Long-Term Control of Oligometastatic Prostate Cancer After Stereotactic Body Radiotherapy in the Absence of Androgen Deprivation Therapy: A Case Report

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Clinical Practice Points

- A subset of patients with oligometastatic prostate may be effectively treated with focal radiotherapy.
- Randomized prospective clinical trials are underway to determine the overall survival benefit of stereotactic radiation in treatment-naive oligometastatic prostate cancer.

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Introduction

Prostate cancer is a common malignancy with favorable clinical outcomes after therapy for localized disease. A subset of men will develop a biochemical recurrence of their cancer with a rising prostate-specific antigen (PSA) value. In the absence of metastases, treatment of biochemically recurrent prostate cancer remains controversial. Several clinical parameters (ie, PSA doubling time, Gleason score, time to biochemical recurrence) may inform clinical decisions in patients with biochemical recurrence, favoring initiation of androgen deprivation therapy (ADT).[1] Upon developing metastatic prostate cancer, continuous ADT is the standard-of-care treatment for what has long been considered an incurable disease. Recently, oligometastatic disease has emerged as a distinct clinical state with a tumor burden intermediate to localized and extensive systemic disease, which can be effectively treated with local therapies.[2] Patients with controlled local sites of disease (ie, prostatectomy) and fewer than 5 metastatic sites may be candidates for stereotactic body radiotherapy (SBRT).[3] A recent prospective study reported that select patients with oligometastatic disease were long-term survivors after SBRT.[4] In prostate cancer, a pooled analysis of multiple studies suggested that SBRT for oligometastatic disease was safe and resulted in prolonged progression-free survival.[5] Moreover, second and third SBRT treatments provided to patients with 3 or fewer sites of metastatic disease were associated with prolonged ADT-free survival.[6] Prospective studies evaluating the effect of SBRT on overall survival in prostate cancer are ongoing.

Treating oligometastatic prostate cancer as a separate disease entity remains controversial. Current evidence suggests that sites of metastatic disease may represent a growth advantage of a particularly lethal clone of the cancer.[7] It will prove especially challenging to determine whether these early sites of metastatic disease represent the first few flakes of a snowstorm or metastatic escape of a single clone. In the latter, SBRT may treat a potential lethal phenotype of the disease, whereas systemic ADT may be of more benefit to the former.

In this case report, we describe a patient with oligometastatic prostate cancer who was treated with SBRT in the absence of ADT and experienced a durable remission. While additional studies are needed, this case report provides anecdotal evidence that oligometastatic cancer is a distinct subset of metastatic disease. Select patients with metastatic prostate cancer may experience long-term disease control after local therapy without further treatment.

Case Presentation

A 73-year-old man with a significant cardiac history was initially found to have an elevated PSA of 4.7 ng/mL on routine laboratory

