Case Report

A case of repeat oligoprogressive castration-resistant prostate cancer treated with pulmonary metastasectomy

Takahiko Soma,[1] Soichiro Yoshida,[1] Ryo Wakejima,[2] Towako Taguchi,[3] Shohei Fukuda,[1] Hajime Tanaka,[1] Minato Yokoyama,[1] Kenichi Ohashi,[4] Kenichi Okubo[2] and Yasuhisa Fujii[1]

Departments of [1]Urology, [2]Thoracic Surgery, [3]Comprehensive Pathology, and [4]Human Pathology, Tokyo Medical and Dental University, Tokyo, Japan

Abbreviations & Acronyms
CRPC = castration-resistant prostate cancer
DTX = docetaxel
Enz = enzalutamide
EORTC = European Organization for Research and Treatment of Cancer
ESTRO = European Society for Radiotherapy and Oncology
GG = Grade Group
IMRT = intensity-modulated radiation therapy
LH-RH = luteinizing hormone–releasing hormone
OP-CPRC = oligoprogressive castration-resistant prostate cancer
PSA = prostate-specific antigen
PSDT = progressive site-directed therapy
RP = radical prostatectomy
VATS = video-assisted thoracic surgery
WB-DWI = whole-body diffusion-weighted imaging

Correspondence: Soichiro Yoshida M.D., Ph.D., Department of Urology, Tokyo Medical and Dental University, 1-5-45, Yushima, Bunkyo-ku, Tokyo 113-8510, Japan. Email: s-yoshida.uro@tmd.ac.jp

How to cite this article: Soma T, Yoshida S, Wakejima R *et al*. A case of repeat oligoprogressive castration-resistant prostate cancer treated with pulmonary metastasectomy. *IJU Case Rep*. 2023; 6: 216–218.

Received 14 November 2022; accepted 29 March 2023.
Online publication 17 April 2023

Introduction: Several retrospective studies have demonstrated the efficacy of progressive site-directed therapy for oligoprogressive castration-resistant prostate cancer. However, eligible patients for progressive site-directed therapy in these studies were limited to oligoprogressive castration-resistant prostate cancer with bone or lymph node metastases without visceral metastases, and little is known about the efficacy of progressive site-directed therapy for oligoprogressive castration-resistant prostate cancer with visceral metastases.

Case presentation: We report a case with castration-resistant prostate cancer previously treated with enzalutamide and docetaxel, in which only a solitary lung metastasis was identified throughout the course of treatment. The patient underwent thoracoscopic pulmonary metastasectomy with a diagnosis of repeat oligoprogressive castration-resistant prostate cancer. Only androgen deprivation therapy was continued and his prostate-specific antigen levels remained undetectable for 9 months after surgery.

Conclusion: Our case suggests that progressive site-directed therapy may be effective for carefully selected repeat OP-CRPC with a lung metastasis.

Key words: CRPC, metastasectomy, oligometastatic disease, progression site-directed therapy.

Keynote message

The efficacy of PSDT for OP-CRPC was reported retrospectively, but these studies mainly targeted lymph node or bone metastases. We reported a case of OP-CRPC with a single lung metastasis that was treated by pulmonary metastasectomy and achieved favorable PSA response. Our case suggests that PSDT may be effective for carefully selected OP-CRPC with a lung metastasis.

Introduction

In 1995, Hellman and Weichselbaum introduced the concept of oligometastatic cancer[1] to describe a condition with metastatic sites that are limited in number and location. The benefits of prolonged survival and delay of systemic therapy by metastases-directing therapy have been suggested. In castration-sensitive oligometastatic prostate cancer, several prospective studies have shown survival benefits from targeted radiotherapy to metastatic lesions.[2,3] No prospective studies have demonstrated the efficacy of PSDT for OP-CPRC, defined as CPRC with only a limited number of lesions progressing. Although several retrospective studies have demonstrated the efficacy of PSDT in indices assessed by PSA, eligible patients for PSDT in these studies were limited to OP-CRPC with bone or lymph node metastases without visceral metastases, and little is known about the efficacy of PSDT for OP-CRPC with visceral metastases.[4–7]

