CASE REPORT PEER REVIEWED | OPEN ACCESS

Dramatic improvement after palliative whole-liver radiotherapy for liver damage caused by diffuse liver metastases from castration-resistant prostate cancer: A case report

Yumi Ogoshi, Kei Ito, Keiko Nemoto Murofushi, Masaya Ito, Shuichiro Kobayashi, Fumitaka Koga

ABSTRACT

Introduction: Whole-liver radiotherapy (WLRT) is performed for palliative purposes in patients with metastatic liver tumors. However, it remains unclear whether the benefits obtained from WLRT surpass the potential disadvantages of radiotherapy-induced liver disease in such patients, particularly those with severe liver damage. We present the case of a 76-year-old man with diffuse liver metastases from castration-resistant prostate cancer.

Case Report: He was diagnosed as having prostate cancer with multiple metastases to the bone, pleura, and para-aortic lymph nodes three years and six months earlier and developed hepatic metastases following a sequence of therapies, including surgical castration, bicalutamide, enzalutamide, and 10 cycles of docetaxel. Despite administering abiraterone acetate for two months, the prostate-specific antigen (PSA) levels increased, and the patient developed symptomatic liver damage, presenting with jaundice, anorexia, and fatigue. His serum total bilirubin (9.5 mg/dL) and liver transaminase (>100 U/L) levels were markedly elevated. The patient received WLRT at 8 Gy in a single fraction for palliative intent. Symptomatic relief was achieved shortly after WLRT, and the total bilirubin and transaminase levels decreased and normalized within two months. Additionally, two months after WLRT, the PSA level decreased from 285 to 23.3 ng/mL, and a robust partial tumor response was observed on computed tomography images. Although the patient died of cancer eight months after WLRT, radiotherapy-induced liver disease was not confirmed during the follow-up period.

Conclusion: In the present case, WLRT successfully relieved the symptoms and reversed the liver damage caused by diffuse metastases, and it was considered to contribute to cancer control without adverse events. Thus, WLRT can be a viable option for patients with liver damage induced by diffuse liver metastases.

Keywords: Liver metastases, Prostate cancer, Radiotherapy, Whole-liver radiotherapy

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INTRODUCTION

Visceral metastases are found in approximately 22–30% of castration-resistant prostate cancers (CRPCs) [1], and the liver is a major visceral metastatic site [2]. Liver metastases cause symptoms such as pain, sweats, nausea, and vomiting [3], substantially compromising patients' quality of life. Moreover, a clinical scenario proposed that the liver damage induced by metastases causes hepatic dysfunction, ultimately leading to liver failure, and death [4]. A meta-analysis evaluating the metastatic sites of CRPC showed that the prognosis was worse for liver metastases than for other visceral metastases [2].

Based on several prospective studies documenting the palliative efficacy of low-dose whole-liver radiotherapy (WLRT) in 48–54% of cases [3, 5], WLRT is recommended to alleviate symptoms induced by liver metastases [6]. Moreover, as WLRT improves hepatic blood test results, which are associated with the degree of liver damage [4], the therapeutic modality may be favorable for improving liver function. In contrast, a study on radiation-induced liver disease (RILD) using the normal tissue complication probability model suggested that patients with poorer hepatic functions are at a higher risk of developing RILD even at low doses [7]. Thus, it is unclear whether WLRT improves liver dysfunction due to the natural course of the disease or exacerbates pre-existing liver damage.

Here, we report a case of CRPC with diffuse liver metastases in which WLRT successfully relieved symptoms and reversed hepatic damage and discuss the potential benefits of WLRT in patients with metastatic liver tumors.

CASE REPORT

A 76-year-old man with metastatic prostate cancer, who previously visited a different clinic after developing acute urinary retention, was referred to our hospital and was diagnosed with prostate cancer. His serum prostate-specific antigen (PSA) level was 159 ng/mL, and a prostate biopsy revealed adenocarcinoma with a Gleason score of 4+5. Chest and abdominal computed tomography (CT), pelvic magnetic resonance imaging, and bone scintigraphy revealed multiple metastases to the bone, pleura, and para-aortic lymph nodes. The patient underwent surgical castration; however, he developed CRPC eight months later. During the following two years and eight months, he received sequential therapies of bicalutamide, enzalutamide, and 10 cycles of docetaxel. The patient also received palliative radiotherapy at 50 Gy in 20 fractions to the primary lesion to relieve gross hematuria and urinary obstruction during bicalutamide therapy. His PSA levels had elevated gradually to over 50 ng/mL, and imaging studies revealed the development of multiple liver metastases during docetaxel therapy. Despite administering abiraterone acetate for two months, PSA levels increased to 285 ng/mL, and the patient developed jaundice, anorexia, and fatigue.

