

# Delayed Development of Radiation Vasculopathy of the Brain Stem Confirmed by F-18 FDG PET in a Case of Anaplastic Astrocytoma

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**Abstract:** We present the imaging findings of a 38-year-old female patient who underwent resection and radiation therapy for an anaplastic astrocytoma in her left temporal lobe 12 years ago. She was symptom-free until 1 month before admission at which time she presented with symptoms of right hemiparesis, right facial droop, and slurred speech. Magnetic resonance imaging (MRI) of the brain showed a new mass lesion in the left pontine region of the brain stem. Magnetic resonance spectroscopy imaging of the lesion demonstrated an increase in choline (Ch)/N-acetyl aspartate (NAA) metabolite values which were nondiagnostic. Since viable tumor recurrence was strongly suspected, a biopsy was planned, although this posed significant risk. Therefore, an F-18 FDG brain PET scan was performed, which demonstrated no metabolic activity in the pontine lesion leading to the less common diagnosis of long-term postradiation vasculopathy. Over the next 6 months, the patient's symptoms slowly improved and a follow-up MRI scan showed a decrease in the size of the lesion, consistent with postradiation vasculopathy and infarction. This case illustrates the importance of considering the rare diagnosis of radiation-induced vasculopathy in the differential diagnosis when symptoms of recurrent brain tumor occur.

**Key Words:** F-18 FDG, brain stem mass, radiation vasculopathy, anaplastic astrocytoma

(*Clin Nucl Med* 2007;32: 527–531)

The incidence of primary intracranial malignancy is approximately 7 cases per 100,000 persons per year.<sup>1</sup> Anaplastic astrocytoma is classified as grade 3 by the World Health Organization (WHO), a category that falls between low (1 and 2) and high-grade<sup>2</sup> astrocytomas.<sup>3,4</sup> Common presenting symptoms are seizures, focal neurologic symptoms, headache, and vomiting among others depending on the location of the tumor. Overall, there is a poor prognosis with

an average survival of 2 years.<sup>2</sup> The peak incidence is in the fifth and sixth decades of life. On magnetic resonance imaging (MRI), anaplastic astrocytomas typically show inhomogeneous, mixed attenuation intensity with rim enhancement, and usually with surrounding edema.<sup>5,6</sup> While these tumors can occur anywhere in the cerebral hemispheres, they are most common in the frontal and temporal lobes. The treatment of astrocytomas can involve surgical resection, radiation therapy, and chemotherapy.<sup>7,8</sup> Long-term complications of radiation therapy include radiation vasculopathy and secondary malignancy. Secondary malignancy development after radiation therapy for the central nervous system has a risk of approximately 1%–3%.<sup>9–14</sup>

The latency from radiation therapy treatment to the development of vasculopathy ranges from 2 to 25 years with peak incidence at approximately 3 years.<sup>15,16</sup> Cases of delayed radiation injury that developed as late as 27 years after radiotherapy are extremely rare.<sup>17</sup> To date, there have been very few cases of radiation-induced neoplasm reported after radiosurgery.<sup>18</sup> In another case report radiation vasculopathy of intracranial major arteries in children has also been described.<sup>19</sup> It has been hypothesized that deterioration in prostaglandin I-2 synthesis plays a key role in the genesis of radiation-induced vasculopathy.<sup>20</sup>

In addition, it has been suggested that accelerated atherosclerosis develops in large arteries leading to repeated small strokes. The histopathology of radiation vasculopathy is thought to be the result of cerebral capillary destruction leading to abnormal permeability of the blood brain barrier.<sup>21</sup>

The brain stem has many vital functions, including consciousness, controlling heart rate, and respiratory rate. Brain stem lesions typically present as gait disturbance, headache, and weakness of the limbs, diplopia, and/or dysphagia. Other symptoms include weakness of one or more limbs, signifying involvement of the corticospinal, and corticobulbar pathways.<sup>22</sup> The brain stem accounts for less than 2% of gliomas and are more common in children than adults.<sup>23,24</sup> On MRI, brain stem tumors are typically isointense or hypointense on T1-weighted images, hyperintense on T2-weighted images, and enhance uniformly after administration of intravenous gadolinium contrast.<sup>25,26</sup> The close proximity of these tumors to the surrounding critical normal structures limits invasive procedures such as biopsy or surgical resection.

