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Case Report

MRI-Guided Adaptive Radiation Therapy for Oligometastatic Prostate Cancer Involving the Adrenal Gland: A Case Report and Literature Review

Fabian J. Bolte[a] Christopher K. Luminais[b] Matthew Mistro[b]
Michael E. Devitt[a]

[a]Division of Hematology and Oncology, Department of Medicine, University of Virginia Cancer Center, Charlottesville, VA, USA; [b]Department of Radiation Oncology, University of Virginia, Charlottesville, VA, USA

Keywords
Oligometastatic prostate cancer · Adrenal gland metastasis · Stereotactic body radiation therapy and adaptive radiation therapy

Abstract
Introduction: Metastasis-directed therapy is an evolving treatment modality for patients with oligometastatic prostate cancer. Although the microenvironment of the adrenal glands is enriched in androgen precursors, isolated adrenal metastases are rare. The application of stereotactic ablative radiotherapy (SBRT) to oligometastatic adrenal lesions has been limited due to toxicity concerns. ***Case Presentation:*** We report a patient with castration resistant prostate cancer and oligometastatic disease recurrence to the adrenal gland who underwent MRI-guided adaptive radiotherapy, which allowed accurate delivery of SBRT while minimizing exposure to adjacent radiosensitive organs. This approach was safe and resulted in long-term local and systemic disease control. ***Conclusion:*** This case highlights the potential role for MRI-guided SBRT in selected patients with oligometastatic prostate cancer to the adrenal glands.

Correspondence to:
Michael E. Devitt, med6m@uvahealth.org

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Introduction

Treatment options for patients with metastatic prostate cancer depend on individual patient characteristics and primarily include androgen deprivation therapy. Metastasis-directed therapy is an evolving treatment modality for patients with oligometastatic disease to lymph nodes and bones. Although the microenvironment of the adrenal glands is enriched in androgen precursors, adrenal metastases are rare with an overall incidence of 1% in a population-based analysis of 74,826 patients with metastatic prostate cancer [1, 2]. The application of stereotactic ablative radiotherapy to oligometastatic adrenal lesions has been limited due to toxicity concerns. Here we report a case of high-risk, castration-resistant prostate cancer and oligometastatic disease recurrence to the adrenal gland treated with MRI-guided SBRT. Additionally, we review and discuss the literature on the management of oligometastatic prostate cancer affecting the adrenal gland.

Case Presentation

The patient is a 70-year-old man who was initially diagnosed with localized prostate cancer. He opted to pursue radical prostatectomy with pelvic lymph node dissection in a curative intent. His final pathologic stage was AJCC 8th Edition Stage IIIC, pT3a, pN0 (0/25), cM0, Grade Group 5. His postoperative PSA levels remained undetectable until 12 months after surgery when his PSA increased to 0.21 confirmed on two separate occasions. His PSA course following radical prostatectomy is shown in Figure 1. The patient proceeded with salvage radiotherapy to the prostate bed (68 Gy in 34 fractions) in the absence of clinical evidence of metastatic disease. He was noted to have a rising PSA again 4 years after his surgery. A 18F-fluciclovine PET/CT showed a right middle lobe lung nodule measuring 0.8 cm with no abnormal uptake. A CT chest was repeated after 3 months in the setting of a rising PSA to 2.43 ng/mL and showed a spiculated right middle lobe nodule (shown in Fig. 2a) and a right middle lobe intrapulmonary lymph node (shown in Fig. 2b). At this time, an endobronchial ultrasound-guided biopsy of the lymph node was performed, and pathology was consistent with prostate adenocarcinoma. After multidisciplinary consultation, the patient opted to pursue an R middle lobe lobectomy. He recovered well from his surgery, and he was started on docetaxel and androgen deprivation therapy for metastatic castration-sensitive prostate cancer. Germline testing was performed and negative for inherited cancer syndromes. The patient received 6 cycles of docetaxel and continued androgen deprivation therapy. Approximately 6.5 years after his radical prostatectomy, he developed castration-resistant metastatic prostate cancer, with a slowly rising PSA to 0.4 ng/mL. At this time, his imaging was significant for an asymptomatic, indeterminate left adrenal nodule measuring 1.9 cm. He was started on abiraterone/prednisone and his PSA became undetectable for another 6 months. By 2023, the patient's PSA was rising to 3.3 ng/mL and abiraterone/prednisone was discontinued. Subsequent imaging showed an increase in the size of the left adrenal nodule to 3.7 cm × 3 cm (Fig. 2c, d). There were no further sites of metastasis identified including a normal bone scan. The patient was evaluated for further treatment options of his metastatic castration-resistant prostate cancer and elected to pursue with SBRT to his left adrenal gland. The gross tumor volume (GTV) was in close proximity (<10 mm) to the large bowel and noted to directly contact the stomach (shown in Fig. 3a–c), both of which are dose-limiting organs that prevent the safe administration of ablative SBRT doses. The dose constraints for organs at risks are summarized in online supplementary Table 1 (for all online suppl. material, see https://doi.org/10.1159/000545983). To deliver an ablative SBRT dose of 40 Gy in 5 fractions while minimizing toxicity to adjacent critical organs, the patient was treated with

