



A Diagnostic Conundrum: Cerebral Radiation Necrosis Masquerading as Tumor in the Contralateral Hemisphere

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Abstract

Cerebral radiation necrosis (CRN) is a recognized late complication following cranial irradiation. This article describes a unique case of CRN occurring contralaterally to the original irradiation site in a male treated for atypical meningioma with surgery and subsequent radiation therapy. This case highlights the diagnostic challenge of differentiating CRN from tumor recurrence or progression and highlights the importance of advanced imaging techniques and biopsy for diagnosis.

Keywords

- ▶ cerebral radiation necrosis
- ▶ contralateral cerebral radiation necrosis
- ▶ radiation-induced brain necrosis

Introduction

Cranial irradiation is an important treatment modality for brain tumors, whether for curative purposes or palliation. However, cerebral radiation necrosis is a well-recognized late complication following irradiation of intracranial and skull-based tumors. It manifests after a latency period of several months, though cases have been documented to occur even up to 10 years after radiation therapy.^{1,2} The reported incidence ranges between 3 and 24%,^{3,4} and it is more likely to occur when high doses per fraction are administered with concurrent chemotherapy. It typically develops at or adjacent to the original site of tumor location that received the highest dose of radiation. There is no shadow of uncertainty that CRN is usually misinterpreted as tumor recurrence, and no single modality other than tissue diagnosis can reliably distinguish CRN from recurrent tumor. Here, we present an unusual case of cerebral radiation necrosis occurring on the contralateral side.

Case

A 32-year-old man, previously treated for an atypical meningioma 5 years before the current presentation, reported with new-onset headaches. Originally, in 2019, he reported experiencing mild holocranial headaches for 6 months, which were intermittent and associated with vomiting and seizures. MRI evaluation identified a broad-based intraparenchymal altered signal intensity in the right frontal lobe, extending into the thalamic-capsulo-ganglionic region, with T2 hyperintensity and postcontrast enhancement, suggestive of meningioma (▶ **Fig. 1**).

The patient underwent a right frontal craniotomy and tumor excision (Simpson's grade 3). Postoperative histopathology labeled it as atypical meningioma (grade II).

Postoperative MRI showed the resection cavity without evidence of gross residual disease. The patient underwent adjuvant radiation therapy at a private hospital. Treatment was delivered by intensity-modulated radiotherapy (IMRT)

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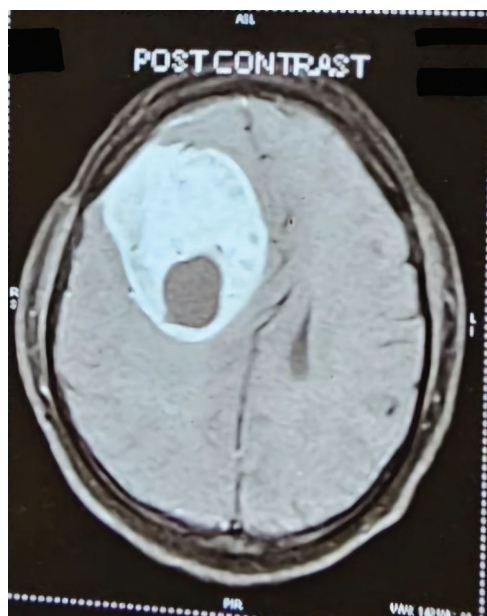


Fig. 1 MRI evaluation identified a broad-based intraparenchymal altered signal intensity in the right frontal lobe, extending into the thalamic-capsulo-ganglionic region, with T2 hyperintensity and post-contrast enhancement, suggestive of meningioma.

to a total dose of 59.5 Gy in 30 fractions, completed by November 2019. He tolerated the treatment well and suffered no long-term neurological sequelae.

Between 2019 and 2023, the patient was monitored with regular clinical examinations and cranial MRI scans. His last MRI scan before re-presentation, in January 2023, showed stable posttreatment changes.

As the patient was not experiencing symptoms at the time of his last visit, he elected not to follow-up until January 2024, when he began experiencing left-sided headaches of moderate severity and occasional dizziness. There was no neurological deficit on physical examination.