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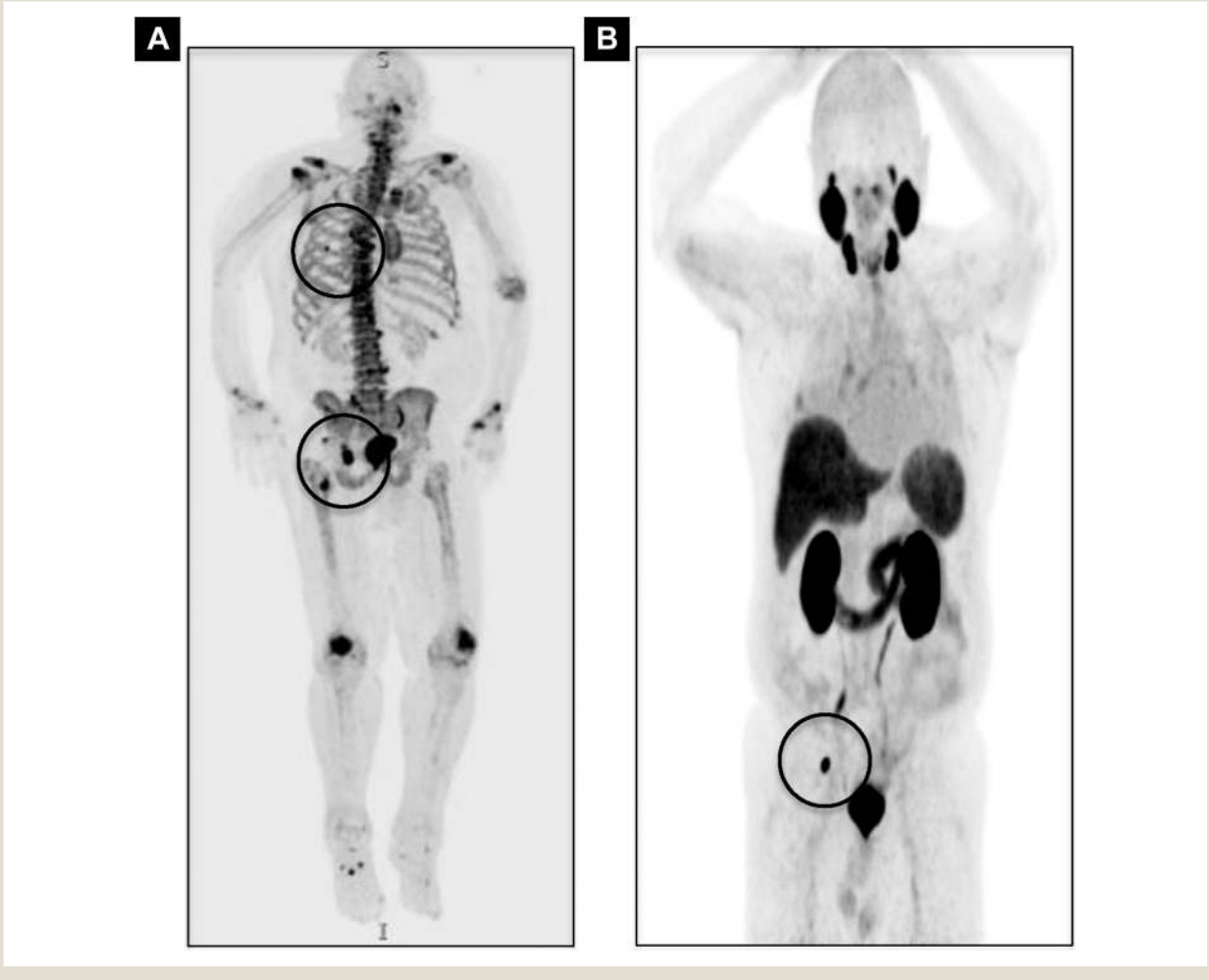
testing. He underwent an ultrasound-guided 12-core biopsy, which revealed Gleason 4 + 3 = 7 prostate adenocarcinoma with perineural invasion. He elected to undergo a radical prostatectomy with surgical pathology showing Gleason 4 + 5 = 9 adenocarcinoma with negative surgical margins and no metastases found in resected lymph nodes. One year after surgery, his PSA was measured at 2.9 ng/mL and continued to rise. The patient refused salvage radiation at the time. Magnetic resonance imaging of the abdomen and pelvis was negative for local recurrence and metastatic disease. ^{18}F NaF positron emission tomography (PET) demonstrated 2 small foci of increased radiotracer uptake in the anterolateral right fifth rib and right iliac bone, as well as intensely active lesions in the right acetabulum and proximal femur consistent with oligometastatic prostate cancer (Figure 1A).

The patient refused ADT as the standard-of-care treatment option for metastatic hormone-sensitive prostate cancer. He was seen in consultation by clinicians in radiation oncology, who offered SBRT to the 4 metastatic lesions. The patient was treated with 24 Gy over 3 fractions to the right femur/acetabulum and 15 Gy to each lesion in the right iliac wing and right fifth rib. Radiotherapy was completed without complication or toxicity. After 8 weeks, his PSA decreased from 6.22 to 2.6 ng/mL (Figure 2). Over the next several months, his PSA continued to decrease to a nadir of 0.24 ng/mL. After 18 months, his PSA began to rise. Repeat ^{18}F NaF and DCFPyL PET imaging demonstrated a 1.1 cm sclerotic lesion in the right iliac wing consistent with a radiographic relapse (Figure 1B). The patient wished to pursue additional SBRT, and his single metastasis was treated to 24 Gy. No toxicities were observed after treatment. Two months after completing radiotherapy, his PSA decreased from 3.7 to 1.23 ng/mL, which has remained stable after additional follow-up.

Discussion

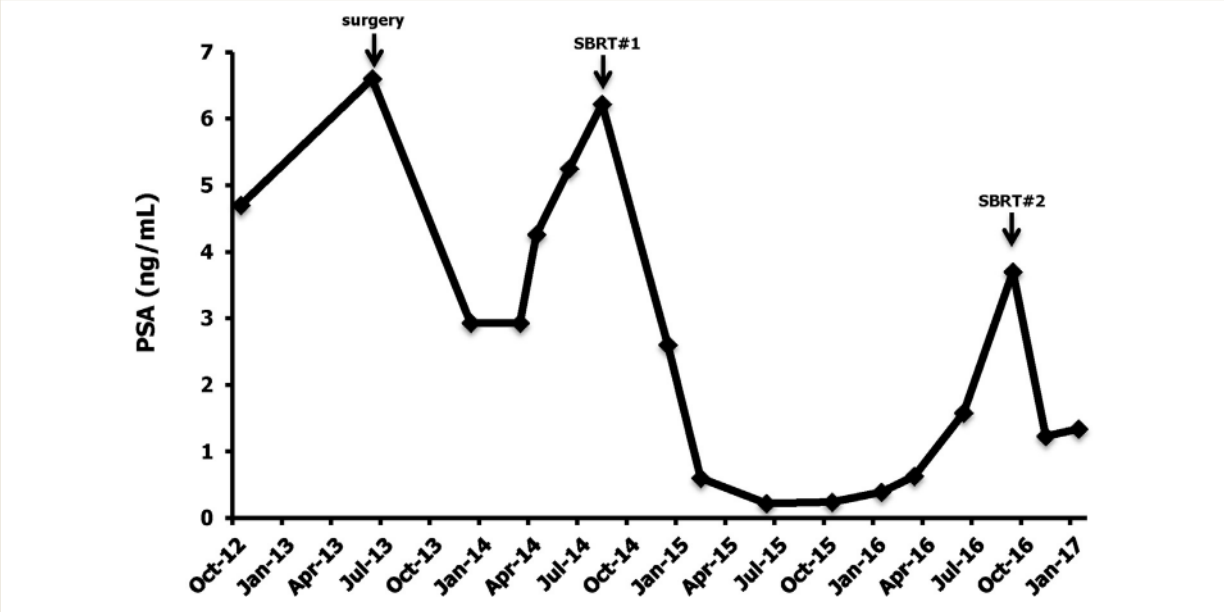
Until recently, the treatment paradigm for metastatic prostate cancer has focused on palliation. Conventional wisdom suggested

