Complete biochemical response following metastasis-directed radiotherapy for oligometastatic prostate cancer: A case report

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ABSTRACT

Localized treatment has recently become an option for treating oligometastatic prostate cancer. Metastasis-directed therapy (MDT) is a new approach for localized treatment, and many clinical trials are ongoing. In the present case, biochemical recurrence occurred 8 months after a radical prostatectomy for localized prostate cancer, and oligometastases were diagnosed via whole-body magnetic resonance imaging. Metastasis-directed radiotherapy (MDRT) was performed on all oligometastatic sites. After MDRT without androgen deprivation therapy, the prostate-specific antigen (PSA) decreased to an undetectable level and did not increase for 24 months.

Introduction

Treatment for men with metastatic prostate cancer (PCa) remains mainly systemic with androgen deprivation therapy (ADT) alone. The STAMPEDE trial showed that prostate radiotherapy improved survival for men with low metastatic burdens of PCa. Oligometastases that cannot be diagnosed by conventional imaging methods, such as computed tomography (CT) and bone scintigraphy (BS), can often be diagnosed via next-generation imaging, especially in patients with biochemical recurrence (BCR) after a prostatectomy. A prospective randomized phase II study comparing metastasis-directed therapy (MDT) to surveillance for oligometastatic PCa after primary treatment with next-generation imaging (NGI) demonstrated that survival without ADT but with MDT was longer than survival with surveillance alone. Here, we report a case of a patient with oligometastatic PCa for whom metastasis-directed radiotherapy (MDRT) after a prostatectomy was highly effective.

Case presentation

A 76-year-old man with PCa (cT2bN0M0, Gleason score: 4 + 4 = 8, and initial prostate-specific antigen [PSA]: 10.7 ng/ml) underwent a robot-assisted laparoscopic radical prostatectomy (RARP). The final pathology was pT3bN0, with a Gleason score of 4 + 5 = 9 and negative resection margins. The postoperative PSA nadir was 0.11 ng/ml. The PSA gradually increased to 0.25 ng/ml after 8 months, and BCR was diagnosed. Salvage radiotherapy (64.8 Gy) was performed at the prostatic fossa. One month later, the PSA decreased by 24% but gradually increased thereafter. CT and BS were performed when the PSA was >1 ng/ml without inducing ADT, but no metastasis was observed. Whole-body magnetic resonance imaging (wbMRI) was performed and showed metastases of the eighth thoracic and second and fourth lumbar vertebrae and the sternum (Fig. 1). MDRT (2.5 Gy x 14 = 35 Gy) was administered to all metastatic sites with PSA levels of 1.58 ng/ml (Fig. 2). After 6 months of MDRT, the PSA levels decreased to <0.008 ng/ml, with no PSA elevation or imaging progression occurring for 24 months afterward.

Discussion

Hellman et al. first proposed the concept of an oligometastatic state as an intermediate state (≤5 metastases) between localized primary and polymetastatic cancers, with no restrictions on primary lesions. The concept of oligorecurrence was defined as the state in which cancer patients have ≤5 metastatic or recurrent lesions with controlled primary lesions. By those definitions, our patient with oligometastasis after RARP and salvage radiotherapy to the prostatic fossa may have experienced oligorecurrence. However, the reason our patient could not be diagnosed with simultaneous oligometastases may have been because no wbMRI was performed before the RARP.

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Diagnosing oligometastases largely depends on the imaging modality. Conventional imaging methods, such as CT and BS, have limited roles in detecting local recurrence or distant metastases in patients with BCR. Evidence shows that NGI is more sensitive and specific than are CT and BS for detecting metastatic disease. The most promising NGI is prostate-specific membrane antigen positron-emission tomography (PSMA PET). A systematic review of $^{68}$Ga-PSMA PET, which included 37 articles with 4790 patients, showed that $^{68}$Ga-PSMA PET improved detection of metastases with BCR at low pre-PET PSA levels of $>$0.2 ng/ml (33%) and 0.2–0.5 ng/ml (45%). Compared with other imaging methods, PSMA PET has high diagnostic accuracy, especially in patients with low PSA values. Unfortunately, PSMA PET has not yet been approved in Japan. However, owing to recent technical improvements in MRI scanners and development of sequences with faster temporal resolution, the whole body can be scanned with MRI within a reasonable time to detect metastases in diseased bone and soft tissues, including the lymph nodes. Robertson et al. reported whole-body studies combining multiparametric prostate MRI and wbMRI for patients with BCR after a prostatectomy. Even in patients with very low PSA levels (median 0.36 ng/ml), disease recurrence was identified in the prostatic bed, lymph...
nodes, and bones in 21% of patients. The American Society of Clinical Oncology provides a guideline for optimum imaging strategies for advanced prostate cancer. In this guideline, when considering local salvage treatment for elevated PSA after a prostatectomy, NGI methods, such as wbMRI or PSMA PET, should be performed if the conventional imaging diagnosis is negative.

In accordance with Hellman et al., targeting oligometastases via MDT might prevent further spread of the metastases and improve survival. Several retrospective studies reported that MDT delayed the start of ADT and its related side effects due to clinical disease progression. The STOMP trial is the only completed multicenter, randomized, phase II study that compared MDT to surveillance in oligometastatic prostate cancer patients after primary treatment. Patients who received MDT experienced longer ADT-free survival than did those who underwent surveillance alone (median 21 versus 13 months, respectively). Furthermore, three of four patients in the interventional arm experienced a PSA response with an excellent safety profile (no grade 2 or higher toxicity).

One limitation in our case is that the oligometastatic sites were not biopsy-confirmed. However, the clinical course showed clear oligometastases, and MDRT was successful. Although the mechanism of the success of MDRT for treating oligometastatic disease, a systemic disease, is difficult to explain, we believe that the abscopal effect, i.e., radiation-induced shrinkage of distant untreated lesions, is involved in addition to the local effect.

Conclusion

This case suggests that treatment with MDRT may benefit select patients with oligometastatic PCa after primary treatment. With further development of diagnostic imaging and ongoing clinical trials, we hope that MDT will become a standard treatment for oligometastatic PCa.

Declaration of competing interest

There are no conflicts of interest or funding to report.

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