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OPEN ACCESS CASE REPORT

DTI-Guided Hypofractionated IMRT for Large Brain Metastasis in Small Cell Lung Cancer: A Case Report

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ABSTRACT

Background: The utilization of diffusion tensor imaging (DTI)-guided radiotherapy represents an innovative approach for detecting tumor invasion while minimizing radiation exposure to critical white matter tracts.

Objective Diffusion tensor imaging (DTI) is a useful technique for visualizing white matter tracts adjacent to the tumor. The application of DTI in conjunction with radiotherapy for large brain metastases has not been reported. Therefore the current case report is discussing this health issue.

Method: This case report discussing a 62-year-old female patient underwent DTI-guided hypofractionated intensity-modulated radiation therapy for a metastasis measuring 4.5 centimeters from small-cell lung cancer in the left frontal lobe.

Results: The tumor showed complete radiological remission with no observed neurological sequelae or treatment-related toxicity.

Conclusion: DTI-guided radiotherapy has the potential to become a safe and effective treatment for large brain metastasis that are adjacent to matter tracts.

Keywords: Small Cell Lung Carcinoma, Brain Neoplasms, Adverse Effects, Diffusion Magnetic Resonance Imaging, Diffusion tensor imaging, Intensity-modulated radiation therapy.

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INTRODUCTION

The utilization of diffusion tensor imaging (DTI)-guided radiotherapy represents an innovative approach for detecting tumor invasion while minimizing radiation exposure to critical white matter tracts [1,2]. Several studies have demonstrated the effectiveness of DTI in brain tumor radiotherapy [3,4]. DTI can be used to identify and delineate critical white matter tracts, such as the corticospinal tract and optic pathways, which are at risk of radiation damage during treatment. By incorporating DTI data into radiotherapy treatment planning, clinicians can optimize radiation delivery to minimize the dose to these critical structures, potentially reducing the risk of neurological complications. Research has shown that DTI-guided radiotherapy can lead to improved preservation of neurological function and quality of life in patients with brain tumors [3,4]. DTI has also been utilized to assess the impact of radiotherapy on white matter integrity, providing insights into the mechanisms of radiation-induced brain injury and potential targets for intervention. Nonetheless, its real-world clinical effectiveness and safety remain a subject of ambiguity. In this report, we present a case involving a sizable brain metastasis, where the implementation of DTI-guided intensity-modulated radiation therapy (IMRT) yielded successful outcomes and demonstrated clear clinical benefits.

CASE PRESENTATION

A 62-year-old woman with an unremarkable past medical history was referred to our institution for evaluation of right hemiparesis. MRI revealed a large expansile tumor 4.5 cm in diameter with focal edema in the left frontal lobe (Figure 1a).
followed up at the gynaecological clinic and was discharged after complete healing.

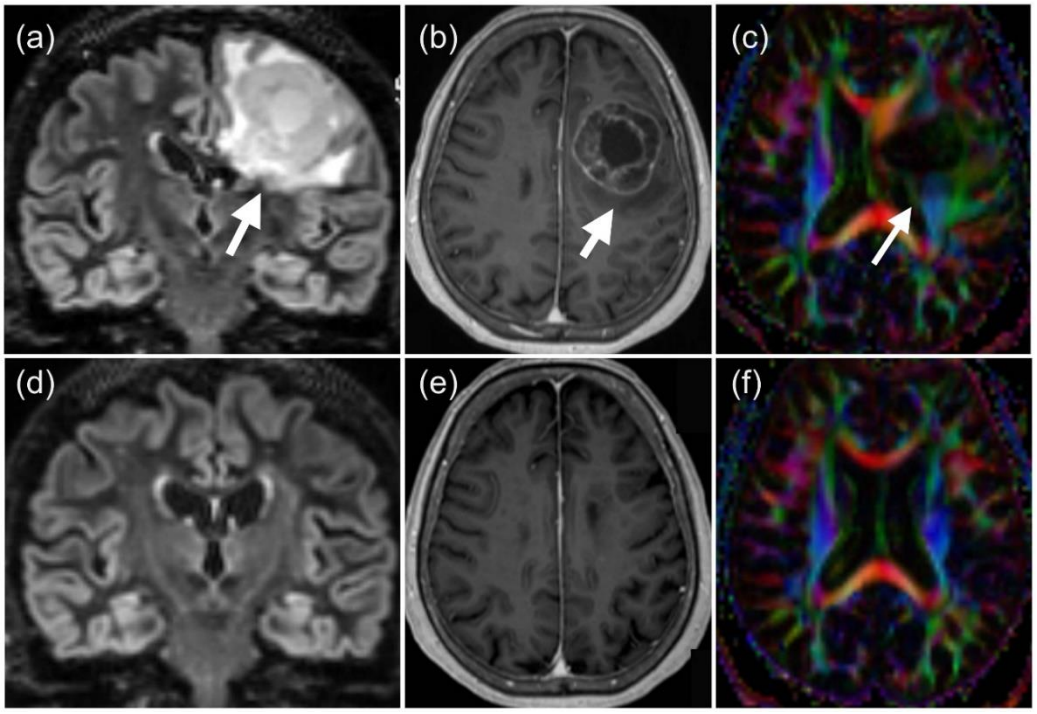

Figure 1. Multiparametric MRI of a solitary brain metastasis from lung cancer. (a)-(c): before radiotherapy. (d)-(f): 6 months after radiotherapy. (a) Coronal fluid attenuated inversion recovery (FLAIR) image showed a large expansile tumor (arrow) with focal edema in the left frontal lobe. (b) Transverse T1-weighted image showed a well-circumscribed tumor (arrow) with contrast enhancement after intravenous administration of a gadolinium-based contrast agent. (c) Diffusion tensor

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imaging showed that the left corticospinal tract, arcuate fasciculus, and corpus callosum were damaged by the large tumor (arrow). (d) Coronal FLAIR image showed complete remission of the tumor without perifocal edema. (e) Post-contrast transverse T1-weighted image showed no residual tumor. (f) Diffusion tensor imaging showed recovery of the left corticospinal tract, arcuate fasciculus, and corpus callosum.