Figure 1 PET Imaging of Patient With Oligometastatic Prostate Cancer Before SBRT. (A) After Rising PSA Values, ^{18}F NaF PET Imaging Was Performed to Evaluate for Metastatic Disease. Metastatic Lesions Were Observed in Right Fifth Rib With 3 Additional Discrete Sites in Right Lower Pelvis and Right Proximal Femur (Circles). (B) DCFPyL PET Imaging Demonstrating Radiotracer Uptake in Right Iliac Crest (Circle)



Abbreviations: PET = positron emission tomography; PSA = prostate-specific antigen; SBRT = stereotactic body radiotherapy.

Figure 2 Trend of PSA Values After Surgery and SBRT in Patient With Oligometastatic Prostate Cancer. After Radical Prostatectomy, Serum PSA Values Remained Persistently Elevated and Began Rising Within 1 Year. Patient Was Treated With SBRT With Subsequent Decrease in Serum PSA. After 18 Months, Serum PSA Rose to 3.7 ng/mL Before Second Course of SBRT. After Radiotherapy, Serum PSA Values Remained Stable



Abbreviations: PSA = prostate-specific antigen; SBRT = stereotactic body radiotherapy.

that metastatic disease was incurable. This case illustrates that select patients with limited metastatic burden may benefit from local treatment with SBRT. Interestingly, the patient we describe remained asymptomatic with low PSA values in the absence of ADT, suggesting that any residual disease is indolent. Whereas certain localized prostate cancers can be followed with active surveillance/watchful waiting as a result of favorable biology, the same principle may hold true in the post-SBRT setting for oligometastatic disease. Prostate cancer has significant intratumor heterogeneity, with certain clones predisposed to metastasize.[7] Upon treatment of a metastatic deposit, the remaining disease may be followed with serial PSA testing and interval imaging, similar to the way patients with biochemically recurrent disease are treated. Systemic treatment may be significantly delayed.

Deferring systemic therapy in the form of ADT may have several advantages. First, by treating with radiation rather than ADT, the time to castration resistance may be delayed, potentially conferring a survival advantage.[8] SBRT has already been shown to improve progression-free survival in oligometastatic prostate cancer, suggesting that the time to ADT initiation would also be increased. Several potential ancillary benefits may also result from delaying systemic therapy. Avoiding ADT may reduce the incidence of cardiovascular disease in at-risk individuals.[9] After SBRT, this patient developed unstable angina, requiring percutaneous intervention with placement of a coronary stent. Foregoing or delaying ADT may prevent worsening of his underlying coronary artery disease. Quality of life after SBRT may also be improved without systemic therapy.[10] Both ADT and chemotherapy can be difficult to tolerate, resulting in significant toxicities and reduced quality of life. Further, early treatment with ADT may select for castration-resistant, aggressive prostate cancer. Within hormone-sensitive cancers, castration-resistant clones exist yet remain at a growth disadvantage.[11] In the setting of low testosterone, castration-resistant clones may be selected for and proliferate, which may theoretically worsen survival.[12] Thus, using radiation as a targeted therapy rather than ADT may slow the development of lethal prostate cancer.

Several areas of research in oligometastatic prostate are ongoing. Most importantly, prospective trials will determine whether there is an overall survival advantage to support the use of SBRT. The ORIOLE trial (NCT02680587) was recently opened to study time to progression in oligometastatic prostate cancer patients treated with SBRT versus observation. This case report provides anecdotal evidence of prolonged survival. Important questions remain, however. For example, the number of metastases that can be effectively treated and the anatomic sites most amenable to SBRT have yet to be established. A reasonable approach at this time is to utilize SBRT in those patients with a small number of metastases (4 or fewer) and easily accessible sites (ie, bone). Prospective studies are required to further characterize the respective roles of ADT and SBRT and the criteria by which to individualize therapy for patients with oligometastatic disease.

Conclusion

This case report supports the emerging evidence for oligometastatic prostate cancer as a distinct clinical state of disease and the effectiveness of SBRT in select patients.

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Disclosure

The authors have stated that they have no conflict of interest.

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