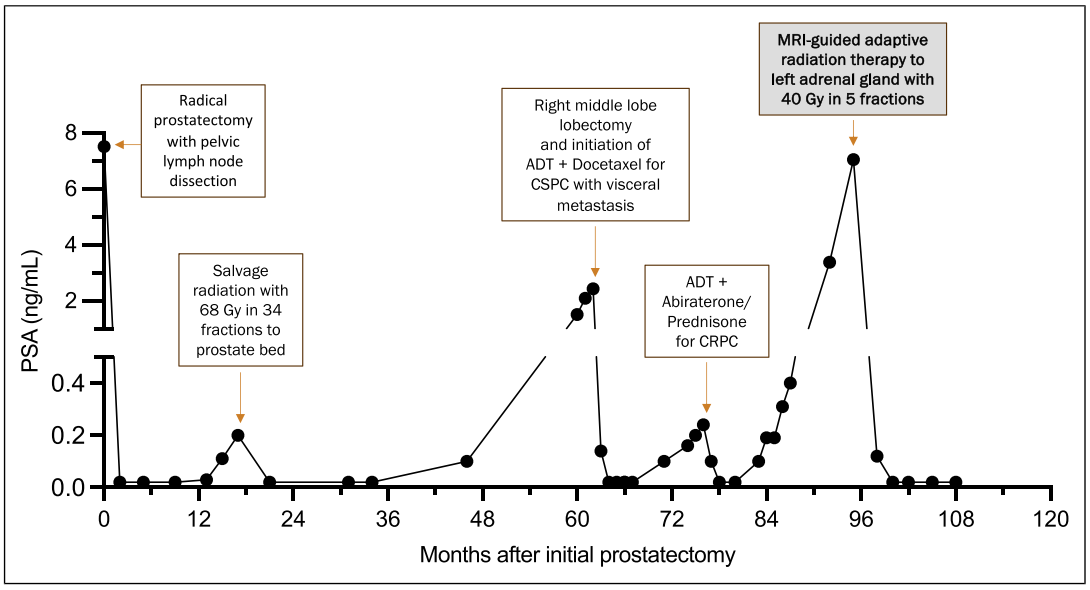

Fig. 1. PSA course following radical prostatectomy with a total follow-up of 8.5 years. ADT, androgen deprivation therapy; CSPC, castration-sensitive prostate cancer; CRPC, castration-resistant prostate cancer.