Contrast-enhanced MRI showed a well-circumscribed tumor with contrast enhancement (Figure 1b). MRI findings were consistent with brain metastasis, and a whole-body CT scan was performed, which revealed primary lung cancer. After transbronchial biopsy and histopathologic and immunohistochemical examination, the lung tumor was diagnosed as small cell lung cancer (SCLC). Due to the risk of cognitive dysfunction and alopecia, the patient declined whole brain irradiation (WBI). Stereotactic radiosurgery (SRS) was not indicated due to the large size of the tumor. Because of concerns about acute brain edema after SRS, hypofractionated IMRT was performed.

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki, and informed consent was obtained from the patient for the use of the clinical data and images. Data for this research were derived from observations of a common daily routine in our hospital. Given the well-established and non-invasive nature of this practice, institutional review board (IRB) approval was waived. Three MRI sequences were used to delineate the target volume and neural pathways and structures: fluid attenuated inversion recovery (FLAIR) (Figure 1a), post-gadolinium T1-weighted images (Figure 1b), and DTI (Figure 1c). CT was used for dose calculation and MRI for identification of brain structures and tumors. Gross tumor volume (GTV) was defined on the post-gadolinium T1-weighted images and clinical target volume (CTV) was defined on the FLAIR images. The planning target volume (PTV) was defined as GTV plus 2 mm margin and CTV plus 1 mm margin, excluding white matter tracts detected by DTI (Figure 1c). The prescribed dose was 30 Gy in 10 fractions to the PTV, and the dose was defined as the minimum dose received by 95% volume (D95%) of the PTV. The maximum dose to the GTV was not specified. D0.1cc (the maximum dose delivered to a volume of 0.1 ml) of the white matter tracts was set at less than 28.5 Gy.

The patient did not experience adverse events during radiotherapy or follow-up. The patient's hemiparesis gradually improved during radiotherapy and was completely resolved three months after the treatment. Systemic chemotherapy was started two weeks after radiotherapy. Follow-up MRI 6 months after IMRT showed complete tumor remission (Figures 1d and e), and DTI showed recovery of white matter tracts (Figure 1f).

DISCUSSION

Radiation therapy is the primary treatment for a solitary brain metastasis in patients with SCLC. It may include SRS or WBI with or without hippocampal avoidance [5,6]. However, tumors larger than 3 cm in diameter can be difficult to control with SRS without damaging surrounding normal structures such as white matter tracts. WBI is associated with excellent rates of intracranial tumor control, but it is associated with higher rates of cognitive decline and adverse effects on quality of life, even when hippocampal avoidance is used [5-7]. To overcome the shortcomings of SRS and WBI, we applied DTI-guided hypofractionated IMRT.

The treatment strategy in this case report has several strengths. First, by not setting a dose limit in the GTV, high doses of radiation were delivered to the center of the tumor, effectively killing the radioresistant cancer cells in the center of the tumor. Second, the use of fractionated IMRT instead of single-fraction SRS reduced normal tissue toxicity and ultimately improved the therapeutic ratio. Third, it has been shown that preferential reduction of radiation dose to white matter tracts adjacent to the GTV does not necessarily result in marginal recurrence, but rather may contribute to white matter tract regeneration.

There are several limitations to this case report. First, a single case report cannot be generalized to other cases of multiple brain metastases or brain metastases amenable to SRS. However, this is the first report to demonstrate the proof-of-principle of hypofractionated IMRT for a large brain metastasis from SCLC while avoiding white matter tracts using DTI. Second, the optimal dose and fractionation for tumors and white matter tracts has not yet been

determined. Further studies are warranted to determine the optimal dose and fractionation schedule for the tumor and white matter tracts.
Expanding on the innovative approach presented, it's worth noting that DTI has shown promise in guiding radiation therapy for various brain tumors beyond SCLC metastases. For instance, studies have utilized DTI to delineate eloquent white matter tracts in patients with high-grade gliomas, allowing for dose escalation to the tumor while minimizing the risk of neurological deficits [8, 9]. Furthermore, DTI-guided radiation techniques have been explored in the context of primary brain tumors and even in prophylactic cranial irradiation for small cell lung cancer, aiming to reduce the potential for long-term neurocognitive sequelae [10]. While this case report focuses on a single instance, the broader literature suggests a growing interest in leveraging advanced neuroimaging like DTI to personalize radiation treatment and improve the therapeutic window. Even in this single case, the observed stability or potential improvement in the patient's neurological status post-treatment, though anecdotal, lends support to the rationale for white matter preservation and the potential benefits of avoiding WBI-related cognitive decline, a well-documented concern in the management of brain metastases.

CONCLUSION

While findings from a single case should be interpreted with caution, this report demonstrates the feasibility and safety of DTI-guided hypofractionated IMRT as a promising alternative therapy for large, eloquent-area brain metastases from SCLC. Large-scale studies are needed to evaluate the safety and efficacy of DTI-guided IMRT compared to conventional radiotherapy approaches, with emphasis on neurological outcomes and tumor control rates.

Conflict of interest

The authors declare that no conflict of interest.

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