Received for publication August 18, 2006; revision accepted March 27, 2007.

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ISSN: 0363-9762/07/3207-0527

In terms of imaging for tumor recurrence, CT and MRI cannot reliably differentiate tumor recurrence from radiation related changes. MR spectroscopy is particularly helpful for the differentiation of locally infiltrative tumor from other types of well-circumscribed intracranial lesions.<sup>27</sup> Measurement of choline (Ch) and *N*-acetyl aspartate (NAA), and their ratio (Ch/NAA) has shown promise in distinguishing high grade from low-grade lesions.<sup>28,29</sup> Magnetic resonance spectroscopy imaging (MRSI) may be helpful in guiding biopsy location within lesions that are heterogeneous in nature or with necrotic or cystic components. F-18 FDG PET scanning has been widely employed in assessment of brain tumors. It has shown tremendous utility in the evaluation and management of patients with brain tumors including grading of such tumors and determination of prognosis.<sup>30-32</sup>

### CASE REPORT

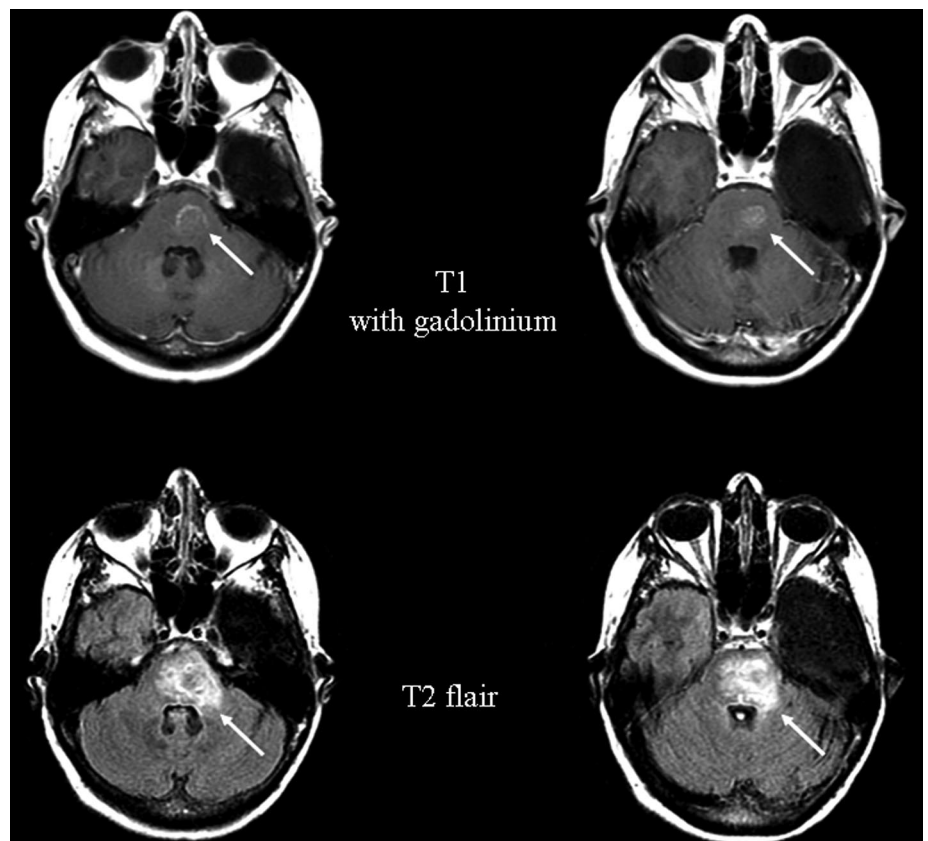
The patient is a 38-year-old female patient who underwent a left temporal craniotomy for resection of an anaplastic astrocytoma 12 years ago for which she received whole brain radiation therapy. Subsequently she underwent periodical clinical and MR follow-ups. The patient was in her usual good state of health, until she suffered progressive right facial droop, dysarthria, and slurred speech as well as right hemiparesis, 12 years after resection. Brain MRI and MRSI were performed, followed by F-18 FDG PET.

