Secondary sarcoma of bone post-prostate brachytherapy: A case report

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Abstract

Malignancies associated with brachytherapy for prostate cancer are largely unreported in the literature. We report a case of post-brachytherapy osteogenic sarcoma in the pelvis 6 years after permanent 125I implant for intermediate-risk prostate cancer. The patient was treated with neoadjuvant chemotherapy, limb-sparing surgical resection and postoperative radiation therapy for unexpected positive margins.

Introduction

Several studies report that prostate cancer patients receiving external beam radiation therapy (EBRT) may be at increased risk for developing second malignancies compared to those who do not receive any radiation therapy.1-3 However, given the relative novelty of brachytherapy, there is considerably less written about the risk of second malignancies after brachytherapy. We report a case of high-grade pleomorphic sarcoma of bone arising 6 years after brachytherapy implant.

Case report

A 54-year-old male presented with a T2b NX MX Gleason 3+4 adenocarcinoma of the prostate, screen detected with an initial prostate-specific antigen (iPSA) of 5.7. His only medical comorbidities were diabetes, hypertension and reflux. The patient opted for brachytherapy. Neoadjuvant androgen deprivation therapy was given to decrease prostate size. He received a transperineal Iodine-125 implant in 2006. A total of 120 sources each containing about 0.33 mCi of I-125 were placed at pre-planned coordinates. At planning, the prostate volume was 43 cc, and the planning target volume was 59 cc. Our planning target volume was defined as the prostate plus a superior 5 mm, lateral 3 to 5 mm and anterior 0 to 3 mm margin. The prescription dose was 144 Gy, with a D90% of 160 Gy. Post-implant, dosimetry showed acceptable V100, V150 and V200 of 100%, 59.4% and 21.3%, respectively. In routine follow-up, his PSA fell to a nadir of 0.06 in July 2012.

Six years after BT implantation, he developed left lower back, hip and thigh pain. Investigation revealed a 9 × 7 × 7-cm soft tissue mass centred on the left inferior pubic ramus, closely associated with the prostate and within the low dose region of the brachytherapy implant (Fig. 1, Fig. 2). Staging computed tomography (CT) scan of the chest, abdomen and pelvis did not reveal any other lesions. CT-guided core needle biopsy revealed a high-grade undifferentiated sarcoma of bone. After a multidisciplinary discussion, a recommendation for neoadjuvant chemotherapy and surgical resection was made.

Three cycles of doxorubicin 75 mg/m² and cisplatin 100 mg/m² every 21 days were planned. Cycle 1 was complicated by nausea requiring intravenous hydration, and febrile neutropenia. Cycle 2 was delayed by 1 week with the dose reduced to 85% and the administration of prophylactic G-CSF. Cycle 3 was given at the same reduced dose, and was also delayed for 1 week due to poor performance status. The tumour decreased (8.4 × 5.4 × 6.8 cm) on post-chemotherapy magnetic resonance image and systemic imaging showed no evidence of distant metastatic disease. He underwent resection of the left anterior hemi-pelvis using computer navigation (Stryker Canada Inc.) to preserve the hip joint laterally. Medially, dissection was taken along the base of the penis and the contralateral pubic ramus divided. The soft tissue defect was filled with a vertical rectus abdominus flap. Pathology revealed a high-grade pleomorphic spindle cell sarcoma with a fascicular storiform growth pattern and sclerotic matrix (Fig. 3). It was undifferentiated with no osteoid or chondroid matrix identified. The tumour was
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95% necrotic and while the osteotomy margin was negative, there was a highly infiltrative growth pattern with focally positive and close soft tissue margins. The postoperative course was complicated by infection requiring percutaneous drainage and long-term ertapenem and vancomycin. This resulted in a delay to the initial plan for 3 further cycles of adjuvant chemotherapy. A discussion about the risks and benefits of chemotherapy was held 12 weeks postoperatively, and the patient refused this option.

As unexpected positive margins are associated with higher local recurrence rates, the multidisciplinary group recommended radiation therapy to the tumour bed to ameliorate this risk. Thirteen weeks after surgery, radiation therapy was delivered with a volume modulated arc therapy (VMAT) technique. The prescription dose was 50.4 Gy in 28 fractions with an additional boost of 6 Gy in 3 fractions to a smaller volume (Fig. 4). Follow-up imaging up to 12 months post-radiation therapy showed no signs of locally recurrent disease.

**Discussion**

To the best of our knowledge, there have been no previous reported cases of osteogenic sarcoma associated with prostate brachytherapy using permanent I125 seeds. The risk of second malignancies from EBRT is more definitively established than with brachytherapy. The Surveillance, Epidemiology, and End Result (SEER) data analysis has shown a small but significant 34% increase in relative risk of second malignancies after EBRT as compared to surgery, beyond 10 years. The increased relative risk of sarcoma within the treatment field was larger at 217%. This translates into an estimated risk of 1 radiation therapy-associated solid tumour among 290 persons at risk.

The association between radiation and sarcomas is well-established both clinically and in the literature. The risk of radiation-induced malignancy is expressed by the Linear No Threshold model, which assumes a proportional relationship between radiation dose and risk of second malignancy, with a safe threshold dose below which a risk does not exist. Multiple mechanistic models for radiation-induced carcinogenesis have been suggested. These mechanisms would apply equally to EBRT and brachytherapy. At our institution, high-grade osteosarcoma of the pelvis has been seen several times after EBRT. Although not previously described with brachytherapy, brachytherapy-associated sarcoma is possible given the association of sarcoma with other forms of radiation exposure, and the literature describing other second malignancies associated with brachytherapy.

There have been previous case reports of rare prostatic malignant histologies developing after a long latency period following brachytherapy alone or in combination with EBRT for treatment of prostatic adenocarcinoma. Other local second malignancies have also been described following brachytherapy, including rectal squamous cell carcinoma in an ulcerated prostatorectal fistula. In addition, a case report describes distant malignancy developing at the site of a migrated brachytherapy seed in the lungs 10 years after combined androgen deprivation, EBRT and brachytherapy.
In contrast, a review of SEER data noted no significant difference in the odds of second cancers for those treated with radioactive implants or isotopes versus those who received no radiation.¹ A Dutch Cancer Registry competitive risk analysis also described no difference in second malignancies incidence for brachytherapy versus prostatectomy, and no increased tumour incidence in comparison to the general population.¹² The specific contribution of brachytherapy to the risk of second malignancies remains unclear.

This case meets the criteria for radiation-induced sarcoma (primary and secondary neoplasm of different histology, arising within the irradiated region, with a latency period of 6 years).⁴ However, given the overall low rates of sarcoma post-radiation (estimated at 0.03%-0.2%⁴), the possibility of an unrelated malignancy remains.

**Conclusion**

Our report describes a case of high-grade undifferentiated sarcoma of bone diagnosed 6 years following brachytherapy implant treated with neoadjuvant chemotherapy, surgery and postoperative radiotherapy. In comparison to EBRT, brachytherapy results in a lower dose delivered to normal tissues; while the absolute risk of second malignancies remains low overall, it remains a reality and should be discussed with all patients.

**Competing interests:** Dr. Ye, Dr. Conway, Dr. Peacock, Dr. Clarkson, Dr. Lee, Dr. Simmons, Dr. Weir and Dr. McKenzie all declare no competing financial or personal interests.

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**References**


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