The patient was admitted to our hospital with severe liver damage and remarkably elevated serum total bilirubin (9.5 mg/dL) and hepatic enzymes; the Child-Pugh score was 9 (class B) (Table 1). Enzalutamide, which had failed previously, was retried because the patient was unfit for cabazitaxel therapy due to severe hepatic dysfunction and a poor Eastern Cooperative Oncology Group performance status of 2.

Palliative WLRT was administered following the restart of enzalutamide (three years and 11 months after the primary diagnosis). Since diffuse liver metastases were observed on CT images (Figure 1A), the gross tumor volume was not defined. The whole liver was encompassed as the clinical target volume (CTV), and a planning target volume (PTV) margin of 5 mm was added to the CTV for set-up error and respiratory motion. The prescribed WLRT dose was 8 Gy in a single fraction, and the PTV was irradiated at 7.5–8.7 Gy (94–109%) using two oblique beams (Figure 2). Prochlorperazine 15 mg and dexamethasone 4 mg in a day were prophylactically administered to prevent nausea, a possible side-effect of radiation therapy.

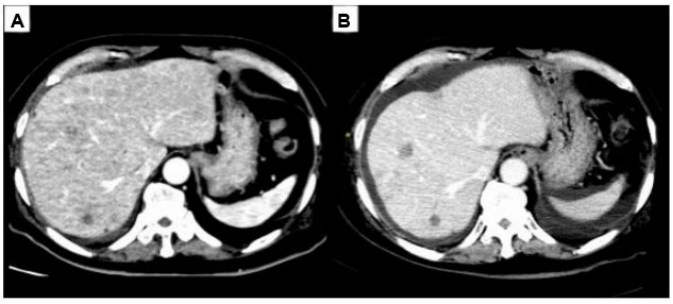

Figure 1: Assessment of liver metastases before and after whole-liver radiotherapy (WLRT). (A) Contrast-enhanced computed tomography (CT) image of the abdomen before WLRT showing diffuse liver metastases. (B) Contrast-enhanced CT image of the abdomen three months after WLRT shows the resolution of most liver metastases.

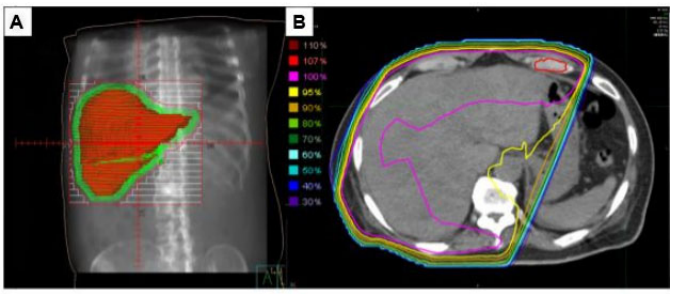

Figure 2: Beam's eye view and dose distribution during whole-liver radiotherapy (WLRT). (A) Beam's eye view of WLRT. The clinical target volume (CTV) is the whole liver, and a planning target volume (PTV) margin of 5 mm is added to the CTV. (B) Dose distribution of WLRT. The prescribed dose is 8 Gy administered in a single fraction. The PTV is irradiated at 7.5–8.7 Gy (94–109%) using two oblique beams.

Jaundice, anorexia, and fatigue resolved within one week after WLRT. The serum total bilirubin level decreased to 1.2 mg/dL, and the level remained within normal limits during the follow-up period of eight months, while the liver enzymes also showed improvement one month after WLRT (Table 1). Furthermore, the diffuse liver metastases showed a robust partial tumor response on CT images three months after WLRT (Figure 1B). The PSA level had decreased to 23.3 mg/mL four months after WLRT; however, it increased one month later (Table 1). The disease progressed systematically, and the patient died of CRPC eight months after WLRT. No adverse effects, including RILD, were observed during the follow-up period.