Contrast-enhanced MRI (CE-MRI) revealed a large, lobulated, irregular, partially cystic lesion within the left frontoparietal region, measuring 5.7 × 6 cm with extensive surrounding vasogenic edema with midline shift (► **Fig. 2**). The radiographic differential diagnosis included high-grade glioma, metastasis, abscess, radiation-induced malignancy, and radiation necrosis. The use of additional imaging modalities such as MR spectroscopy revealed a significant lactate peak, and it favored the impression of radiation necrosis on the contralateral side over tumor recurrence (► **Fig. 3**).

The detailed radiation plan from the original treating center for radiotherapy was unavailable. The patient subsequently underwent biopsy from the lesion, and microscopic features were suggestive of radiation necrosis (► **Fig. 4**).

Discussion

CRN is a common complication encountered after radiation therapy for intracranial malignancies; additionally, it can rarely occur after irradiation of extracranial lesion of the

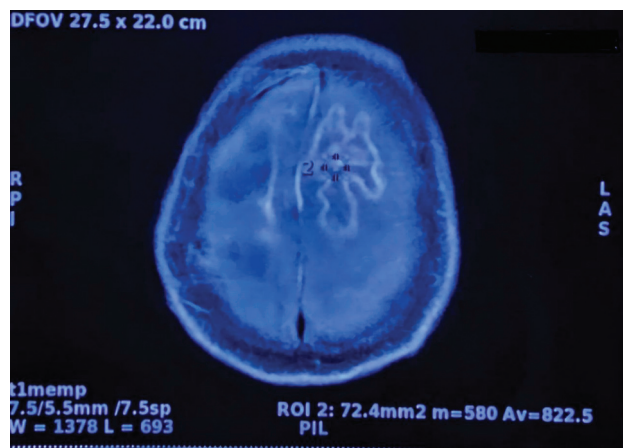


Fig. 2 Contrast-enhanced MRI (CE-MRI) revealed a large, lobulated, irregular, partially cystic lesion within the left frontoparietal region, measuring 5.7 × 6 cm with extensive surrounding vasogenic edema with midline shift.

head and neck. It usually occurs 2 years after irradiation.⁵ Reported risk factors relate to the total dose of radiation, dose per fraction, irritated volume, biologically effective dose (BED) ≥85.5 Gy, concomitant chemotherapy administration, and susceptibility of underlying genes such as variations in the Cep128 gene.⁶

Typically, lesions are observed at or adjacent to the location of the primary tumor, though in rare instances contralateral lesions have also been documented, such as the case presented here.⁷ In such cases, a detailed analysis of the isodose distribution is essential to assess if the dose delivered to the contralateral hemisphere was unusually high. In our situation, since the patient received treatment at a private facility and we did not have access to the isodose distribution data, potential errors in planning and other unknown factors influencing the unusual high dose to the contralateral hemisphere should be considered.

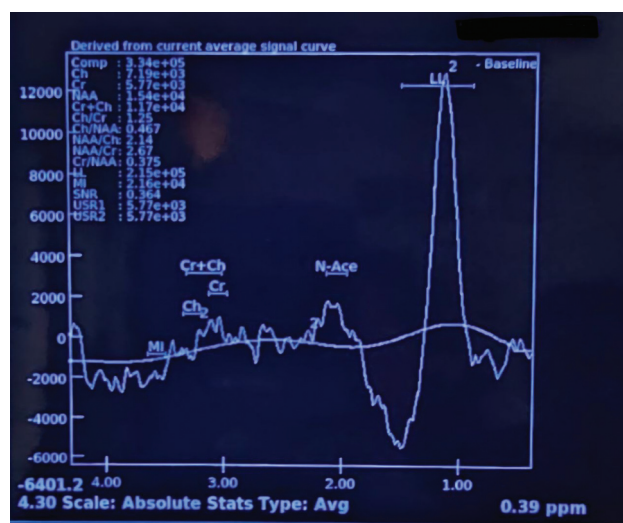


Fig. 3 MR spectroscopy revealed a significant lactate peak, and it favored the impression of radiation necrosis on the contralateral side over tumor recurrence.

