

Case Report

Running Title: WLRT- An Underutilized Weapon

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Whole Liver Radiotherapy- an Underutilized Weapon for Diffuse Liver Metastasis: A Case Report

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Abstract

A 56-year-old female patient was presented with abdominal distension and decreased appetite. Diagnosis confirmed breast cancer, a mastectomy, and multiple lines of chemotherapy. Later on, the patient developed liver metastasis and received whole liver radiotherapy (WLRT) for diffuse liver metastasis. This phenomenon is still the most prevalent site of metastases, particularly in lung, breast, and gastrointestinal cancers owing to its rich, dual blood supply and its role as a filter in the portal circulation. Conventional treatment approaches are not effective in such patients due to diffuse liver involvement; thus, the use of low-dose WLRT is considered as a good alternative. In practice, palliative liver irradiation is a rare modality due to radiation-induced hepatitis. However, WLRT treatment aims at the palliation of symptoms and improving the patients' quality of life rather than enhancing survival. Results of the present case report also showed that WLRT in patients with poor performance status would ultimately improve their palliative symptoms and overall quality of life with acceptable morbidity.

Keywords: Radiotherapy, Whole liver irradiation, Liver metastasis, Quality of life, Palliative care

Introduction

Liver is one of the most common sites of involvement in the metastatic setting; the disease frequently arises from lung, breast, and gastrointestinal tract and other sites.¹ In patients with extensive involvement of the liver, pain and derangement of liver functions is common due to liver enlargement and obstruction. These patients are not suitable candidates for surgical resection, radiofrequency ablation, trans-arterial chemoembolization, or chemotherapy because of diffuse liver involvement. Although systemic chemotherapy is a mainstay of treatment in these patients, it is often delayed due to impaired liver function and increased bilirubin levels.² Low-dose whole-liver

radiotherapy (WLRT) is a good treatment option for patients with extensive liver involvement to relieve symptoms and improve the quality of life. We report a 56-year-old female patient who received WLRT for diffuse liver metastasis.

Case Presentation

A 59-year-old female patient was presented to our hospital with abdominal distension and reduced appetite. She was diagnosed with breast cancer in 2015 and had undergone right modified radical mastectomy followed by four cycles of epirubicin and cyclophosphamide (EC). The hormonal status was ER/PR negative and Her-2 positive. The subject developed

multiple hepatic metastases in 2016. She received 12 weekly cycles of paclitaxel and trastuzumab followed by maintenance trastuzumab. The disease progressed despite multiple lines of chemotherapy. The subject presented with abdominal pain in the right hypochondriac region and jaundice in November 2018. Positron emission tomography-computed tomography (PET-CT) showed extensive liver with retroperitoneal lymph node metastasis. The patient was clinically assessed prior to radiation therapy. The liver was palpable almost four fingers (5 cm) below the right costal margin in mid-clavicular line. The bilirubin and SGOT levels were 14.8 mg/dl and 116.2, respectively. There was no ascites or sign of hepatic encephalopathy. She was classified as a Child-Pugh class A as per clinical and serological findings and was planned for WLRT to a dose of 21 Gray (Gy) in seven fractions over two weeks.

Radiotherapy

Clinical target volume (CTV) for radiotherapy was specified (Figure 1) through transferring the computed tomography (Siemens Biograph, PA, USA) data to the Linac-based planning system (Eclipse 3D version 13.7; Varian Medical Systems Inc., Palo Alto, USA). Organs at risk (OAR) were determined and constraints were given as follows:

- (1) Spinal cord - $D_{max} \leq 30$ Gy
- (2) Kidneys (Left and Right)-mean dose to bilateral kidneys should be < 16 Gy
- (3) Liver-mean liver dose must be ≤ 21 Gy
- (4) Stomach and duodenum - $D_{max} \leq 32$ Gy

Helical tomotherapy IGRT plan (Tomotherapy Inc., Wisconsin, USA) was generated with a field width of 2.512 cm, a pitch of 0.3, and a modulation factor of 2 (Figure 2). Later on, the patient received palliative external radiotherapy with IGRT with helical tomotherapy using 6MV photons with a helical manner to a dose of 21Gy/7 daily over nine days.

Following three fractions of radiotherapy, the subject reported symptomatic pain relief. The patient had complete pain relief after the completion of radiotherapy while the pain medications were discontinued. After treatment, the patient's appetite significantly improved, and the liver span decreased from 5 cm to 1 cm. Her icterus was significantly

reduced and her performance was also enhanced.

