Case Report

A patient with oligometastatic hormone-sensitive prostate cancer who achieved long-term progression-free survival following cytoreductive radical prostatectomy and metastasectomy

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Abbreviations & Acronyms
ADT = androgen deprivation therapy
CAB = combined androgen blockade
cRP = cytoreductive radical prostatectomy
CRPC = castration-resistant prostate cancer
CT = computed tomography
FDG-PET = fluorodeoxyglucose-positron emission tomography
MRI = magnetic resonance imaging
omPCa = oligometastatic prostate cancer
PCa = prostate cancer
PSA = prostate-specific antigen
Th7 = seventh thoracic vertebra

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How to cite this article: Mamiya D, Kijima T, Takada-Owada A *et al*. A patient with oligometastatic hormone-sensitive prostate cancer who achieved long-term progression-free survival following cytoreductive radical prostatectomy and metastasectomy. *IJU Case Rep*. 2024; 7: 165–168.

Received 30 November 2023; accepted 14 January 2024.
Online publication 29 January 2024

Introduction: Oligometastatic prostate cancer can be well-controlled through combined local and metastasis-directed therapies. However, the effects of cytoreductive radical prostatectomy and metastasectomy remain unclear.

Case presentation: A 52-year-old man presented with prostate cancer and isolated bone metastasis to the thoracic spine. Six months after neoadjuvant hormonal therapy, the patient underwent cytoreductive radical prostatectomy and total en bloc spondylectomy. The postoperative course was uneventful. Hormonal therapy was terminated 5 years after surgery, and no biochemical or radiological progression was observed at 7 years postoperatively.

Conclusion: Although careful patient selection is necessary, cytoreductive radical prostatectomy and metastasectomy are effective treatments for well-selected patients with oligometastatic prostate cancer.

Key words: cytoreductive surgery, metastasectomy, oligometastasis, progression-free survival, prostate cancer.

Keynote message

Long-term control of oligometastatic prostate cancer can be achieved through appropriate treatment targeting primary and metastatic lesions. Cytoreductive radical prostatectomy for oligometastatic prostate cancer is feasible and can improve survival and reduce local symptoms. Metastasis-directed therapy for oligometastatic prostate cancer often involves stereotactic ablative radiotherapy; however, metastasectomy may be performed for selected cases.

Introduction

omPCa is characterized by a low metastatic burden within a specific location. Oligometastasis, initially proposed in 1995,[1] is a condition that may be cured through combined surgery and radiotherapy of both primary and metastatic lesions. As evidenced by whole-genome sequencing data of patients with PCa, cross-talk between metastatic foci exists and may lead to the emergence of new metastatic lesions.[2] Furthermore, the primary tumor secretes compounds that support tumor cell proliferation at distant sites, leading to overt metastases.[3] Additionally, tumor self-seeding can lead to colonization and priming of circulating tumor cells at the primary organ.[4] Targeting primary and oligometastatic lesions is performed based on the hypothesis that excision and/or irradiation of these lesions could prevent the aforementioned vicious cycles. Therefore, primary radiation therapy has become a standard treatment for omPCa.[5] We report a case of omPCa with a single metastasis to the vertebral bone in a patient who achieved long-term progression-free survival after cRP and total en bloc spondylectomy.[6]

