CASE REPORT

Secondary spindle cell sarcoma following external beam radiotherapy for prostate cancer: a rare but devastating complication

Matthew Farag,¹ Anthony Ta,¹ Siva Shankar,² Lih-Ming Wong¹

¹Department of Urology, St Vincent's Hospital Melbourne, Melbourne, Victoria, Australia
²Peter MacCallum Cancer Institute, Melbourne, Victoria, Australia

Correspondence to
 Dr Matthew Farag,
 mattfarag@hotmail.com

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SUMMARY

We report a case of rapidly growing sarcoma that resulted in mortality only 6 years after radiotherapy for low-grade prostate cancer. At the age of 69 years and a prostate-specific antigen (PSA) that had risen to 9.0 µg/L, transrectal ultrasound-guided biopsy of the prostate found a single core of Gleason 3+3 disease involving 4 mm of a 10 mm core. The patient declined active surveillance and completed 78 Gy of external beam radiotherapy over 39 fractions to a prostate volume of 46 mL. His PSA nadir was 0.62 µg/L 1-year postradiation; however, in April 2017, his PSA began to rise satisfying the definition of biochemical recurrence. He underwent cystoscopy, biopsy favoured an undifferentiated pleomorphic sarcoma. Restaging scans (CT/bone scan) were completed showing no metastasis, and repeat MRI showed rapid growth of the lesion in 3 months. He underwent palliative pelvic exenteration, however, 1 month later presented with large volume tumour recurrence and was subsequently palliated and died.

BACKGROUND

Defining the optimum therapeutic algorithm for localised prostate cancer remains a unique challenge in urological oncology. The vast majority of men with prostate cancer will die from causes unrelated to their malignancy.¹ Advances in the grading and subsequent management of prostate cancer have meant the number of prostate cancer survivors is increasing.² Studies have shown that modern external beam radiotherapy can be as effective as modern surgical and brachytherapy techniques.^{2,3} Therefore, patients considering treatment for localised prostate cancer are commonly referred to a radiation oncologist by their urologist to discuss external beam radiotherapy as an equivalent option.

We present a case of postexternal beam radiotherapy sarcoma, approximately 6 years after treatment for low-grade prostate cancer. The development of radiation-induced second primary cancers (SPCs) has long been recognised as a possible late side effect following radiation therapy,⁴ and prostate cancer radiotherapy is therefore a risk factor for secondary malignancies. It is often difficult to determine the exact rate of SPC because of the long latency time between irradiation and SPC development, hence the exact rate of secondary sarcoma is unknown. This is concerning

in diseases such as localised prostate cancer, particularly low-grade, which often have more indolent courses and high rates of long-term survival.

CASE PRESENTATION

Our patient had a medical history significant for transurethral resection of prostate (TURP) in 1996 for urinary symptoms and had undergone an appendectomy in 1970. Histology from the TURP was benign. He had never smoked and had no known family history of malignancies. He underwent routine testing of his prostate-specific antigen (PSA) from 2008, which was initially around 6 µg/L and gradually increased to 9.0 µg/L (2011), his prostate remained benign on digital rectal examination. At the age of 69, he underwent a prostate biopsy (24 January 2011) and was diagnosed with low-risk prostate adenocarcinoma in the left transition zone comprising 4 mm out of a 10 mm core (T1c Gleason 3+3). It was discussed by his urologist that he was a candidate for active surveillance, surgery or external beam radiotherapy. After appropriate counselling, he decided against active surveillance as both he and his wife felt that they would not like to take the risk of disease progression; instead he expressed a preference to have radiotherapy.

He completed 78 Gy of external beam radiotherapy over 39 fractions (completed 27 November 2011) to a prostate volume of 46 mL, without neoadjuvant androgen deprivation therapy due to low-risk disease. The radiation comprised the use of intensity-modulated radiation therapy to the 'prostate only' which routinely included the superior 2 cm of the seminal vesicles. He was well in the immediate period postradiotherapy apart from urgency that slowly improved and nocturia that was well managed. Otherwise, he had no other rectal symptoms, and his international prostate symptom score (IPSS) was 4/35 at the completion of radiotherapy. A radiation oncologist along with his urologist followed up closely during the period following treatment, his PSA nadir was 0.62 µg/L 1-year postradiation.

During the period of 2013–2017, he had several episodes of haematuria, thought to be secondary to radiation cystitis. Rectal cancer was excluded with imaging and scopes in 2013, with rectal bleeding thought to be secondary to haemorrhoids. He also had a normal rigid cystoscopy in 2013 along with

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Figure 1 A pelvic exenteration specimen comprising an en bloc resection of bladder, prostate/periprostatic tissue, postprostatic urethra, penis, rectum and anus (22 August 2017). No gross tumour is seen on the specimen exterior. There is no gross evidence of full thickness bladder wall involvement identified, and tumour grossly appears to be at least 2 mm clear of specimen edge in the bladder. The prostate is largely replaced by tumour with an ill-defined edge and a firm pale grey cut surface.

urethral dilatation and commencement of tamsulosin to treat poor urinary flow.