In 2020, the EORTC and ESTRO OligoCare project proposed a comprehensive system to characterize and classify oligometastatic cancer based on its clinical course.[8] In this classification, OP-CRPC was divided into genuine OP-CRPC, which has never been a polymetastatic

disease throughout its course, and induced OP-CRPC, which is a polymetastatic disease but has only limited progressing foci resistant to systemic therapy. This classification may reflect the biological characteristics of oligometastatic disease, and PSDT has been found to be more effective in genuine OP-CRPC compared with induced OP-CRPC.[9] Genuine OP-CRPC can be classified into *de novo* OP-CRPC with an initial diagnosis of oligometastasis and repeat OP-CRPC with a previous diagnosis of oligometastatic disease.

Here, we report a case of repeat OP-CRPC that achieved an undetectable PSA level for 9 months after partial lung resection of a solitary lung metastasis.

Case report

A 67-year-old male visited his previous doctor for a PSA level of 4.78 ng/mL. He underwent prostate biopsy and was diagnosed with prostate cancer with GG 3. Under a diagnosis of having no metastasis on imaging, he underwent radical prostatectomy in February 2011 (Fig. 1). Pathological examination revealed adenocarcinoma with GG 4, extracapsular extension, and positive resection margins. Postoperative PSA nadir was 0.11 ng/mL. Three months postoperatively, the patient was diagnosed with a biochemical recurrence. When he was referred to our hospital in March 2012, his PSA had increased to 1.07 ng/mL. Salvage radiotherapy with 66 Gy to the prostate bed was performed as of April 2012. PSA response was achieved and the PSA nadir was 0.09 ng/mL at 4 months after radiotherapy.

In October 2015, a solitary lung metastasis appeared in the right lung on WB-DWI (Fig. 1a), and luteinizing hormone–releasing hormone agonist monotherapy was started. Although remission of the lung metastasis was obtained, WB-DWI identified lung metastasis enlargement in 2018. Under the diagnosis of CRPC, enzalutamide and docetaxel were introduced sequentially. After 10 courses of docetaxel, the right lung metastasis disappeared on WB-DWI at the PSA level of 0.007 ng/mL (Fig. 1d). Then, only androgen deprivation therapy (ADT) was continued.

In September 2021, the right lung metastasis was enlarged again with a PSA level of 0.349 ng/mL (Fig. 1e,f). Under a diagnosis of repeat OP-CRPC, thoracoscopic partial lung resection was performed in December 2021. Pathologically, the lung tumor was adenocarcinoma, and immunohistochemical staining was positive for PSA and NKX3.1 and negative for thyroid transcription factor-1 (TTF-1) and Napsin A, findings consistent with prostate cancer metastasis (Fig. 2). After resection of the lung metastasis, only ADT was continued and the PSA level remained undetectable for more than 9 months after the surgery.

Discussion

In the case of repeat OP-CRPC presented here, the disease progressed only in the same site as the initial metastasis and did not appear in other sites during the treatment course, and partial lung resection was effective. This suggested that the treatment-resistant clone was confined to a resected lung metastasis, and that carefully selected OP-CPRC with a lung metastasis can be a candidate for PSDT as well as OP-CRPC with bone metastases or lymph node metastases.

Fonseca et al. reported the results of an analysis of 10 cases of metastatic castration-sensitive prostate cancer that recurred after radical treatment, in which biopsy or resection of the lung metastases was performed.[10] They found that recurrent lung metastases did not contain the deleterious mutations in *TP53* and DNA damage-repair genes that characterize aggressive cancer, and that copy number changes and clonal mutations were highly conserved between metastases and primary lesions. This report suggests that selected metastatic castration-sensitive prostate cancer with recurrence in the lung may have different biological features than metastatic cancers with aggressive features, although these patients were carefully selected based on their clinical course and underwent biopsy or resection for lung metastases.