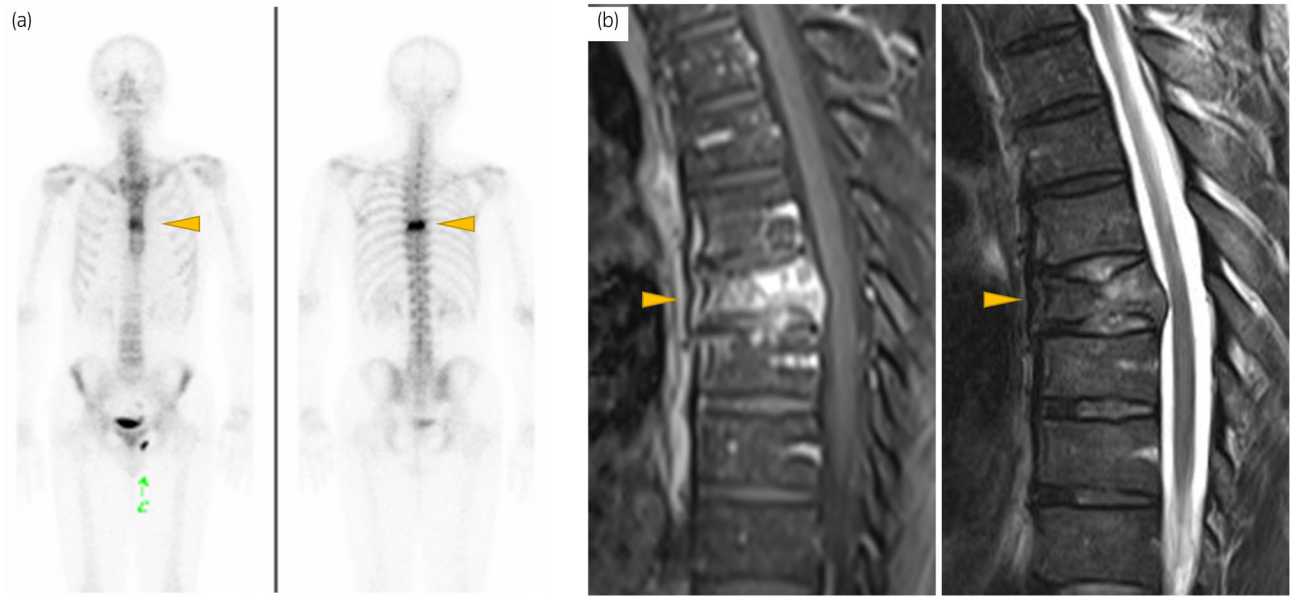

Fig. 1 (a) Bone scintigraphy image revealing isolated bone metastasis to the Th7 vertebral body. (b) T1-weighted (left) and T2-weighted (right) MRI images showing isolated bone metastasis to the Th7 vertebral body.

Case presentation

A 52-year-old man with no medical or family history of cancer presented with a high PSA level (37.4 ng/mL). A prostate biopsy revealed PCa with a 4 + 4 Gleason score. CT did not detect any obvious lymph node or visceral metastases. Bone scintigraphy revealed accumulation in the (Fig. 1a) that was confirmed by MRI as a bone metastasis (Fig. 1b). Although the patient experienced pain at the metastatic site, neurological symptoms were not observed.

Based on the omPCa diagnosis (clinical stage T2aN0M1b), CAB therapy with degarelix and bicalutamide was initiated. The PSA level decreased favorably to 0.112 ng/mL at 3 months and 0.022 ng/mL at 6 months. Six months after CAB therapy, MRI revealed no reduction in the Th7 metastasis; however, the compression fracture progressed slightly. Conversely, 18F-FDG-PET/CT and whole-body MRI revealed no new metastatic lesions.

Because the patient had a good initial PSA response to CAB therapy, limited metastatic volume, good performance status, and long life expectancy, aggressive treatment targeting both primary and metastatic lesions was performed. For the Th7 metastasis, total en bloc spondylectomy was planned because of compression fracture progression and because the lesion was confined to a single vertebral body amenable to complete resection.

Seven months after CAB therapy, a robot-assisted radical prostatectomy was performed. The pathological diagnosis was PCa with a 4 + 4 Gleason score (treatment effect grade 0b), pathological stage T3aN0, and negative resection margins (Fig. 2a). Total en bloc spondylectomy was performed 9 months after CAB therapy. After Th7 removal, a titanium mesh was inserted with autogenous bone transplantation, followed by posterior fixation from Th5 to Th9. The pathological diagnosis was tubular adenocarcinoma with a 3 + 3 Gleason score (treatment effect grade 0b) in the bone marrow throughout the vertebral body with negative surgical margins (Fig. 2b,c). No postoperative complications occurred, and the patient returned to performing activities of daily living at 1 month postoperatively.

CAB therapy was continued, and the patient underwent regular CT, MRI, and FDG-PET/CT examinations during follow-up. The PSA level remained undetectable, and imaging studies revealed no recurrence. CAB therapy was discontinued at 5 years postoperatively, and the serum testosterone level returned to the eugonadal level (2.45 ng/mL) 6 months thereafter. After testosterone recovery, the PSA level remained undetectable. No recurrence was observed 7 years postoperatively.