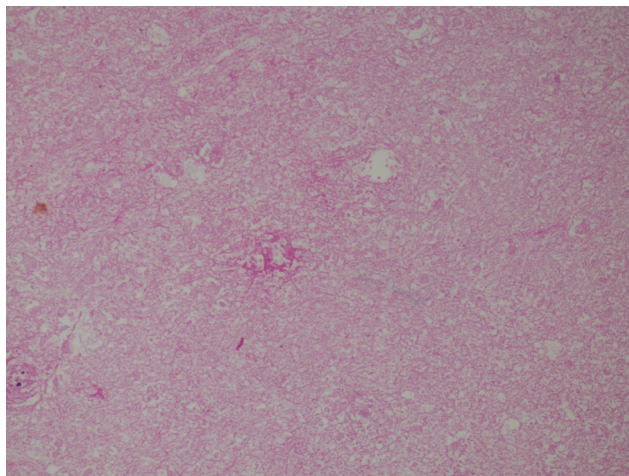


Fig. 4 Section shows areas of necrosis, possibly glial origin. A viable blood vessel with intimal fibrosis and perivascular lymphocyte aggregates. No viable cells and tumor were seen. The microscopic features were suggestive of radiation necrosis.

Symptoms vary depending upon the size, location, and mass effect on adjacent structures. Characteristic symptoms include seizures, headache, vomiting, altered level on consciousness, and motor dysfunctions. If allowed to progress, radiation necrosis can result in small vessel occlusive disease and bleeding from fragile vessels, worsening the clinical presentation.

The exact pathogenesis of radiation necrosis remains unclear; several theories offer explanations. The most widely accepted hypothesis suggests that radiation inflicts damage on the endothelial cell, triggering an increase in ceramide levels in the brain. The endothelial cell function is compromised, leading to disruption of the blood–brain barrier, resulting in vascular insufficiency and infarction.^{8,9} Consequently, there is entry of inflammatory cells that secrete cytokines that further intensify the immune response and fuel uncontrolled inflammation. Additionally, the release of vasoactive substances such as vascular endothelial growth factor (VEGF) can further impair the blood–brain barrier and promote brain edema.¹⁰

Distinguishing CRN from tumor progression or recurrence is a frequent challenge, as both the clinical presentation and imaging can appear similar. Kumar et al identified patterns such as diffuse “Swiss cheese” and isolated “soap bubble” formations as characteristic of necrosis.⁴ Advanced imaging techniques like multivoxel MR spectroscopy and fluorine-18 fluorodeoxyglucose positron emission tomography (¹⁸F-FDG-PET) can enhance lesion differentiation, but tissue biopsy remains the gold standard for diagnosis.

Since the exact mechanism of radiation-induced injury is not fully understood, there is no definitive treatment available. For small, asymptomatic lesion, a conservative approach with close follow-up supplemented with imaging can be adopted. However, for symptomatic brain necrosis, the treatment strategy revolves around surgery and medical management, including glucocorticoids and anticoagulants. Additionally, researchers are also exploring alternative treatments like hyperbaric oxygen, high dose of

vitamins and novel interventions like bevacizumab, nerve growth factor, gangliosides, Shenqi Fuzheng injection, and laser interstitial thermal ablation.¹¹ Among the various treatments explored, bevacizumab, an anti-VEGF drug, has demonstrated the strongest evidence for treating CNS radiation necrosis. A placebo-controlled, double-blinded clinical trial by Levin et al demonstrated that administering bevacizumab at a dose of 7.5 mg/kg every 3 weeks, with the treatment repeated twice a week, led to significant symptom improvement and a reduction in necrotic lesion volume on MRI scans.¹⁰

Conclusion

We present the first reported case of cerebral radiation necrosis following radiation treatment for a meningioma on the contralateral hemisphere. The circumstances for this unusual fashion of complication on the contralateral to the radiation port remain unknown. The case highlights the potential importance of considering radiation necrosis in the differential diagnosis of any patient with the clinical and imaging features of a new intrinsic mass, regardless of time or location from previous irradiation.

Authors' Contribution

T.D. contributed to literature search and manuscript preparation. S.M. contributed to manuscript preparation. D.S. was the operating surgeon. R.K.S. was the pathologist. The manuscript has been read and approved by all the authors, requirements for authorship have been met, and each author believes that the manuscript represents honest work.

Conflict of Interest

None declared.

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