PSDT for OP-CRPC has been shown in retrospective studies to prolong PSA progression-free survival by 8–9 months in cohorts of androgen receptor axis targeting therapy failure.[4–7] However, these studies focus on lymph node and bone metastases. Among visceral metastases, lung metastases have a better prognosis than liver metastases.[11,12] We found only one case report showing a favorable PSA reduction after resection of a solitary lung metastasis of CRPC.[13]

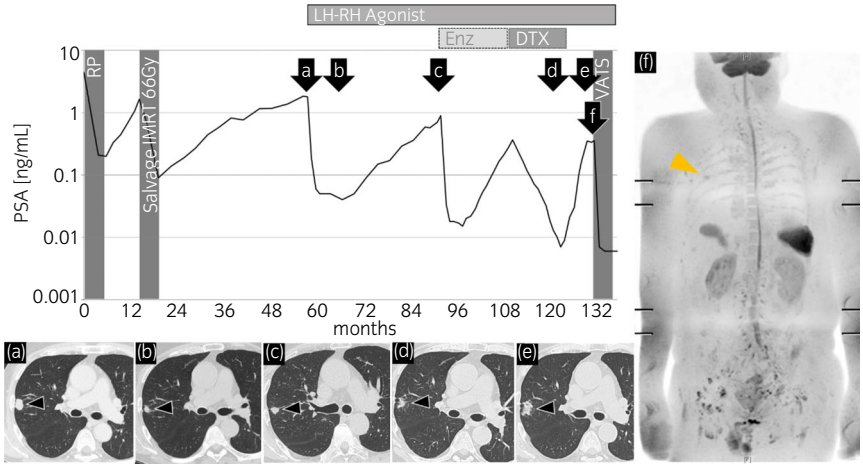

Fig. 1 Treatment course and trends of serum PSA and CT images of lung metastasis. The vertical axis is logarithmic. (a–e) CT images of the lung tumor (arrowheads). There was correlation between the tumor size and serum PSA level. (f) Whole body diffusion-weighted MRI before lung surgery. No metastatic lesions other than Lung tumor (Yellow arrowhead) was identified.

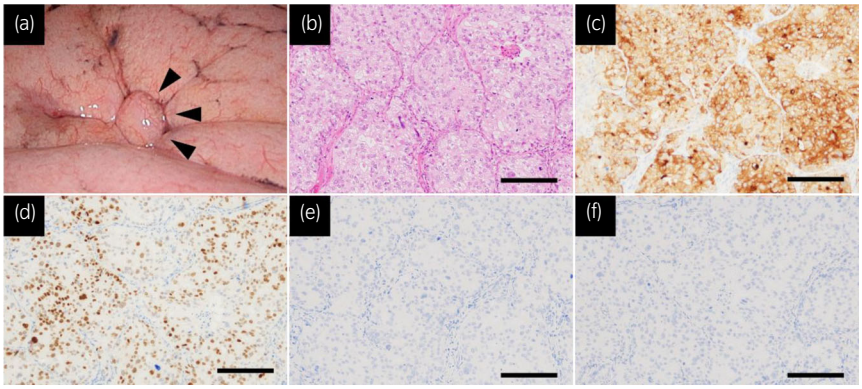

Fig. 2 Thoracoscopic image and pathological findings of the lung tumor. (a) Thoracoscopic image of lung metastasis (black arrowhead). (b) Hematoxylin and eosin staining lung tumor, (c–f) Immunostaining of PSA (c) and NKX3.1 (d) were positive. These results were compatible with this tumor being metastasis of prostate cancer. Immunostaining of thyroid transcription factor-1 (TTF-1) (e) and Napsin A (f) were negative. These results were compatible with this tumor not being a primary pulmonary tumor. Scale bar: 200 μm.

A metastatic lesion of genuine OP-CRPC is a tumor consisting of treatment-resistant subclones but with a limited number and locations of metastatic lesions, and targeted therapy of metastatic foci may be an option. In particular, repeat OP-CRPC, in which no new lesions appear during the course of the disease, are considered to have more limited potential lesion spread. Although in clinical practice it is not common to biopsy lung metastatic lesions and select treatment options based on the results of genetic analysis, the comprehensive system to characterize and classify oligometastatic cancer proposed by the EORTC/ESTRO OligoCare project can help select cases for targeted therapy.