Discussion

Our patient achieved long-term progression-free survival after cRP and vertebral bone metastasectomy. He remained biochemically progression-free even after ADT termination, suggesting that aggressive treatment of local and metastatic lesions may be curative or provide long-term disease control.

Currently, there is no standard definition of omPCa. However, omPCa generally refers to a limited number of metastases (≤3) to the bones and/or lymph nodes, but not to visceral organs; this is because visceral metastases are associated with a significantly worse prognosis.[7] The bone metastasis location may affect the omPCa prognosis. One study reported that a solitary metastasis and limited extension to metastatic sites (limited to the axial skeleton and lymph nodes) were associated with a better prognosis for patients with metastatic PCa treated with hormone and metastasis-directed therapies.[8] Accordingly, this case was a good candidate for aggressive local and metastasis-directed therapies.

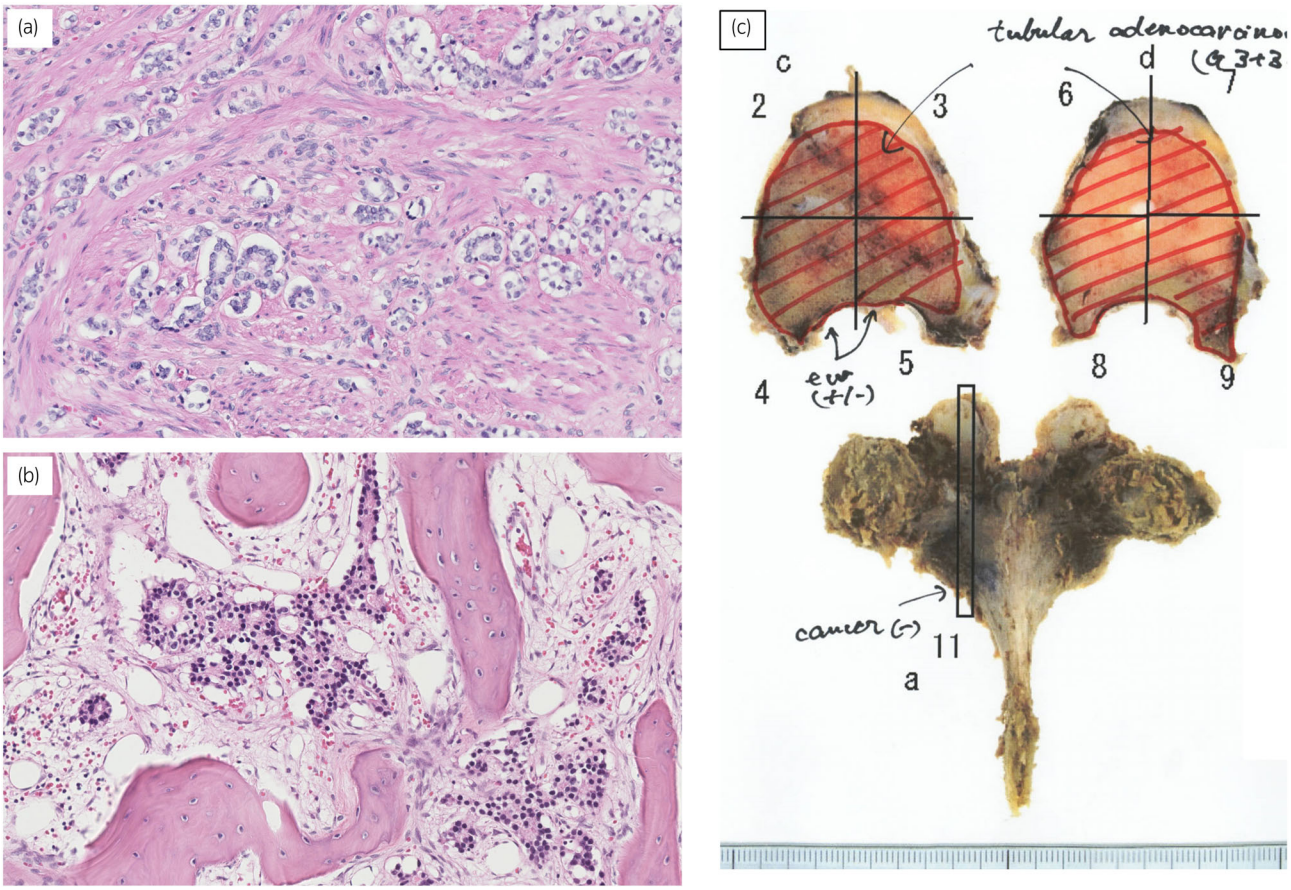

Fig. 2 (a) Histopathological findings of the prostate (200-fold) indicating adenocarcinoma with a Gleason score of 4 + 4. (b) Histopathological findings of the Th7 vertebral body (200-fold) indicating adenocarcinoma with a Gleason score of 3 + 3 in the bone marrow. (c) Macroscopic view of the Th7 specimen indicates that the entire vertebral body is engulfed by the tumor.

For de novo low-volume metastatic PCa, radiation therapy of the primary organ is one treatment option.[5] Evidence of the success of cRP for omPCa has been limited to retrospective and small prospective studies, which have consistently reported improved survival of patients who have undergone cRP. One study reported that patients who underwent cRP achieved significantly better CRPC-free survival than those who received ADT alone (40 *vs* 29 months).[9] Another study reported better CRPC-free survival of patients in the cRP arm compared with that of patients in the ADT arm (53 *vs* 21 months).[10] Reduction in the local tumor burden by cRP is expected to improve the prognosis and local symptoms. Several studies have reported that patients who underwent cRP experienced fewer local complications than those who received ADT.[11] Another important issue regarding cRP is perioperative morbidity. Several studies have shown that cRP is technically feasible for omPCa.[12] To determine the efficacy and feasibility of cRP for omPCa, it is necessary to evaluate the results of ongoing randomized clinical trials.