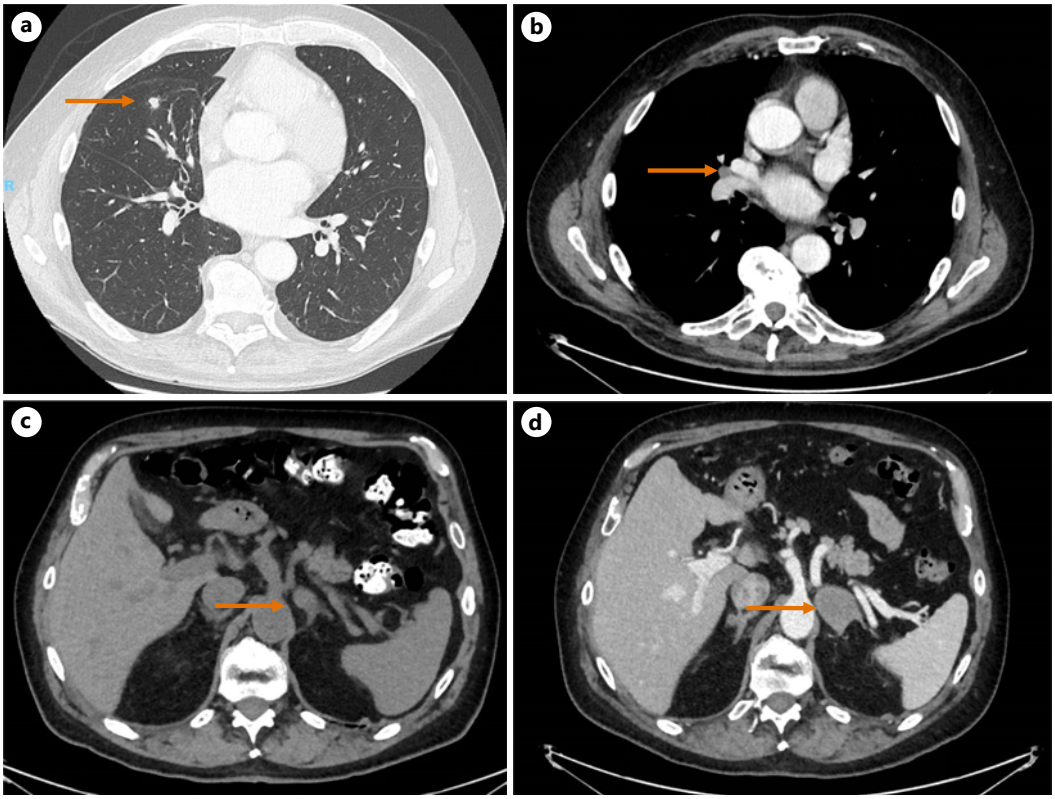

Fig. 2. Contrast-enhanced computed tomography scan showing a spiculated right middle lobe nodule measuring 0.9 cm (**a**, axial view) and a right middle lobe intrapulmonary lymph node (**b**, axial view). Computed tomography scan demonstrating interval growth of left adrenal mass from 1.9 cm (**c**, axial view) to 3.7 cm (**d**, axial view).