Conclusions

PSDT is expected to be effective in selected repeat OP-CRPC with a lung metastasis. Further evaluation of the molecular biology of OP-CRPC in a large number of cases and the course after targeted therapy based on the type of oligometastases are needed.

Acknowledgments

None.

Author contributions

Takahiko Soma: Visualization; writing – original draft. Soichiro Yoshida: Conceptualization; project administration; supervision; writing – review and editing. Ryo Wakejima: Resources; writing – review and editing. Towako Taguchi: Resources; writing – review and editing. Shohei Fukuda: Writing – review and editing. Hajime Tanaka: Writing – review and editing. Minato Yokoyama: Writing – review and editing. Kenichi Ohashi: Supervision; writing – review and editing. Kenichi Okubo: Supervision; writing – review and editing. Yasuhisa Fujii: Supervision; writing – review and editing.

Conflict of interest

The authors have no conflicts of interest.

Approval of the research protocol by an Institutional Reviewer Board

Not applicable.

Informed consent

Written informed consent was obtained from the patient.

Registry and the Registration No. of the study/trial

Not applicable.

References

1 Hellman S, Weichselbaum RR. Oligometastases. *J. Clin. Oncol.* 1995; **13**: 8–10.
2 Ost P, Reynders D, Decaestecker K *et al*. Surveillance or metastasis-directed therapy for oligometastatic prostate cancer recurrence: a prospective, randomized, multicenter phase II trial. *JCO* 2018; **36**: 446–53.
3 Phillips R, Shi WY, Deek M *et al*. Outcomes of observation vs stereotactic ablative radiation for oligometastatic prostate cancer: the ORIOLE phase 2 randomized clinical trial. *JAMA Oncol.* 2020; **6**: 650–9.
4 Yoshida S, Takahara T, Arita Y *et al*. Progressive site-directed therapy for castration-resistant prostate cancer: localization of the progressive site as a prognostic factor. *Int. J. Radiat. Oncol. Biol. Phys.* 2019; **105**: 376–81.
5 Deek MP, Taparra K, Phillips R *et al*. Metastasis-directed therapy prolongs efficacy of systemic therapy and improves clinical outcomes in oligoprogressive castration-resistant prostate cancer. *Eur. Urol. Oncol.* 2021; **4**: 447–55.
6 Nozaki K, Kawai T, Fujimura T *et al*. Carbon 11-choline positron emission tomography/computed tomography and palliative local therapy for castration-resistant prostate cancer. *Int. Urol. Nephrol.* 2019; **51**: 1763–9.
7 Lohaus F, Zöphel K, Löck S *et al*. Can local ablative radiotherapy revert castration-resistant prostate cancer to an earlier stage of disease? *Eur. Urol.* 2019; **75**: 548–51.
8 Guckenberger M, Lievens Y, Bouma AB *et al*. Characterisation and classification of oligometastatic disease: a European Society for Radiotherapy and Oncology and European Organisation for Research and Treatment of Cancer consensus recommendation. *Lancet Oncol.* 2020; **21**: e18–28.
9 Yoshida S, Matsushima H, Fujii Y *et al*. Classification of oligometastatic prostate cancer with additional consideration for hormone sensitivity. *World J. Urol.* 2022; **40**: 871–3.
10 Fonseca NM, Van der Eecken K, Herberts C *et al*. Genomic features of lung-recurrent hormone-sensitive prostate cancer. *JCO Precis. Oncol.* 2022; **6**: e2100543.
11 Pond GR, Sonpavde G, de Wit R, Eisenberger MA, Tannock IF, Armstrong AJ. The prognostic importance of metastatic site in men with metastatic castration-resistant prostate cancer. *Eur. Urol.* 2014; **65**: 3–6.
12 Goodman OB, Flaig TW, Molina A *et al*. Exploratory analysis of the visceral disease subgroup in a phase III study of abiraterone acetate in metastatic castration-resistant prostate cancer. *Prostate Cancer Prostatic Dis.* 2014; **17**: 34–9.
13 Izawa M, Kosaka T, Nakamura K *et al*. Pulmonary metastasis secondary to abiraterone-resistant prostate cancer with homozygous deletions of BRCA2: first Japanese case. *IJU Case Rep.* 2021; **4**: 14–7.