Diving Into Radiation Necrosis: Hyperbaric Oxygen Therapy in Cerebral Radiation Necrosis

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INTRODUCTION

Radiotherapy is a major treatment modality for CNS malignancies. Radiation necrosis is a common long-term toxicity of radiation therapy to the CNS, occurring in up to 50% of patients. It can be debilitating and may be complicated by headaches, seizures, cognitive decline, or focal neurologic deficits.[1]

CASE REPORT

A 43-year-old man with a history of right temporal anaplastic astrocytoma presented for surveillance 18 months after completing adjuvant radiation. He reported a new daily headache that had worsened since onset 3 months prior. His cancer therapy included a gross total resection, adjuvant radiotherapy (5,940 cGy), and adjuvant temozolomide that was discontinued after 8 of 12 planned cycles because of prolonged leukopenia and varicella zoster outbreak. Postoperative and surveillance magnetic resonance imaging (MRI) previously showed stable T2 hyperintensity along the resection margin consistent with postsurgical gliosis, but no evidence of radiation necrosis (Fig 1A). Surveillance MRI, however, revealed marked T2 hyperintensity in the right temporal lobe extending across midline and a new 2.7-cm area of restricted diffusion medial to the right ventricle (Fig 1B). Subsequent biopsy revealed necrotic tissue, inflammation, and gliosis consistent with radiation necrosis.

Given his worsening headache (rated 8 of 10 at maximum), he was offered treatment with glucocorticoids, bevacizumab, and/or hyperbaric oxygen therapy. After weighing these treatment options and potential toxicities, he elected for hyperbaric oxygen therapy alone. Each treatment consisted of 3 30-minute sessions at 2.0 atmospheres absolute with 100% oxygen. After 32 treatments, reported headache severity was 4 to 5 of 10, and surveillance MRI showed significant decrease in white matter T2 hyperintensities (Fig 1C). After all 60 treatments, MRI showed further improvement, with decreased edema and minimal residual enhancement (Fig 1D). Notably, he experienced improvement in frequency and intensity of headaches, with pain rating of 0 of 10 recorded 2 months after hyperbaric oxygen therapy.

DISCUSSION

Cerebral radiation necrosis typically develops 1 to 3 years after radiation, with higher dose per fraction being a major risk factor; however, the dose-response relationship may vary by brain region.[2] Radiation necrosis is hypothesized to occur via 2 primary mechanisms. Radiation disrupts the blood–brain barrier, causing vasogenic edema and vascular endothelial growth factor upregulation leading to pathological angiogenesis and cerebral edema. In addition, damage to small and midsized vessels causes reduction in microvasculature, chronic ischemia, and, ultimately, tissue necrosis.[1,3] These mechanisms may perpetuate indefinitely, causing necrosis of adjacent tissue.[1]

There is limited high-quality evidence to guide management of radiation necrosis. Surgical management is indicated for severely symptomatic cases to rapidly decrease intracranial pressure. Corticosteroids have been used in the treatment of radiation necrosis for decades; however, long-term use frequently leads to hyperglycemia, immunosuppression, and other adverse effects. The efficacy of bevacizumab is supported by class 1 evidence, but serious adverse effects, such as cerebral hemorrhage and thromboembolism, can limit use. Bevacizumab may lead to higher rates of radiographic response and symptomatic improvement compared with glucocorticoids; however, 6-month recurrence rates approach 30% with either treatment.[4]

Hyperbaric oxygen therapy has demonstrated the ability to return capillary density of irradiated tissues to 80% of normal; nonblinded prospective studies report radiographic and symptomatic improvement of radiation necrosis with hyperbaric oxygen therapy.[5] In many cases, the effect attributed to hyperbaric oxygen therapy is obscured by concomitant glucocorticoids or bevacizumab; studies evaluating hyperbaric oxygen therapy alone are scarce. Barotrauma, reversible myopia, and oxygen toxicity complicate less than 2% of cases, and seizures, while serious, are rarely reported.[3] This toxicity profile compares favorably with those of glucocorticoids and bevacizumab. Our patient experienced significant radiographic and clinical

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on March 30, 2020 and published at ascopubs.org/journal/op on June 15, 2020: DOI https://doi.org/10.1200/OP.20.00058

