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Case report

Treatment of steroid refractory, Gamma Knife related radiation necrosis with bevacizumab: Case report and review of the literature

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1. Introduction

Radiation necrosis is the most significant complication associated with Gamma Knife radiosurgery. It typically becomes manifest as a necrotic white matter lesion 3 or more months following treatment [3]. Treatment volume and radiation dose are the two most important predictors of radiation necrosis. Once radiation necrosis has become clinically apparent treatment has historically been limited to corticosteroids. Antiplatelet agents, anticoagulants and hyperbaric oxygen have been studied but there is currently minimal high quality evidence to support their use in routine clinical practice [6]. If the radiation necrosis fails to respond to steroid treatment therapeutic options are limited.

Recent trials have highlighted a potential role for bevacizumab, a monoclonal antibody directed against vascular endothelial growth factor (VEGF) in the treatment of radiation necrosis from conventional radiation therapy [14]. We present a case of symptomatic radiation necrosis following Gamma Knife radiosurgery for multiple atypical WHO grade II meningiomas initially unresponsive to steroid treatment and ultimately responsive to bevacizumab therapy.

2. Case report

History: This 38 year old man was referred to the University of Pennsylvania in 2005 after presenting to an outside hospital with dizziness. Magnetic resonance imaging (MRI) at the time revealed a large, extra-axial biparietal mass (Fig. 1). He underwent a craniotomy and pathology confirmed the diagnosis of atypical WHO grade II meningioma. He subsequently received external beam radiation therapy to a total dose of 59.5 Gy. His tumor recurred in two separate areas adjacent to the resection cavity in 2007 and he was treated with Gamma Knife radiosurgery to each area with a dose of 18 Gy to the 50% isodose line.

Two years later, in 2009 the patient suffered a third recurrence outside of the Gamma Knife radiosurgery field but within the external beam field and received a second Gamma Knife radiosurgery treatment with 18 Gy to the 50% isodose line (Fig. 2). Three months later a separate recurrence was treated with repeat surgery with pathology revealing a mix of radiation necrosis and tumor recurrence.

Presentation and examination: The patient presented to the emergency department at the University of Pennsylvania 6 months after his last surgery and 9 months after the most recent Gamma Knife radiosurgery treatment with 4 days of progressive lower extremity weakness, multiple falls and urinary incontinence. Examination revealed bilateral lower extremity spasticity with 3/5 strength in his hip flexors, knee flexors and knee extensors on the right and 2/5 on the left. He also exhibited pronounced proximal 2/5 weakness in his right upper extremity and 4/5 in his proximal

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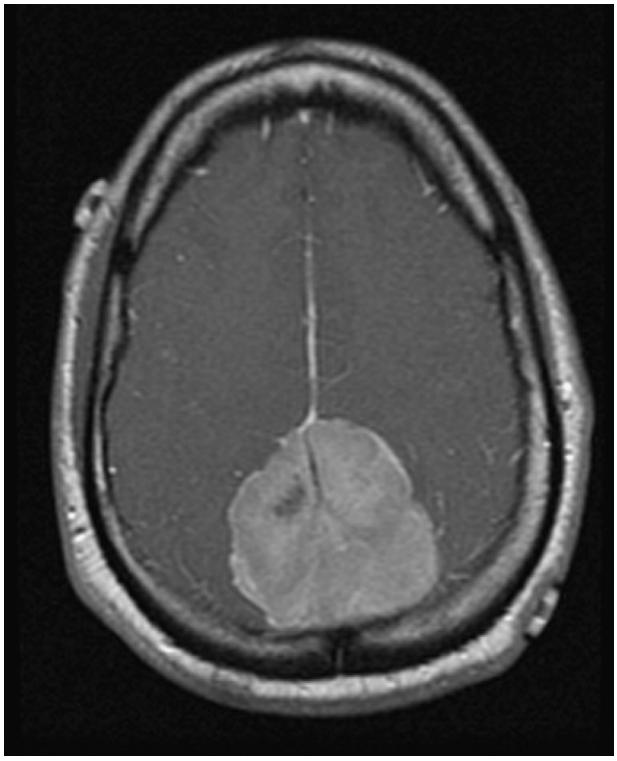

Fig. 1. T_1 weighted post-gadolinium image demonstrating a large extra-axial parietal mass extending from the falx and sagittal sinus bilaterally.

left upper extremity. Babinski signs were present bilaterally. He exhibited sustained clonus bilaterally.