Table 1: Time course of laboratory blood data

Laboratory variable	Normal range	Time after whole-liver radiotherapy											
		−1 mo	0[a]	3 days	5 days	2 wks	1 mo	2 mos	3 mos	4 mos	5 mos	6 mos	7 mos
T-Bil (mg/dL)	0.4–1.5	0.7	9.5	6.5	5.0	2.4	1.2	0.8	1.0	1.1	0.8	0.6	0.6
D-Bil (mg/dL)	0–0.4	N/A	7.0	5.1	3.9	2.0	0.8	0.4	N/A	0.5	0.3	0.3	N/A
AST (U/L)	13–30	36	128	105	74	45	30	29	31	30	35	49	98
ALT (U/L)	10–42	21	103	64	52	42	15	11	12	11	11	14	19
GGT (U/L)	13–64	274	1105	783	670	489	177	66	63	50	46	56	64
ALP (U/L)	106–322	1025	1238	773	718	615	504	479	496	640	752	997	1332
PSA (ng/mL)	0–3.5	157.3	284.8	N/A	N/A	N/A	132.9	33.4	25.8	23.3	25.3	47.8	247.7

Abbreviations: wks, weeks; mo: month; mos: months; T-Bil, total bilirubin; D-Bil, direct bilirubin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyl transpeptidase; ALP, alkaline phosphatase; PSA, prostate-specific antigen; N/A, not available.
The values with green backgrounds represent levels deviant from the normal range.
[a]"0" (baseline) is when the WLRT was performed.

DISCUSSION

In the present case of metastatic CRPC, palliative WLRT for diffuse liver metastases dramatically improved the symptomatic liver damage, PSA response, and tumor burden. In addition, the hepatic blood test results, which reflect the degree of liver damage [8, 9], showed improvement and suggested that WLRT positively influenced liver function.

Some published case series demonstrated a significant improvement in several liver enzymes and related factors by WLRT [8, 9]. Theoretically, the improvement in blood test results could have contributed to the improved liver function and subsequent prolongation of survival. Moreover, WLRT may have contributed to the patient's survival time by enabling the administration of systemic therapy in instances where a specific antitumor agent is contraindicated due to liver metastases-induced hepatic dysfunction. A retrospective study found that 4 of 10 patients with severe liver damage due to liver metastases from colorectal cancer showed improved liver function test results and could resume systemic chemotherapy when WLRT was administered at 21 Gy in three fractions [9]. A trend of longer survival time was noted in the 4 patients who resumed chemotherapy after WLRT than in the 6 patients who did not (mean survival time: 143 vs. 38 days, p = 0.127) [9]. Although our patient's liver enzymes and related factors improved sufficiently to be able to administer cabazitaxel, he proved unfit for cabazitaxel therapy due to poor performance status.

Notably, the PSA level drastically decreased after local WLRT treatment. Although enzalutamide was administered concurrently with WLRT, it was expected to be ineffective as it had failed previously, particularly in a sequence of docetaxel and abiraterone acetate [10]. Metastases to the bones, pleura, and para-aortic lymph nodes had been stable on CT images prior to WLRT, indicating that the liver was the oligo-progressive site. Therefore, we can assume that the decrease in the PSA level may have been the effect of WLRT instead of enzalutamide. In the present case, cancer status may have been more accurately evaluated with prostate-specific membrane antigen (PSMA) positron emission tomography (PET). Unfortunately, PSMA PET has not yet been approved for use in Japan.

Whole-liver radiotherapy has several advantages in patients with liver metastases. First, it is only a single fraction treatment, which reduces the financial burden and hospitalization time for the patient. Second, high-precision equipment and human resources are not required to administer WLRT when using conventional techniques. Third, WLRT with low-dose radiation has low toxicity; severe toxicity has been noted in only 0–7% of patients [3, 5, 8, 9]. As nausea is the most common adverse effect [3, 5, 8, 9], we prescribed prophylactic antiemetics.

CONCLUSION

In conclusion, we presented a case of CRPC with liver metastases that was successfully palliated with WLRT. Liver function test results, including serum total bilirubin levels and PSA levels, and imaging findings dramatically improved after palliative WLRT. We consider WLRT a critical treatment option for patients with liver damage caused by diffuse liver metastases.

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Author Contributions

Yumi Ogoshi – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Kei Ito – Conception of the work, Design of the work, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Keiko Nemoto Murofushi – Conception of the work, Design of the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Fumitaka Koga – Conception of the work, Design of the work, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

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Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Kei Ito has performed educational seminars with Varian medical systems. The other authors declare that there is no conflict of interest regarding the publication of this article.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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