Prostate Cancer With Isolated Bony Metastasis: Sternal Struggle

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A 70-year-old man presented with lower urinary tract symptoms including nocturia and frequency. Digital rectal examination revealed a 3+ prostate with bilateral increased firmness with no nodules, concerning for malignancy. The prostate-specific antigen (PSA) was elevated at 80 µg/L. There was no bony pain and no constitutional symptoms.

Transrectal ultrasound-guided prostate biopsy was performed. Examination of the biopsy specimen revealed Gleason 9 (5 + 4) prostate adenocarcinoma involving 12 of 12 cores and 90% of prostatic tissue with evidence of perineural and periprostatic fat invasion.

Fig. 1. Total body bone scan demonstrating increased tracer uptake in the sternum. C6 vertebral body tracer uptake was found to be due to osteophytosis, and the remainder of tracer uptake was degenerative.

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Bone scan demonstrated a solitary bone metastasis in the sternum. Magnetic resonance imaging of the spine was ordered to characterize C6 vertebral body tracer uptake, determined to be osteophytosis. Other findings were degenerative. Computed tomography (CT) of the abdomen and pelvis did not demonstrate lymphadenopathy.

The patient was given hormone therapy with a GnRH agonist. After discussion with medical oncology, the patient was given docetaxel chemotherapy for 6 cycles, and no adverse events occurred. His PSA became undetectable (<0.1 μg/L) after chemotherapy, and ongoing hormone therapy was planned.

His urinary symptoms improved with medical management. A posttreatment bone scan demonstrated decreased but persistent tracer uptake in the sternum (Fig. 1). Repeated CT of the chest, abdomen, and pelvis demonstrated a 2.8 × 1.8 cm sclerotic metastasis in the sternum without other metastases (Fig. 2). He had mild sternal pain with coughing. His medical history was significant for hypertension, dyslipidemia, and type II diabetes without evidence of end-organ damage. A referral to radiation oncology was made. His performance status was excellent, and he was willing to consider all treatment options.

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This patient (1) presents with oligometastatic, Gleason 5 + 4 adenocarcinoma, with a presenting prostate-specific antigen level of 80 μg/L. On the basis of the biopsy extension into periprostatic fat, he has T3a disease. He has been treated initially with androgen deprivation therapy and docetaxel. On the basis of the STAMPEDE data, he can expect a median response duration of 3 years and survival of 6 years (2). He may, however, not achieve this having a high-grade tumor, which predicts for a shorter response to androgen deprivation therapy. He is 70 years old with limited comorbidities, which are unlikely to compromise his survival over the next 10 years.

The patient’s prostate-specific antigen level is currently undetectable, which will reflect his response to androgen ablation, and his performance status is excellent. The only abnormality is persistent uptake on isotope bone scan in the sternum, which may reflect osteoblastic healing rather than active tumor.

In this setting, I would offer the patient radical ablative radiation therapy. Local treatment to the sternum with a stereotactic or electron technique to minimize dose to the heart and lungs delivering 21 Gy in 3 fractions will achieve local control in >90% of cases (3). I would also treat the pelvis with high-dose radiation therapy. The patient’s risk of occult seminal vesicle and lymph node metastases is high, and improved failure-free survival has been demonstrated from nodal radiation therapy in patients with N+ disease (4). In high-risk disease, the combination of external beam radiation therapy and brachytherapy has a better outcome than external beam radiation therapy alone (5, 6). I would therefore offer radiation therapy to the prostate, seminal vesicles, and regional lymph nodes with intensity modulated radiation therapy delivering 46 Gy in 23 fractions, followed by high-dose-rate brachytherapy implanting the prostate, periprostatic tissues, and seminal vesicles delivering a boost of 15 Gy.

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References


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Prostate-Specific Membrane Antigen PET Before Aggressive Local Therapy to the Sternum

In the absence of major competing medical comorbidities, durable local control will be a significant issue during the projected lifetime of this man (1). In men who present with such high-volume and high-grade (group 5) prostate disease concurrently with lower urinary tract symptoms, insufficient control long term is often observed with medical management alone.

Therefore, after discussion at a multidisciplinary tumor board, I would recommend local treatment of the prostate alone with radiation therapy. A hypofractionated schedule of 55 Gy in 20 fractions to the prostate is likely to provide adequate palliation and is commonplace in Australia and
the United Kingdom. As the sternal disease is asymptomatic, however, I would first arrange functional imaging with positron emission tomography (PET) before entertaining a more aggressive treatment paradigm. PET with 68Ga-labeled prostate-specific membrane antigen (PSMA) is a highly promising imaging technique with higher sensitivity for metastatic disease than 18F-fluoromethylcholine PET (2). This would be the ideal choice for detection of additional disease that is occult on conventional radiographic modalities.