Imaging findings: An MRI was obtained demonstrating an increase in size of the enhancing mass centered along the superior falx with multiple small foci of enhancement within the bilateral parietal lobes (Fig. 3a). FLAIR imaging revealed significant edema within the bilateral frontal and parietal lobes (Fig. 3b). MR perfusion imaging did not show a visible increase in regional cerebral blood volume (rCBV) in the region of evolving edema and enhancement.

Hospital course: The patient was admitted to the neurosurgical service and started on 4 mg of dexamethasone every 6 h. After 8 days of hospitalization and treatment with dexamethasone there was minimal improvement in his neurological exam. Following consultation with the patient and his family he was given bevacizumab (10 mg/kg). Four days following administration a follow-up MRI demonstrated markedly reduced T_1 post-contrast enhancement (Fig. 3c) and FLAIR signal (Fig. 3d). There was also a substantial improvement in the neurological exam, with strength returning to 5/5 in the upper extremities and right lower extremity and to 4/5 in the left lower extremity. He remained incontinent of urine and was discharged to a rehabilitation facility where he experienced a transient improvement in his symptoms. He was readmitted 4 months after his treatment with bevacizumab with increased seizures; imaging revealed disease progression with increased edema. His neurological exam had deteriorated to the point that he was no longer ambulatory and he elected to forego further surgery or medical treatment with bevacizumab and enter hospice care.

3. Discussion

Radiation therapy is generally effective in delaying recurrence of atypical and malignant meningiomas [10]. In addition, Gamma Knife stereotactic radiosurgery can be used to treat meningiomas

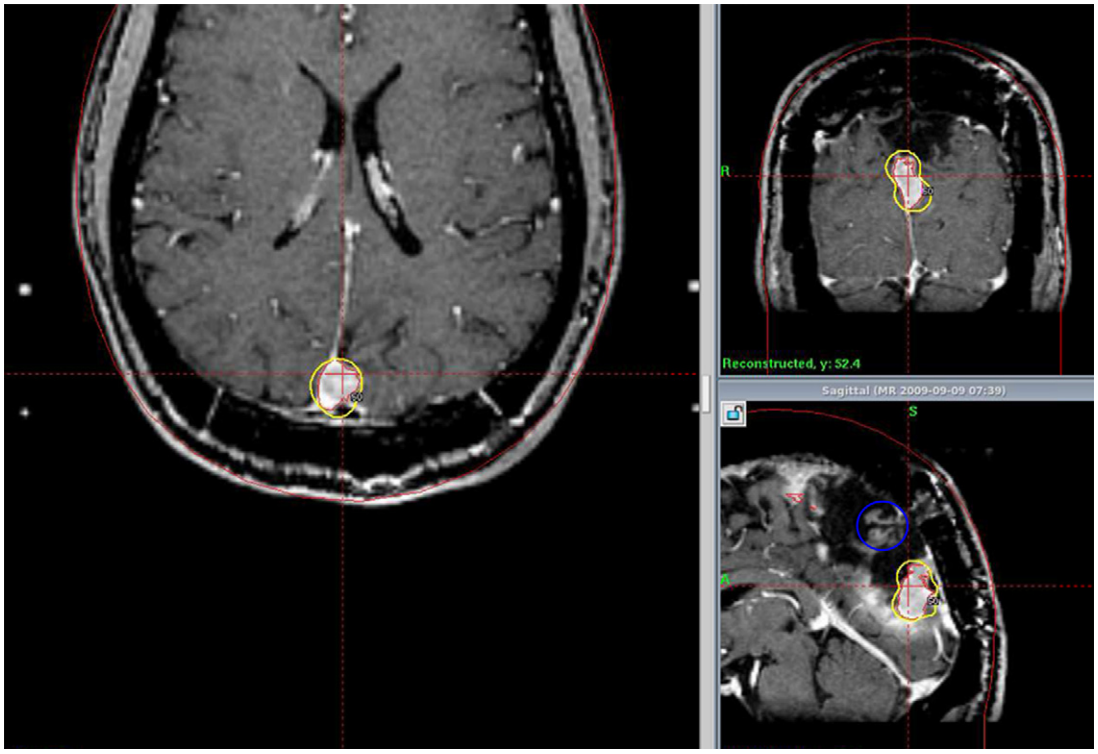

Fig. 2. Axial, coronal and sagittal MR images used in planning the patient's second treatment in the Gamma Knife. The yellow circles delineate the 50% isodose lines. The blue circle marks the approximate location of prior Gamma Knife radiosurgery. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)