Angiosarcomas are high-grade sarcomas of vascular origin that rarely arise in the prostate. We describe a unique case of angiosarcoma arising in the prostate 10 years after radiotherapy for adenocarcinoma of the prostate. A review of literature regarding angiosarcomas of prostate is also discussed.

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Angiosarcoma is a malignant endothelial neoplasm with vasosformative architecture characterized by atypical, multilayered, or solid endothelial proliferation. They are rare malignant neoplasms comprising only 2% of all soft tissue sarcomas. Several agents are known to predispose to angiosarcoma formation, including ionizing radiation. To our knowledge, we report the first case of angiosarcoma of prostate 10 years after therapeutic irradiation for prostate cancer and only the seventh case of prostatic angiosarcoma. Multiple criteria have been proposed for considering a tumor to be radiation related, and all have been fulfilled in our case.

REPORT OF A CASE

A 77-year-old man presented in April 2002 with gross hematuria of 2 weeks’ duration. He also complained of urinary frequency, bladder spasms, and pain on urination for 2 months. He denied history of fever, chills, pain, or loss of weight.

The patient’s history was significant for stage B prostatic adenocarcinoma (Gleason score 7) in 1992 treated with external radiation therapy (6680 rad [66.8 Gy]). He received regular follow-up, and his latest serum prostate-specific antigen level (January 2002) was 0.0023 ng/mL (normal 0–0.4). His past medical history was significant for senile dementia, atherosclerotic coronary artery disease, status post-coronary artery bypass surgery in 1998, thoracic aortic aneurysm, hypertension, and chronic obstructive pulmonary disease. He had no history of exposure to chemicals, including vinyl chloride, diphenols, or thorium dioxide.

Physical examination was unremarkable. Computed tomographic scan of the pelvis showed a large mass arising from the prostate. A plain chest radiograph and computed tomographic scan of thorax and abdomen were negative for metastatic disease.

Urethrocystoscopy was performed and showed trilobular prostatic hyperplasia with irregular prostatic tissue encroaching into lumen of the prostatic urethra. The bladder lumen was filled with a significant amount of well-formed blood clots. Transurethral resection of the prostatic tissue infiltrating into urinary bladder was performed and sent for histopathologic examination.

The patient continued to have bouts of hematuria, and numerous units of blood were given, followed by generalized bleeding and evidence of disseminated intravascular coagulation. He died 4 days after the urethrocystoscopy. No autopsy was performed.

PATHOLOGIC FINDINGS

The specimen consisted of 15 g of tan-brown soft tissue mixed with clotted blood. The entire specimen was submitted for histopathologic examination. Microscopically, most of the tissue was necrotic; less than 10% was viable tissue. This consisted of proliferating vascular channels lined by atypical endothelial cells, which in turn were surrounded by spindle-shaped cells. The tumor cells were pleomorphic, varying from elongated and spindle-shaped to large and plump. The nuclei were large and pleomorphic with clumped chromatin and prominent nucleoli. Mitoses were fairly frequent and some were atypical (Figure 1). The prostatic urethral area, however, showed prominent Brunn nests and no evidence of atypia. Immuno-
Figure 1. Tumor consisted of pleomorphic cells and large nuclei with clumped chromatin and prominent nucleoli. Mitoses are easily seen (arrows). Vascular channels lined by atypical endothelial cells are present within the tumor (hematoxylin-eosin, original magnification ×400).

Figure 2. Tumor cells show positive staining for factor VIII–related antigen (Figure 2) and CD34 (Figure 3) (immunohistochemistry, original magnification ×400).

Human oxidase staining for factor VIII–related antigen (Figure 2), CD34 (Figure 3), and vimentin showed positive reactivity in tumor cells. There was negative immunoreactivity for prostate-specific antigen, S100 protein, and cytokeratin. (Factor VIII–related antigen and CD34 were purchased from Cell Marque Corporation, Hot Springs, Ark; all other immunostains were from Ventana Medical Systems, Inc, Tucson, Ariz.) Based on our findings, a diagnosis of angiosarcoma of prostate was made.

COMMENT

Sarcoma of the prostate is rare and constitutes less than 0.1% of all prostatic malignancies. Angiosarcoma of the prostate is extremely rare; to our knowledge, the literature contains only 6 reliable reports of angiosarcoma of prostate. We report the first case of postirradiation angiosarcoma of the prostate.

In considering the diagnosis of irradiation-induced sarcoma, Cahan et al suggested the following criteria: (1) the sarcoma should arise in the area previously subjected to irradiation, (2) a latent period (in years) must exist between the time of irradiation and development of the sarcoma, and (3) the sarcoma must be confirmed histologically. The present case satisfies all of these criteria and, thus, can be considered radiation related.

Kim et al, after an extensive review of literature, found 66 reported cases of radiation-associated angiosarcoma. The most common primary disease for which radiation was used in therapy was breast cancer (44%), followed by gynecologic cancer (21%). Eighty-five percent of radiation-associated angiosarcoma developed in the cutaneous area. The median age at diagnosis was 65 years, and the median latency period from irradiation to diagnosis was 96 months. In their study, the median survival period of radiation-associated angiosarcoma was 12 months.

The causal relationship between previous irradiation and angiosarcoma was debated in the earlier literature. Now, however, little doubt exists that there are bona fide postirradiation angiosarcomas. In addition to the direct oncogenic effect of ionizing radiation, prolonged cellular stimulation during repair of tissue damage resulting from radiation-induced ischemic change may play a role in development of angiosarcoma.

With regard to the 6 previously reported cases of prostatic angiosarcoma, we have recorded the following general observations (Table). At the time of diagnosis, the patient's ages ranged from 2 to 60 years (mean, 34.5 years); only 1 case involved a 2-year-old child. Rhabdomyosarcomas are the most frequent sarcomas of the prostate, accounting for more than 75% of cases, and are typically seen in infants, children, and young adults. Presenting complaints in the 6 reported cases included dysuria and hematuria. Three patients died within the first 6 months, 2 were disease-free for a period of 24 and 36 months, and no follow-up was available for 1 patient.

After an extensive review of the literature, we found 1 case of angiosarcoma of urinary bladder that developed 13 years after therapeutic irradiation for prostate cancer. Although this is only the second report of an angiosar-
Angiosarcoma arising after radiation therapy for prostate carcinoma, we speculate that as therapy of prostatic adenocarcinoma improves survival, the incidence of postirradiation sequelae can be expected to increase. The estimated risk of developing postirradiation sarcoma with long-term follow-up appears to be 0.03% to 0.8%. From a review of the literature that compared mortality risks of chemotherapy, general surgery, and anesthe sia, the risk of postirradiation sarcoma appears no worse. Thus, given the large number of patients who can be cured or who receive palliative treatment with radiation therapy, concern regarding postirradiation sarcoma should not be a major factor influencing treatment decisions in patients with cancer.

There is a need for pathologists to be aware of the possibility of angiosarcomas in patients presenting with hematuria and/or dysuria after radiation therapy.

References