

# Pearls & Oy-sters: Large vessel ischemic stroke secondary to glioblastoma multiforme

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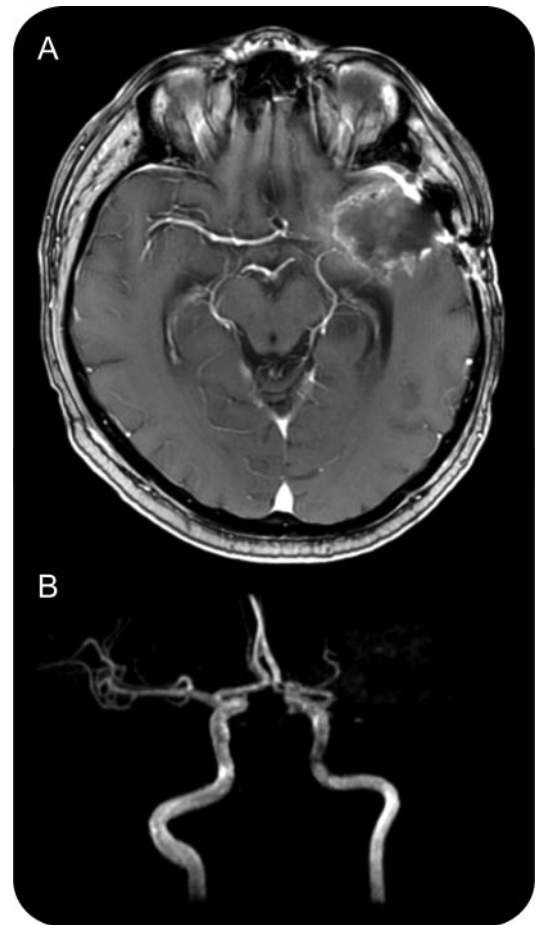
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## PEARLS

- Large vessel ischemic strokes uncommonly account for new focal deficits in patients with primary brain tumors, mimicking intratumoral hemorrhage, tumor progression, or Todd paralysis.
- Stroke occurring in the context of a primary brain tumor is usually a postoperative complication, a late complication of radiation therapy, or embolic due to a hypercoagulable state induced by the tumor.
- Rarely, direct vessel occlusion by an adjacent primary brain tumor may cause a large vessel ischemic stroke.

**CASE REPORT** A 41-year-old right-handed non-smoker with glioblastoma multiforme and no known vascular risk factors developed sudden onset right upper extremity weakness 7 months after he was diagnosed with left temporal glioblastoma multiforme by stereotactic biopsy, 5 months after treatment with radiation therapy and temozolomide, and 4 months after gross total resection with placement of Gliadel™ wafers. His past medical history was negative for hypertension, hyperlipidemia, diabetes, or coronary artery disease. On examination, he was unable to lift his right arm against gravity. MRI revealed a left corona radiata infarct. Gadolinium-enhanced T1 images revealed complete occlusion of the left middle cerebral artery (MCA) at M1 (figure, A). No secondary stroke prevention therapy was initiated. Two months later, he presented with transcortical motor aphasia due to an acute extension of his previous stroke, as evidenced by new diffusion-weighted imaging findings. Magnetic resonance angiography (MRA) showed an occluded left MCA, with some indistinct distal filling from collaterals (figure, B). A workup included 48-hour telemetry which revealed no arrhythmias, and a transthoracic echocardiography which revealed no clots, and no patent foramen ovale. He was not started on aspirin because of temozolomide-related thrombocytopenia.

**Figure** Left MCA occlusion on brain MRI and magnetic resonance angiography



(A) Occlusion of the left middle cerebral artery (MCA) in close proximity to the tumor on gadolinium-enhanced T1-weighted MRI sequences. (B) Magnetic resonance angiography revealing complete occlusion of the left MCA proximally, with some distal indistinct filling from collaterals. The intracranial vascular arterial tree is otherwise normal.

**DISCUSSION** New neurologic deficits in patients with primary brain tumors can be secondary to tumor progression (edema, necrosis, hemorrhage), Todd paralysis, or rarely strokes. A sudden clinical onset suggests a vascular etiology rather than tumor progression. How-

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ever, differentiating between these entities on clinical grounds is usually challenging, and we often rely on imaging. Interpretation of imaging can be challenging itself; for instance, when DWI hyperintensities are anatomically adjacent to the tumor, they can be related to changes around the tumor, and are not necessarily ischemic in nature. Moreover, DWI hyperintensities can be secondary to prolonged seizure activity. Follow-up imaging is needed in these cases.

Ischemic strokes in patients with primary brain tumors are usually a postoperative complication, a late complication of radiation therapy, or embolic due to the hypercoagulable state induced by the tumor. In addition, there are case reports relating certain chemotherapeutic agents to an increased risk of strokes, notably L-asparaginase, cisplatin, 5-fluorouracil (5-FU), and methotrexate. Infectious vasculopathies (varicella zoster and syphilis) can also cause strokes in immunosuppressed patients.

While in our patient vessel occlusion occurred in the field of previous radiation, the occurrence of the stroke a few months after radiation therapy excludes radiation as the culprit, as radiation vasculopathy usually develops years after radiation therapy.<sup>1,2</sup> In addition, radiation-induced large vessel occlusive vasculopathy occurs predominantly in patients exposed to radiation as young children.<sup>2</sup> In situ atherosclerotic disease of the MCA is unlikely in this relatively young man with no cardiovascular risk factors, and an otherwise normal vascular tree on MRA. No cardiac or proximal arterial embolic source could be identified. While a transesophageal echocardiogram would have been more sensitive for cardioembolic sources, and particularly for nonbacterial thrombotic endocarditis (NBTE), patients with primary brain tumors do not seem to be at high risk for NBTE, as do patients with systemic cancers.<sup>3</sup> In addition, the stepwise extension of the stroke area, at a 2-month interval, favors a local progressive mechanism. The large vessel ischemic stroke was therefore attributed to a direct effect of the tumor on the MCA.

In a recent retrospective study on 68 stroke patients with known brain tumors, postoperative complications and radiation therapy accounted for 48% and 25% of stroke etiologies.<sup>4</sup> In that series, of the total 4 reported nonpostoperative large vessel ischemic strokes, 3 were attributed to previous radiation therapy, but the authors did not comment on the underlying stroke mechanism in the remaining patient. Five other cases with a brain tumor as the likely primary cause for a large vessel ischemic stroke have been published.<sup>5-8</sup> They all had a temporal glioblastoma multiforme, and an MCA territory stroke on the same side.

The intimate anatomic relation between the vessel and the tumor in our case, as well as the other similar

reported cases in the literature, suggest 3 possible stroke mechanisms: mechanical compression, vessel infiltration by tumor cells, or a local procoagulant effect mediated by tumor-secreted factors. The third mechanism seems more appealing as all the cases occurred in the setting of a glioblastoma—a tumor with known procoagulant properties. Indeed, glioblastomas have been shown to express tissue factor, the body's most potent procoagulant, in response to hypoxia,<sup>9</sup> and they were associated with the highest rate of intravascular thrombosis (92%) in a recent histopathologic study that included primary and metastatic brain tumors.<sup>10</sup>

Strokes in brain tumor patients are often not considered the neurologic priority, which leads to incomplete evaluations and treatments. With the advent of new oncologic therapeutic modalities leading to prolonged survival in these patients, it is becoming increasingly important to thoroughly evaluate stroke and initiate secondary prevention with antiplatelets when possible.

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