### METHODS

The patient was imaged with GE LX Echospeed (General Electric Medical Systems, Milwaukee, WI) high-field strength 1.5 Tesla (T) MRI scanner, Sagittal T2-weighted, axial FLAIR, proton density, axial T1 weighted, without and with IV Gadolinium-DPTA (Gd) enhancement. <sup>1</sup>H MR spectroscopic Imaging (PRESS 2D CSI, TR: 1000–1500 milliseconds, TE: 35,144,288 milliseconds) was performed at 1.5 T over the lesion. Volumes of interest ( $1.6 \times 1.6 \text{ cm}^3$ ) selected from the lesion center were analyzed for Ch and NAA in each zone. F-18 FDG PET scan was obtained on a Siemens ECAT EXACT HR+ in 3D mode, with an in-plane resolution of 6 mm, full width half maximum, matrix size of  $128 \times 128$ , 25 cm field-of-view. In a quiet and dimly lit room, with minimal ambient noise to decrease any stimulation of the brain, 406 MBq (10.97 mCi) of F-18 FDG was injected intravenously. Following a 30-minute uptake period, transmission images were obtained for the initial 10 minutes followed by a 30-minute emission acquisition. The images were reoriented in the transverse, sagittal, coronal, and canthomeatal planes. The PET data was coregistered with the MR images using the Siemens Syngo software suite.

### RESULTS

Interval postsurgery imaging and follow-up MRI of the brain showed a thin rim of T2 prolongation within the parenchyma adjacent to the resection bed in the inferotemporal fossa,



**FIGURE 1.** Axial T1 with gadolinium contrast, and axial T2 flair images show abnormal signal throughout the uncus and into the pons, concerning for tumor spread.

frontal and parietal lobes with no evidence of enhancing tumor. The findings have been consistent with radiation-induced leukomalacia. When the patient presented with progressive neurologic symptoms, MRI of the brain revealed a new focus of enhancement in the left pons with surrounding edema suggestive of possible tumor recurrence (Fig. 1). Again there was evidence of leukomalacia in the surgical bed. MRSI of the lesion showed diminished NAA/Ch peak and an increase in Ch/NAA metabolite values which were nondiagnostic (Fig. 2). Because of worsening symptoms, consideration was made to perform a biopsy. However, because of the critical location of the mass in the pons that was close to other vital structures noninvasive evaluation with F-18 FDG PET was recommended to confirm suspected tumor. The F-18 FDG PET scan showed diminished F-18 FDG uptake in the left pons (Fig. 3). The PET findings were consistent with long-term radiation vasculopathy resulting in brain stem infarction. The most recent follow-up MRI of the brain after the PET scan showed a decrease in enhancement in the area of abnormal signal in the left pons (Fig. 4).

### DISCUSSION

Diffuse leukodystrophy with confluent regions of subcortical gliosis and demyelination can occur secondary to chronic radiation injury.<sup>33,34</sup> Cerebral capillaries may be destroyed leading to abnormal permeability of the blood brain barrier. This leads to enhancement on cerebral MRI in regions of radiation changes, which frequently renders delineation between radiation-induced necrosis and tumor recurrence very obscure. The confounding medical problem is that these patients often present with clinical symptoms similar to those of tumor recurrence. On radiologic imaging, diffuse white matter injury appears hypointensifying on CT and hyperintense on MR imaging.<sup>18,19,35</sup>