Metastasis-directed therapy for omPCa primarily comprises stereotactic ablative radiotherapy; however, resection of non-nodal metastases with omPCa has been studied. One study of patients with omPCa who underwent surgical metastasectomy for skeletal or visceral lesions reported that 65% (11/17) experienced a PSA level decline of at least 70%, and that two-thirds of patients who experienced recurrence had oligometastatic recurrence amenable to repeat metastasis-directed therapy.[13]

Our patient underwent total en bloc spondylectomy[6] for a solitary metastasis to Th7. This procedure was designed to achieve complete oncological en bloc tumor resection including main and satellite microlesions in the vertebral compartment. Treatment for spinal metastases ranges from en bloc spondylectomy to palliative radiation; therefore, the treatment strategy should be carefully determined. Fisher *et al.*[14] advocated the spine instability neoplastic score, which is used to objectively evaluate the stability of spinal metastasis. The total score of our patient was 11 (intermediate instability) because of the semi-rigid location (score 1), pain (score 3), mixed bone lesion (score 1), normal alignment (score 0), more than 50% collapse (score 3), and bilateral involvement (score 3). Other studies have proposed scoring models to determine the prognosis of patients with spinal metastases to guide treatment. Based on the models of Tomita *et al.*,[15] Tokuhashi *et al.*,[16] and Katagiri *et al.*,[17] our patient had the best possible score, indicating a good long-term prognosis; therefore, excisional surgery was recommended. Importantly, treatment decisions should be based on discussions among

urologists, orthopedic surgeons, and radiation therapists. Furthermore, not only spine stability and the prognosis but also neurologic symptoms, pain, and patient preferences should be considered.

Surgical treatment of primary and metastatic lesions contributes to long-term progression-free survival, as shown by this case. Although careful discussions and patient selection are necessary, cRP and metastasectomy are effective treatments for well-selected patients with omPCa.

Acknowledgments

None.

Author contributions

Daisuke Mamiya: Writing – original draft. Toshiki Kijima: Conceptualization; writing – original draft; writing – review and editing. Atsuko Takada-Owada: Investigation. Hidetoshi Kokubun: Data curation. Toshitaka Uematsu: Data curation. Kohei Takei: Data curation. Tsunehito Kambara: Conceptualization. Kazuyuki Ishida: Investigation; supervision. Hiroshi Taneichi: Conceptualization; supervision. Takao Kamai: Conceptualization; supervision; writing – review and editing.

Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an Institutional Reviewer Board

Not applicable.

Informed consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images.

Registry and Registration No. of the study/trial

Not applicable.

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