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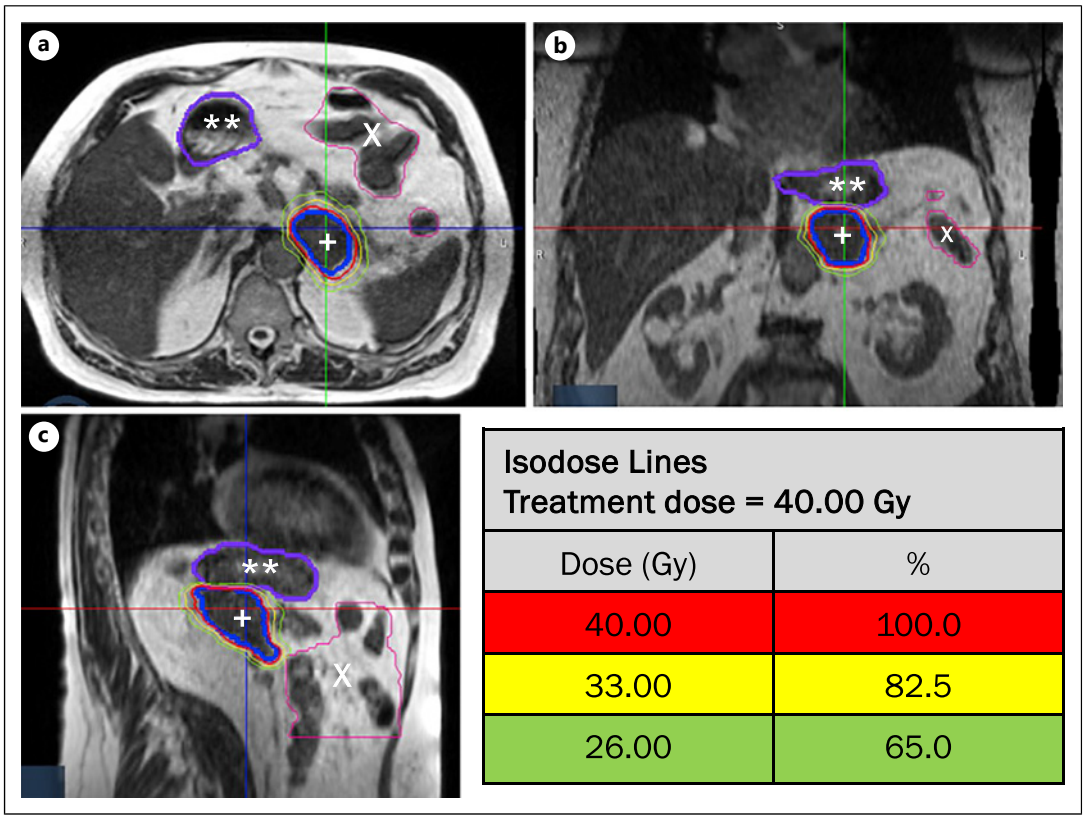

Fig. 3. a–c MRI-guided SBRT treatment plan. Blue lines (+) represent the GTV. Purple lines and asterisks (**) indicate the stomach, while the magenta line (X) represents the small and large intestines.

daily breath-hold MR image guidance on an MRI linear accelerator (ViewRay MRIdian system). On each treatment day, the base plan was applied to the new MR image using the sequence protocol from the initial planning (vendor-specific TRUFI sequence for 3D volumetric images with 5 mm × 1.5 mm in-plane resolution and 3 mm slice thickness), with updated contours in a 3 cm ring region around the GTV. A 3 mm isotropic margin around the GTV was generated daily for the planning target volume (PTV). The plan was re-optimized using an isotoxic approach, allowing reduced PTV coverage to ensure all gastrointestinal organs remained below a maximal dose of 38 Gy and 0.5 cc of each respective organ below 33 Gy. Table 1 summarizes the MRI-guided adaptive radiation therapy including PTV coverage and stomach dose constraints with the predicted and re-optimized plan. In fraction 2, the large bowel was significantly closer and the dose limiting structure, while all other fractions were adjusted to meet the dose-limiting constraint for the stomach. Treatment delivery was gated using 2D cine imaging (8 frames/s with 2.5 mm × 2.5 mm in-plane resolution and 7 mm slice thickness) to track the GTV, allowing movement within a fixed 3 mm boundary based on the tumor's position on daily MR imaging, with up to 5% outside the boundary. With this approach, the patient received an ablative dose of 40 Gy in 5 fractions, adhering to dose limits for all adjacent abdominal organs (shown in Fig. 3). Detailed information on the relationship between volume and dose for target structures and organs is shown in online supplementary Table 2. The therapy was well tolerated, with no acute or delayed adverse effects. The patient's PSA peaked at 7.04 ng/mL at the start of MRI-guided SBRT and became undetectable within 3 months. Imaging at 6 months after therapy revealed a significant decrease in the size of the left adrenal nodule from 3.7 cm × 3 cm to 2.2 cm × 1.7 cm. The patient is more than

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Table 1. Summary of MRI-guided adaptive radiation therapy including PTV coverage and stomach dose constraints with the predicted and re-optimized plan

