothelium of a blood vessel characterized by atypical, multilayered, or solid endothelial proliferation.

Angiosarcomas are rare malignant neoplasms comprising only 2% of all soft tissue sarcomas, occur more often among older adults, and usually involve the skin, soft tissue, breast, or liver [1]. Angiosarcoma of the prostate is very rare, and only nine cases have been reported in the literature to date [2–9]. We present the 10th case of prostate angiosarcoma, and to our knowledge, this is also the first case of prostate angiosarcoma with recurrent adenocarcinoma of the prostate.

Very little is known regarding the natural history and prognosis of prostate angiosarcoma. It can develop at any age; however, a bimodal peak has been noted between the 4th and 5th decade and 7th and 8th decade of life. Factors known to predispose to angiosarcoma include prior radiation treatment, chronic lymphedema, and chemical exposure to vinyl chloride, thorium dioxide, and arsenic. Cahan et al. [10] suggested that radiation-induced sarcoma should arise in an area previously subjected to irradiation with a latent period of at least 7 years. Radiation exposure has been suggested to be the main risk factor for angiosarcoma development in the literature [11, 12]; however, the supporting evidence is weak due to the limited number of cases.

Patients with prostate angiosarcoma can present with symptoms of dysuria, hematuria, and pelvic pain. On physical examination, the prostate can be enlarged, tender, or unremarkable. Diagnosis is usually made upon prostate biopsy, while serum PSA levels are not diagnostic. Abnormal, pleomorphic, malignant endothelial cells are the hallmark of angiosarcoma [13]. Angiosarcomas typically express endothelial markers, including factor VIII, CD34, CD31, Ulex europaeus agglutinin 1, and vascular endothelial growth factor (VEGF). Therefore, immunohistochemistry is an important part of the diagnosis.

Mortality is very high, and prognosis is poor as evidenced by the case reports [2–9]. Tumor size (>5 cm), tumor grade, advanced age, and metastatic disease are considered poor prognostic factors [14].

Treatment for prostate angiosarcoma is a challenge and in general follows the guidelines for other soft tissue sarcomas, such as those published by the National Comprehensive Cancer Network (NCCN) and the European Society for Medical Oncology (ESMO). Radical surgery with complete (R0) resection is the primary treatment of choice for localized prostate angiosarcoma. Although complete resection with wide margins is recommended, clean margins sometimes can be difficult to achieve (resulting in R1 or R2 resections) because of diffuse tissue invasion, tumor size, and relationship to adjacent organs [15–18]. The role of adjuvant chemotherapy to reduce the risk of metastasis in sarcomas also has been controversial due to the lack of prospective clinical trials. No survival benefit has been shown for the use of chemotherapy in abdominal or retro-peritoneal tumors. Cytotoxic chemotherapy is the primary treatment for metastatic angiosarcoma. The main agents used for treatment are anthracyclines, ifosfamide, and taxanes.

The current treatment options for prostatic angiosarcoma are limited, with surgery being the main curative modality. Radiation therapy is currently not a recommended treatment. Primary care physicians and urologists should be aware of this rare entity and refer these patients to specialist centers where they can be managed by a multidisciplinary team that includes an urologist, medical oncologist, and surgical oncologist.

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Fig. 1.

a Prostate core biopsy showing prostate adenocarcinoma with Gleason score $3 + 3 = 6$, H&E $\times 200$. **b** Biopsy showing prostate angiosarcoma on H&E, with proliferating vascular channels lined by atypical and malignant-appearing endothelial cells. The tumor cells stain positive for factor VIII (**c**) and CD31 (**d**), supporting a diagnosis of prostate angiosarcoma