Radiation Necrosis of a High-grade Glioma
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A 64 year old male was referred to the Neurosurgical Service at Rhode Island Hospital for evaluation of a left frontal mass. Given proximity of the lesion to eloquent cortex, resection was not performed and a histopathologic diagnosis of grade III anaplastic oligoastrocytoma was made through biopsy. The patient was enrolled in an experimental treatment protocol that included Paclitaxel Poliglumex (PPX; a microtubule stabilizer and mitotic inhibitor with a radiosensitization index of 4-8), temozolomide, and radiation. The patient also underwent two cycles of maintenance temozolomide therapy and a third cycle of dose-intensive temozolomide therapy. Serial MR imaging with perfusion-weighted imaging was performed at multiple time points throughout treatment.

Imaging Findings
Initial pre-biopsy brain MRI (Figure 1a) demonstrated a 2.7 cm heterogeneously enhancing mass in the left posterior frontal operculum (white arrow), and a second smaller enhancing nodular lesion (Figure 1b) in the left frontal lobe (white arrowhead). Both of these enhancing lesions demonstrated significantly elevated relative cerebral blood volume (rCBV) on perfusion-weighted imaging (Figures 1c and 1d). Follow-up MRI at three months following completion of PPX therapy demonstrated substantial response to treatment at the site of the left frontal opercular mass (not shown), with minimal residual enhancement and reduced mass effect. The left frontal nodular lesion was shown to have slightly increased enhancement with persistent but stable, elevated rCBV. (Figures 2a and 2c)

Follow-up imaging at 8 months following completion of PPX therapy demonstrated significantly increased enhancement associated with the left frontal satellite lesion. (Figure 2b, white arrowhead) However, the corresponding rCBV was substantially smaller, approximating that of normal appearing contralateral white matter (Figure 2d), consistent with radiation necrosis and not tumor progression. The patient underwent a brain biopsy nine days after the MRI, and histopathology confirmed the imaging findings, demonstrating

Figure 1: Preoperative contrast-enhanced T1-weighted MRI imaging was obtained with additional corresponding MR perfusion-weighted images. A heterogeneously enhancing left frontal opercular lesion is demonstrated (A, white arrow) with an additional enhancing satellite lesion in the left frontal lobe (B, white arrowhead). Both of these lesions demonstrate increased rCBV on the corresponding perfusion-weighted images (C and D).

Figure 2: Serial follow-up contrast-enhanced T1-weighted MRI imaging as well as corresponding perfusion-weighted imaging was obtained at 3 months as well as 8 months after resection and initiation of chemotherapy and radiation. 3 month follow-up imaging demonstrates slightly increased enhancement of the left frontal opercular lesion (A, white arrowhead) with stable rCBV (C, white arrow). Follow-up imaging at 8 months demonstrates significantly increased enhancement of the left frontal satellite lesion (B), however the associated rCBV had significantly decreased, approximating that of normal contralateral white matter (D). These findings were most suggestive of radiation necrosis, which was confirmed by histology.
“quiescent” tumor with foci of necrosis and positive Ki-67 (a marker of cellular proliferation) in only approximately one percent of tumor cells.

**DISCUSSION**

Radiation therapy and chemotherapeutic agents that act as radiation sensitizers are often used in the treatment of patients with high-grade gliomas. Following treatment, patients may deteriorate clinically with progression of enhancement on follow-up brain MRIs that looks similar for both radiation necrosis and true progression of tumor. Recurrent tumor demonstrates angiogenesis and microvascular proliferation, and indicates treatment failure. Radiation necrosis is a sign of treatment response manifested as endothelial cell damage and decreased capillary perfusion and may actually be associated with longer survival than in cases without radiation necrosis. Therefore, distinguishing between these two entities carries significant clinical implications. Traditionally, serial MRI and stereotactic biopsy have been the primary methods of diagnosing radiation necrosis. MR perfusion-weighted imaging (PWI) may help differentiate radiation necrosis and recurrent or residual neoplasm, and this remains an active area of investigation.

PWI measures cerebral perfusion by utilizing the transient microscopic magnetic field disturbances that are induced by a bolus injection of exogenous paramagnetic contrast material. Rapid MRI acquisition permits estimation of contrast concentration-time curves utilizing modified tracer kinetic principles. A variety of hemodynamic parameters can subsequently be computed. Of these parameters, rCBV has been the most widely used and has been demonstrated to correlate with tumor grade and tumor microvascular density. Preliminary investigations have demonstrated that decreasing rCBV values over time is indicative of response to treatment, whereas increasing rCBV values suggests tumor progression and treatment failure. In the case above, the enlarging enhancing lesion had decreasing rCBV, consistent with treatment effect or “pseudoprogression,” and this was confirmed on biopsy.

**REFERENCES**


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**Disclosure of Financial Interests**

The authors and/or their spouses/significant others have no financial interests to disclose.

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