If the sternum truly had an isolated “oligometastasis” on PSMA-PET, then one could consider treating this with stereotactic body radiation therapy. Given the high-grade disease, worrisome PSA level elevation, and synchronous presentation with metastases, it is highly unlikely that this patient will have long-term disease control, and he must be fully informed prior to embarking on this treatment approach. Our institution has observed through a prospective clinical trial that a single fraction of 20 Gy is associated with local control rates >90% and minimal toxicity in patients with bony prostate oligometastases (3).

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References


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Intriguing, but Not the Right Setting

Stereotactic body radiation therapy (SBRT) offers an intriguing treatment option for men with oligometastatic prostate cancer. Several series document that treatment of bony and nodal targets is associated with high local control and minimal toxicity (1). The use of SBRT to defer treatment with androgen deprivation therapy (ADT) (median 28 months in reference [1]) suggests a significant quality of life benefit.

Retrospective population-based studies suggest improvements in disease-specific and overall survival with definitive prostatic management (surgery or radiation therapy) in metastatic disease; however, there is likely significant selection bias, with <5% of the presenting population treated (2). Randomized data are lacking.

Prostate SBRT is a convenient treatment approach for patients with metastatic disease but is unproven for high-risk disease, and concerns regarding potential gastrointestinal toxicity with inclusion of pelvic lymph nodes were noted in the only reported prospective series.

Our patient (3) has already been exposed to systemic chemotherapy and ongoing ADT; thus the ability to defer these treatments (and toxicities) has passed. In the absence of data showing a convincing benefit to treating the primary cancer in upfront oligometastatic disease (such as the ongoing study NCT01751438), we are concerned about potential toxicity in treating his significant primary disease. With his ongoing ADT (and expected excellent palliative benefit to conventional radiation), we also have no benchmark to assess the efficacy of SBRT in this patient once delivered. Had he presented with delayed and isolated sternal metastasis after primary management, we would have considered SBRT (30 Gy in 3 fractions). At present, we recommend ADT and conventional palliative radiation therapy if symptoms warrant.

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References


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Sternum First, Perhaps Pelvis Later

To consider the questions regarding further management and consideration of radiation therapy, additional patient history and evaluation may be appropriate including the following:

- History of urinary obstructive symptoms before and after systemic therapy with the International Prostate Symptom Score.
- Measurement of the serum testosterone level to document effective androgen deprivation and the castrate testosterone level.
- Measurement of chromogranin A levels. If incomplete response to androgen deprivation is observed, suspicion of the development of neuroendocrine dedifferentiation should be addressed. Chromogranin A levels may identify such dedifferentiation.
- Advanced positron emission tomography (PET) imaging as available that may include $^{11}$C or $^{18}$F choline, $^{68}$Ga prostate specific membrane antigen, $^{18}$F fluciclovine, or $^{11}$C acetate to determine if there is evidence of active nodal, visceral disease, or other sites of bone metastases. If other sites appear involved, then biopsy, if feasible, should be considered. In the context of an undetectable prostate-specific antigen level, active disease on PET and biopsy may confirm neuroendocrine dedifferentiation or a second malignancy. If further evidence of neuroendocrine dedifferentiation of prostate cancer is identified, then fluorodeoxyglucose PET may also be useful.

If all other workup findings are unremarkable and the clinical picture of an isolated symptomatic bone metastasis is confirmed, then delivering palliative radiation therapy consistent with updated American Society for Radiation Oncology guidelines would be recommended (1). At our institution, the preferred method would be to deliver stereotactic body radiation therapy (SBRT) to the sternum lesion with the patient being entered into a registry study or an ongoing phase 2 prospective trial for $^{11}$C choline PET—positive lesions (National Cancer Institute CA200551). While data are retrospective and limited, single-fraction SBRT with a minimum dose of 18 to 20 Gy is associated with high local control rates and favorable logistics. The discussion with the patient should acknowledge there is no high-level evidence of the superiority of SBRT over conventional external beam radiation therapy for pain control. To avoid unnecessary lung irradiation, one may consider delivery with proton irradiation if available and, if feasible, affordable and within the context of a prospective clinical trial or registry study.

If the patient (3) has demonstrated worsening urinary obstructive symptoms, there are retrospective data supporting the use of high-dose prostate radiation therapy to provide local control and prevent the development of urinary retention or worsening obstructive symptoms. While radiotherapeutic management of patients with oligometastatic disease is an active area of investigation (2), delivery of prophylactic radiation therapy to the primary and adjacent nodal sites outside the scope of a clinical trial would not be routinely recommended for such a patient at this point in time.

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References


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