His PSA began to slowly rise in 2014, and he satisfied the definition of biochemical recurrence in April 2017 (PSA 2.67 µg/L), a rise by more than 2 ng/mL above the nadir.⁵ Concurrently, he developed new obstructive voiding symptoms prompting further evaluation. CT imaging revealed bladder wall thickening and multiple bladder diverticula, with no evidence of local, regional or distant recurrence. Bone scan was unremarkable. Cystoscopy to further investigate the CT findings revealed a bladder neck mass and subsequent transurethral resection was performed. The histopathology favoured an undifferentiated pleomorphic sarcoma (26 July 2017).

Further local staging with MRI (4 August 2017) was performed and demonstrated a large rapidly growing pelvic mass, measuring 16 cm and infiltrating the urinary bladder, prostate bed, urethra and base of the penis. Repeat MRI (21 August 2017) demonstrated further progression, now measuring 6.2×7.1×16 cm. A fat plane could be observed between the tumour and the pubic bone anteriorly, however, posteriorly the tumour appeared to invade into the anterior rectal wall. It was demonstrated to pass in close proximity to the sigmoid colon, passing beneath the pubic symphysis along the penis to within 7 cm of the external urethral meatus.

TREATMENT

Our patient underwent palliative pelvic exenteration with ileal conduit and end colostomy on 22 August 2017 (figures 1 and 2). Histopathology of the specimen favoured a sarcomatoid carcinoma or undifferentiated sarcoma, with positive margins where tumour was infiltrating the pubic ramus.

OUTCOME AND FOLLOW-UP

He presented again on 15 September 2017 with urosepsis and a small bowel obstruction. A CT AP showed a large extensive tumour recurrence (figure 3). He was managed conservatively

Figure 2 The tumour cells have pleomorphic round-to-spindled nuclei with open chromatin and prominent nucleoli, with dense eosinophilic cytoplasm. Mitotic activity is conspicuous, reaching up to 20 per 10 high-power fields.

and was palliated after a family meeting (19 September 2017). Our patient died on 24 September 2017.

DISCUSSION

The definition for the diagnosis of a radiation-induced malignancy has previously been well described.⁶ Initially, the lesion must be localised in a previously irradiated area, and there must be a clear cytological difference between the primary and the new lesion. In addition, there must be a latent interval between the radiation therapy and the presence of a new lesion. These criteria were met in this case, and although our latent interval is perhaps less than the average cited, it is consistent with a case published by Scully *et al*, where secondary spindle cell sarcoma occurred 8 years postirradiation.⁷

Studies have estimated that one of 70 patients undergoing radiation for prostate cancer will develop a secondary cancer if they survive more than 10 years.⁸ The most common sites for secondary cancers are bladder, rectum and lung.⁸ These secondary

Figure 3 CT of the abdomen and pelvis (15 September 2017), showing extensive tumour recurrence less than 1 month postpelvic exenteration.

cancers are late complications occurring after radiotherapy treatment, affecting survivors of the primary prostate cancer. This is especially significant for patients with primary cancers who have high rates of long-term survival, such as prostate cancer. The exact mechanisms leading to radiation-induced malignant transformation of cells are not well defined in the literature.⁹ However, technology in radiotherapy techniques is developing to lower the irradiation dose to normal tissues, this may reduce complications of radiotherapy on normal tissue, including secondary malignancy.

Although the risk of a secondary radiation-induced malignancy is modest, patients should be aware of this risk when making a treatment decision. Here we report a case of rapidly growing sarcoma that occurred only 6 years after treatment. This tumour showed aggressive recurrence only 1 month post an extensive palliative resection, leading to palliation and subsequent mortality of this patient.

Patient's perspective

Next of kin (wife)

28 March 2018: "I am devastated, truly devastated, we had a few good years after the radiotherapy, and then it all happened so quickly. My husband succumbed to this, this second cancer struck like lightning, he got unlucky, I hope we can prevent this from happening to others."

Learning points

- Despite its rarity, secondary sarcoma following external beam radiotherapy can be rapidly growing and have devastating outcomes, this case occurred only 6 years after radiotherapy treatment.
- Low-grade prostate cancer presents the patient with options and challenges regarding the choice of treatment, a specialist multidisciplinary prostate cancer centre should direct care.
- There is value of MRI over CT in local staging of malignancy.

Patients are currently encouraged to meet with different prostate cancer care specialists (urologists, radiation/medical oncologists) to promote informed decision-making. This patient's disease involved a single core of Gleason 3+3 comprising 4 mm of a 10 mm core. His devastating outcome highlights the need to select a management strategy for localised prostate cancer incorporating shared decision-making and explicitly considering primary prostate cancer severity.

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Contributors Dr Matthew Farag is the surgical resident present on the case and main author collating data and writing up report. Mr Lih-Ming Wong is the head of the urological surgical team. Dr Anthony Ta is the urological surgical registrar involved with this case. Dr Siva Shankar is the radio-oncologist administering radiotherapy for this case.

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