Objective	Original plan	Plan type	Fraction 1	Fraction 2	Fraction 3	Fraction 4	Fraction 5
PTV V95%	92.8	Predicted	88.4	89.7	89.2	87.5	87.1
		Re-optimized	89.2	87.3	93.9	87.6	92.6
Stomach	0	Predicted	1.50	0.02	0	2.65	0.87
V38 Gy, cc		Re-optimized	0	0	0.03	0.03	0
Stomach	0.5	Predicted	3.99	0.64	1.88	4.64	2.94
V33 Gy, cc		Re-optimized	0.50	0.10	0.50	0.45	0.50

12 months out from his adaptive radiation therapy and clinically doing well on androgen deprivation therapy with undetectable PSA levels and no evidence of local or systemic disease progression. Adrenal testing showed normal serum cortisol levels. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material.

Discussion

A review of the literature revealed 10 cases of patients with oligometastatic prostate cancer to the adrenal glands (Table 2). Adrenal metastasis occurred predominantly unilaterally (8 out of 10 cases) and more frequently in patients with poorly differentiated, higher-grade prostate cancer (6 out of 10 cases with Gleason Group 5). The diagnostic workup included conventional imaging, PET imaging, as well as CT-guided biopsy to confirm metastatic disease of prostate origin. The management of oligometastatic disease to the adrenal glands varied significantly. Five patients with unilateral metastasis underwent surgery with adrenal gland resection. Two patients with bilateral adrenal metastases received 4 cycles of PSMA radioligand therapy. Two patients with unilateral adrenal metastasis were treated with systemic therapy and only 1 patient with unilateral adrenal metastasis was treated with radiotherapy. Most of the patients (9 out of 10 patients) achieved local disease control with varying times to systemic disease progression.

The long-term outcomes of metastasis-directed therapy in patients with prostate cancer from the pooled STOMP and ORIOLE trial demonstrated a significant improvement of median progression-free survival of 11.9 months with stereotactic ablative radiotherapy versus 5.9 months with observation [13]. The STOMP trial defined oligometastatic disease as 1–3 asymptomatic metastases after curative-intent therapy and enrolled 31 patients in the metastasis-directed therapy arm, with 18 (58.1%) having a single site of metastasis. However, only 1 patient had distant metastasis other than lymph nodes and bone [14]. The ORIOLE trial included 54 patients with recurrent prostate cancer and 1–3 asymptomatic metastasis involving only bone and lymph nodes [15]. Consequently, there is insufficient evidence to support the efficacy and safety of metastasis-directed therapy for oligometastatic prostate cancer isolated to the adrenal gland. The application of stereotactic ablative radiotherapy to adrenal gland metastasis has been limited by toxicity concerns. The SABR-COMET trial on stereotactic ablative radiotherapy to oligometastatic cancers included patients with prostate cancer and reported 3 treatment-related deaths due to serious toxicities [16]. Thus, the application of metastasis-directed therapy requires a careful balance between therapeutic efficacy and toxicity. Our case highlights the potential role for MRI-guided SBRT in selected

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Table 2. Reported cases of prostate cancer and oligometastatic disease solely to the adrenal glands