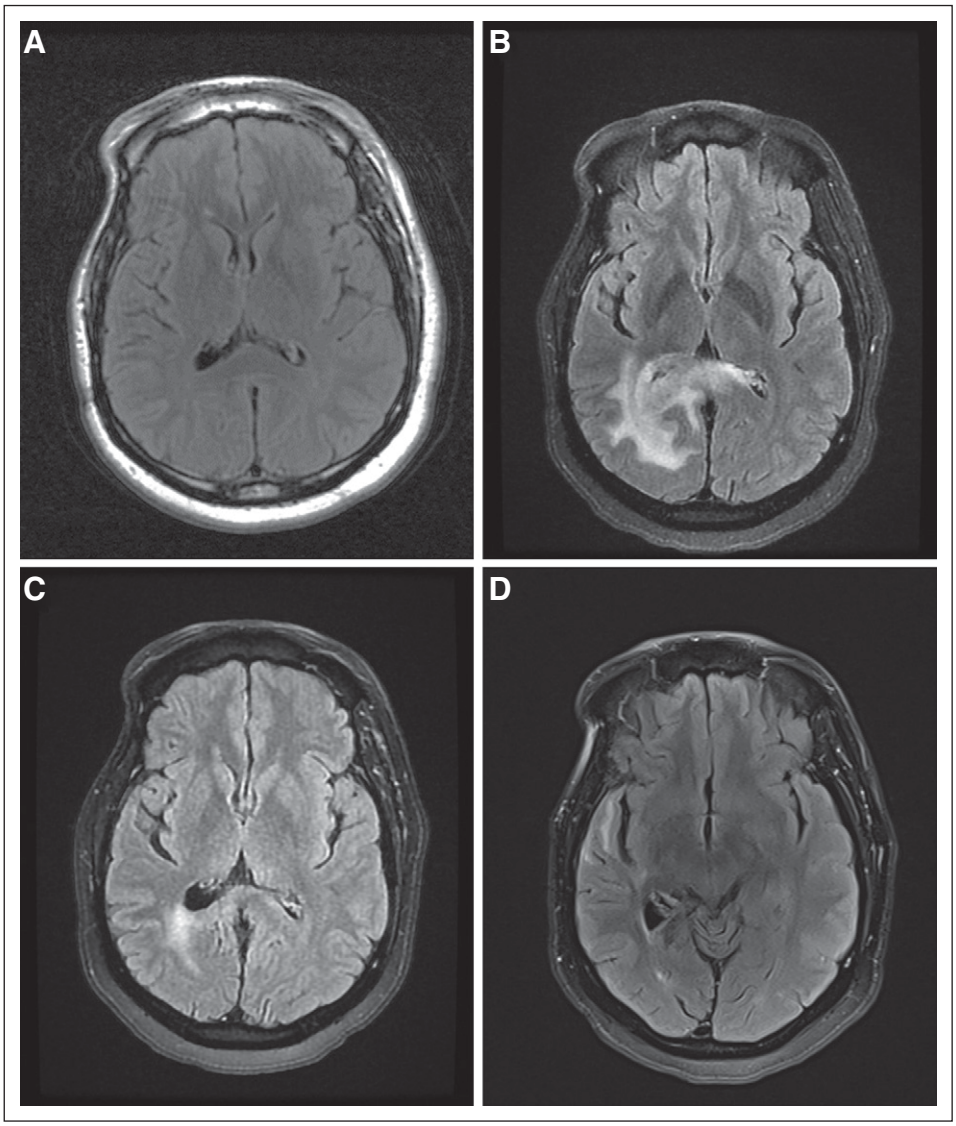

FIG 1. Axial T2-weighted magnetic resonance imaging scans from a patient who developed cerebral radiation necrosis 18 months after gross total resection and adjuvant radiation for treatment of anaplastic asrocytoma. (A) Surveillance imaging showed postoperative gliosis with no evidence of radiation necrosis. (B) Surveillance magnetic resonance imaging revealed abnormal white matter signal in the right temporal lobe with extension across midline. (C). Radiation necrosis was confirmed with biopsy and images obtained after 32 and (D) 60 treatments with hyperbaric oxygen monotherapy showed marked radiologic improvement.

improvement of radiation necrosis with hyperbaric oxygen therapy as monotherapy. Hyperbaric oxygen therapy may be effective as monotherapy in select patients with radiation necrosis. However, high-quality studies are needed to elucidate optimal dosing, patient selection, and to confirm safety and efficacy.

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PRIOR PRESENTATION

Presented at the American College of Physicians Air Force-Army Chapter Scientific Meeting, San Antonio, TX, September 5, 2019.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

Disclosures provided by the authors and data availability statement (if applicable) are available with this article at DOI https://doi.org/10.1200/OP.20.00058.

AUTHOR CONTRIBUTIONS

Conception and design: All authors
Collection and assembly of data: All authors
Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

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Stock and Other Ownership Interests: Editas Medicine, Intellia Therapeutics, Bristol-Myers Squibb, AbbVie, Odonate Therapeutics
Travel, Accommodations, Expenses: DAVA Pharmaceuticals

No other potential conflicts of interest were reported.