At day 30 of follow-up, the CT scan showed a 60% reduction in the volume of liver due to the decrease in gross disease (Figure 3). Her bilirubin decreased from 14.8 mg/dl to 1.8 mg/dl. Based on the improvement in the previous phase, the patient was started on the next line of chemotherapy.

Discussion

Depending on the location and size, liver metastases are associated with significant pain or obstructive symptoms that often require palliative interventions.³ Palliation of symptoms is a key aspect in the management of patients with metastatic liver disease. Patients with extensive liver metastases have a poor prognosis with a median survival of six months.⁴ Therefore, it is of utmost importance to improve the palliative symptoms and overall quality of life. In a radiation therapy oncology group (RTOG) pilot study comprised of 109 patients receiving dose-fractionation schedules ranging from 21 to 30 Gy in 7 to 19 fractions, 55% of the patients had reduced pain while 40% had partially improved liver chemistries.⁵ Although there were no cases of radiation-induced nephritis, hepatitis, or pneumonitis, 16% of the patients showed aggravated nausea. Performance status improved in 25% of the patients while complete response rates for individual symptoms ranged from 7% to 34%.⁵ Low-dose palliative radiation therapy showed a good palliative effect with pain relief varying from 55% to 80% as per prospective clinical studies.^{5,6,7,8} A retrospective study conducted by Ito et al., also confirmed the WLRT as an effective approach in cases with hepatic dysfunction.⁹ However, there is no evidence on the survival advantage of WLRT; thus, it should be reserved for symptom control only. Patient selection is another important aspect of low-dose WLRT. The Child-Pugh system evaluates the liver dysfunction level based on clinical and serum markers prior to the radiation treatment. Patients with Child-Pugh Class B or C have less organ reserve and run significantly higher risks of developing radiation-induced hepatitis.

Whole/partial liver RT is occasionally employed in clinical practice due to the misbelief that it inevitably entails radiation-

induced hepatitis (RILD). However, various studies have reported that low-dose WLRT is safe and effective and does not lead to impairments in liver function.^{5,7,8,9}

This procedure is well tolerated if performed at doses equivalent to 2 Gy fractions of up to 30-35 Gy. Liver tolerates WLRT doses below 30 Gy in 15 fractions, 21 Gy in 7 fractions, or 10 Gy in 2 fractions with supportive medications, such as steroids and antiemetic prior to treatment.^{5,7,8,10} At least one (functioning) kidney should be excluded from the treatment volumes. With the use of pre-treatment antiemetic and low-dose WLRT, toxicity rates are expected to be low.

To conclude, WLRT in patients with poor performance status can improve their palliative symptoms and overall quality of life with acceptable morbidity. Large scale studies should be carried out to corroborate and clarify the effectiveness of WLRT in end-stage liver cancers. Over the past few years, there have been significant improvements in radiation delivery technology, allowing for treatment with focal, high-dose radiation to the lesion with escalated doses. The overall process spares normal liver parenchyma and offers excellent local control with a limited toxicity profile. At present, there is no clinical data to show the survival advantage of WLRT in patients with diffuse liver involvement. Randomized clinical studies of low-dose WLRT are warranted. In the future, this approach requires further exploration.

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Informed Consent

Written informed consent was obtained from the patient.

Conflicts of Interest

None declared.

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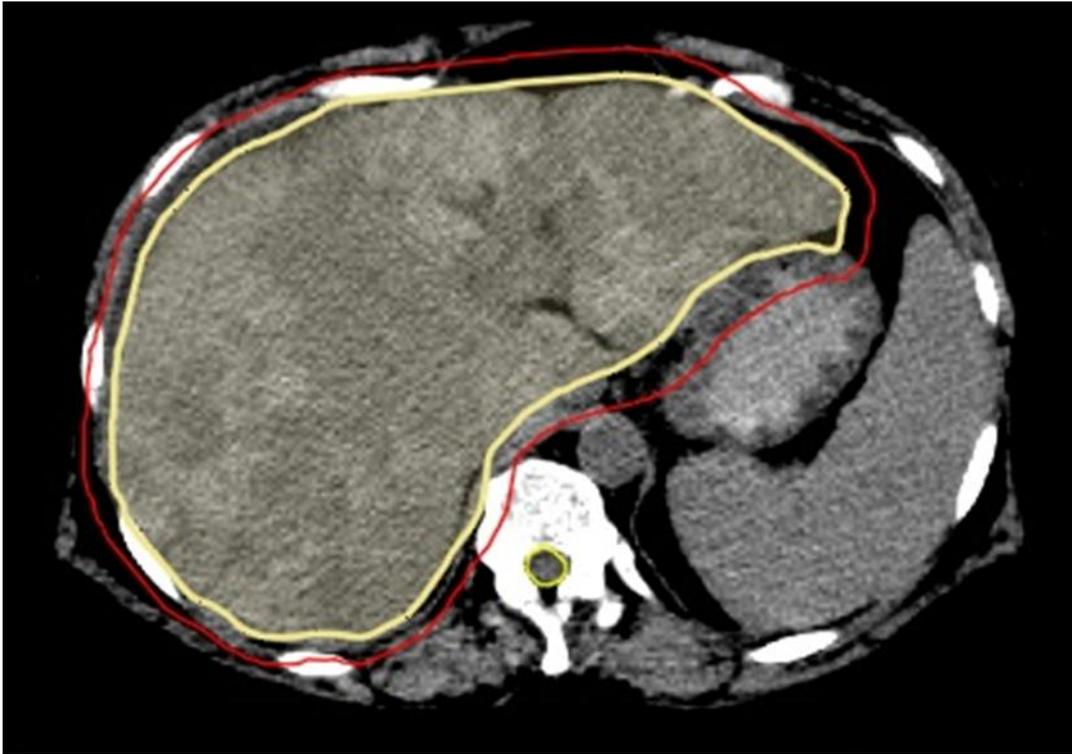