Initial diagnosis	Treatment modality	Treatment response	Ref.
67-Year-old man with metastatic CRPC, Gleason score 9 (4+5), iPSA 647 ng/mL, and bilateral adrenal metastasis	4 cycles of PSMA radioligand therapy	Reduction in volume and PSMA uptake of adrenal metastasis; no disease progression by 3 months of follow-up; no evidence of adrenal insufficiency	[3]
66-Year-old man with CRPC, iPSA 61.9 ng/mL, and bilateral adrenal metastasis	4 cycles of PSMA radioligand therapy	Reduction in volume and PSMA uptake of adrenal metastasis; no disease progression by 6 months of follow-up	[4]
39-Year-old man with prostate cancer, Gleason score 9 (5+4), iPSA 40 ng/Ml, and unilateral adrenal metastasis	Adrenal resection complicated by local infiltration of surrounding structures	Disease progression 6 weeks after surgery due to incomplete resection	[5]
71-Year-old man with prostate cancer, Gleason score 10 (5+5), iPSA 23 ng/mL with metastatic recurrence and unilateral adrenal metastasis	Adrenal resection	Reduction in serum PSA; no further follow-up reported	[6]
79-Year-old man with prostate cancer, Gleason score 9 (4+5) s/p EBRT to prostate with metastatic recurrence and unilateral adrenal metastasis	Adrenal resection	Reduction in serum PSA followed by systemic disease progression at 12 months of follow-up requiring treatment intensification	[7]
69-Year-old man with prostate cancer, Gleason score 8 (3+5), iPSA 459.6 s/p EBRT to prostate and pelvic lymph nodes with metastatic recurrence and unilateral adrenal metastasis	Adrenal resection	Reduction in serum PSA and undetectable PSA levels by 15 months of follow-up	[8]
64-Year-old man with metastatic CSPC, iPSA 1,020 ng/mL, and unilateral adrenal metastasis	Adrenal resection and adjuvant chemotherapy with vinblastine and estramustine	Reduction in serum PSA and no disease progression by 12 months of follow-up	[9]
64-Year-old man with metastatic CRPC, Gleason score 8 (4+4), iPSA 98.6 ng/mL, and unilateral adrenal metastasis	Real-time tracking radiotherapy (6 Gy in 8 fractions)	Reduction in serum PSA and disease progression 8 months after radiotherapy	[10]
65-Year-old man with prostate cancer, s/p radical prostatectomy and pelvic lymph node dissection, Gleason score 9 (4+5), iPSA 387, and metastatic recurrence to bilateral adrenal glands	ADT + docetaxel chemotherapy	Reduction in serum PSA and size of adrenal metastasis on imaging by 9 months of follow-up	[11]
68-Year-old man with prostate cancer, Gleason score 9 (4+5) s/p radical prostatectomy with metastatic recurrence and unilateral adrenal metastasis	Systemic therapy not otherwise specified	Reduction in serum PSA; no further follow-up reported	[12]

ADT, androgen deprivation therapy; CSPC, castration-sensitive prostate cancer; CRPC, castration-resistant prostate cancer; iPSA, initial prostate-specific antigen; EBRT, external beam radiation therapy.

patients with oligometastatic prostate cancer to the adrenal glands. A radiation dose of 40 Gy in 5 fractions was selected based on its established effectiveness as an ablative dose both for the prostate and prostate cancer metastases, as demonstrated in the PACE-B trial (Prostate SBRT trial using 40 Gy in 5 fractions) and ORIOLE trial [15, 17]. The key advantage of MRI-guided SBRT was its ability to provide real-time, high-resolution imaging of soft tissues during treatment, real-time tumor tracking, and daily treatment plan adaptation to account for observed anatomical changes. Together these abilities allowed accurate delivery of ablative doses of SBRT while minimizing exposure to adjacent radiosensitive organs including the stomach, duodenum, the small and large intestines, which would not have been feasible using standard CT-guided c-arm linac [18, 19].

In conclusion, isolated adrenal metastases in prostate cancer are rare. Diagnosis requires careful correlation with the patient's history, serum PSA level, and imaging findings to distinguish them from primary adrenal tumors in the absence of a biopsy. Metastasis-directed therapy with MRI-guided SBRT can be considered in selected patients with adrenal metastasis to achieve long-term disease control. This study is inherently limited by its case report nature and conclusions may not be applicable to larger patient populations. Further prospective studies for oligometastatic prostate cancer are required to determine the role of MRI-guided SBRT in a larger and more diverse patient population with different sites of oligometastatic disease.

Statement of Ethics

This study was reviewed by the Institutional Review Board for Health Sciences Research (IRB-HSR) at the University of Virginia and has been granted exemption from requiring ethics approval. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

F.J.B. reviewed the patient's case, performed a literature review, and wrote the manuscript. F.J.B., C.K.L., and M.E.D. contributed to the data collection, editing of the manuscript, and review of the literature. C.K.L. and M.M. provided information on planning of adaptive MRI-guided radiation therapy and contributed to editing and reviewing of the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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