Figure 1. Axial computed tomography scan of abdomen indicating clinical target volume of liver and planning target volume contours prior to whole liver radiotherapy.

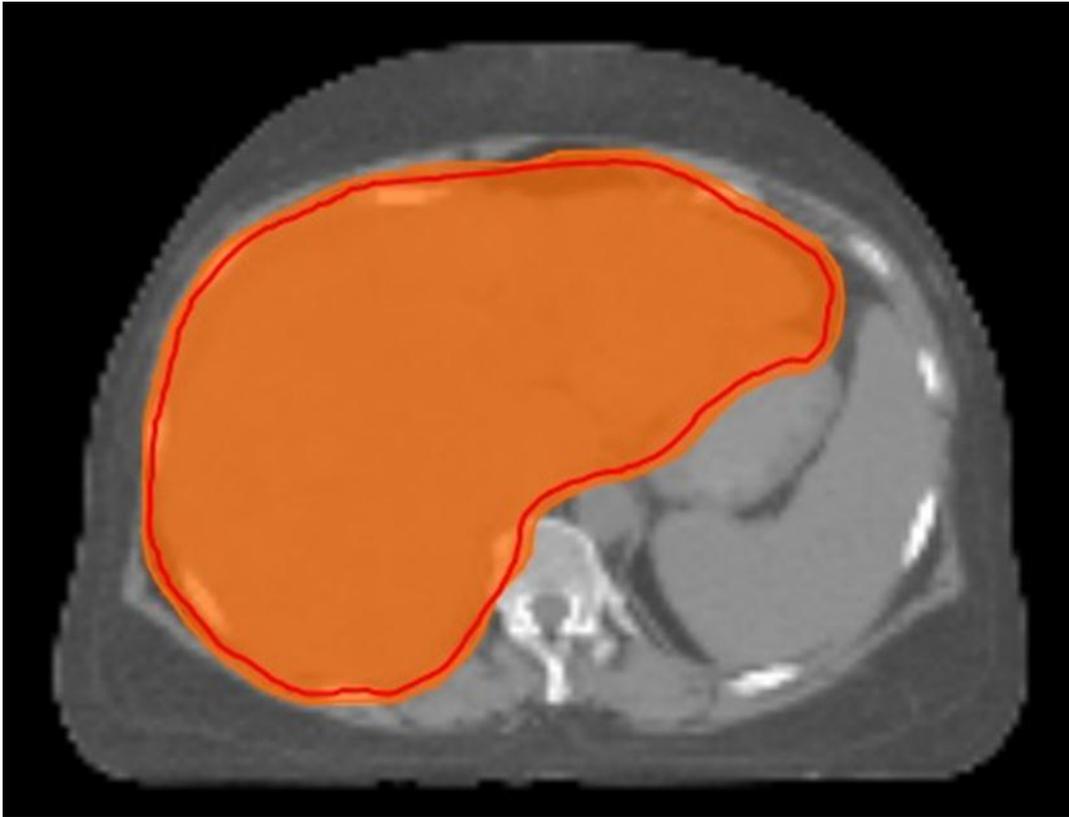


Figure 2. Axial computed tomography scan of abdomen showing 95% coverage of planning target volume of liver generated with helical tomotherapy planning system.



Figure 3. Axial computed tomography scan of abdomen indicating the shrinkage of whole liver volume after completing month of whole liver radiotherapy.