On F-18 FDG PET, recurrence of the tumor in brain stem typically appears as an area of increased uptake more than the white matter. This case highlights the importance of considering radiation vasculopathy in the differential diagnosis of recurrence of symptoms in patients with brain stem tumor status postradiation. In this illustrated example, radiation vasculopathy occurred as a long-term complication extremely late and had symptoms similar to recurrent disease and in a different location other than the original site of the tumor. MR imaging to confirm the diagnosis is usually sufficient, however, as depicted here, the MRI and even MRS were inconclusive. The findings on the follow-up MR scan, 12 years after resection of the primary tumor, along with the clinical presentation, prompted high suspicion for recurrent disease, or for a primary brain stem glioma, albeit less likely. The evaluation of F-18 FDG PET in this case demonstrated hypometabolism of the mass in the pons, with intensity of FDG uptake less than normal white matter activity, consistent with a benign entity. Stereotactic biopsy of cerebral tumors can provide a pathologic diagnosis but this can be invasive with a complication rate lower than that of craniotomy. Diagnostic yield depends on safe sampling of the most representative region of the mass.<sup>32</sup> The fact that the lesion in question was ametabolic spared the patient from having a biopsy of the mass located in a strategically dangerous area.

### CONCLUSIONS

Patients who present with clinical symptoms akin to tumor recurrence long after radiation pose a complex diagnostic problem. Routine anatomic imaging modalities like MR may reveal new mass lesions that obligate the clinician to take the biopsy route. F-18 FDG PET imaging should be performed in

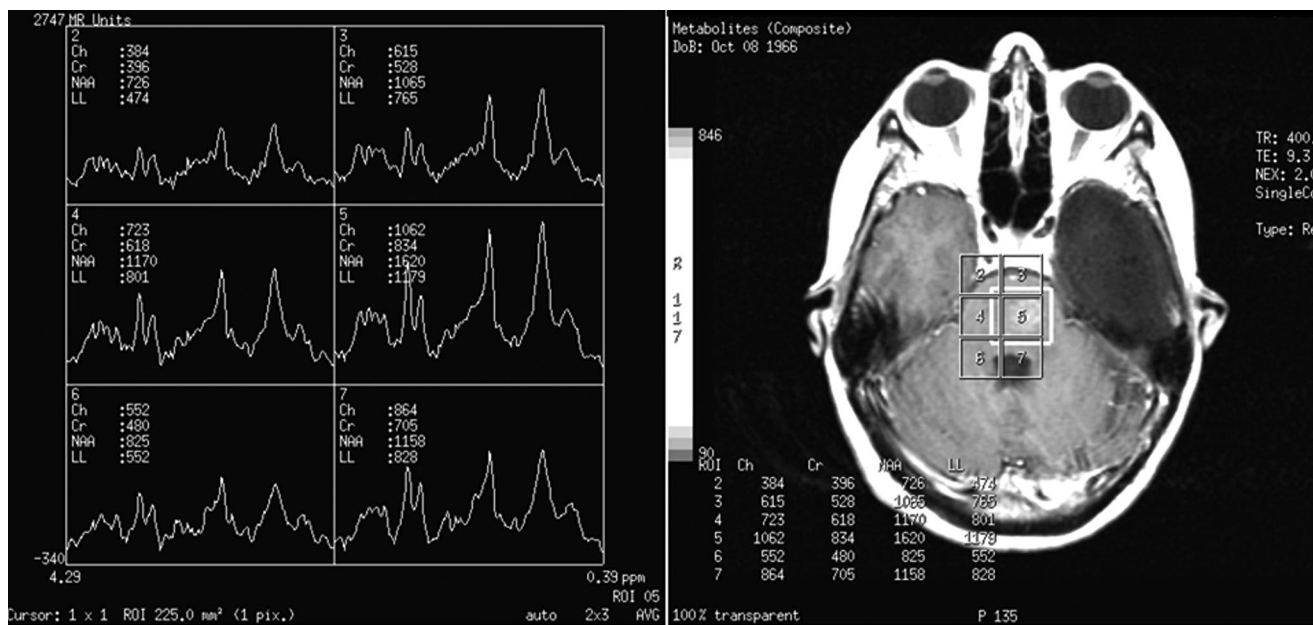
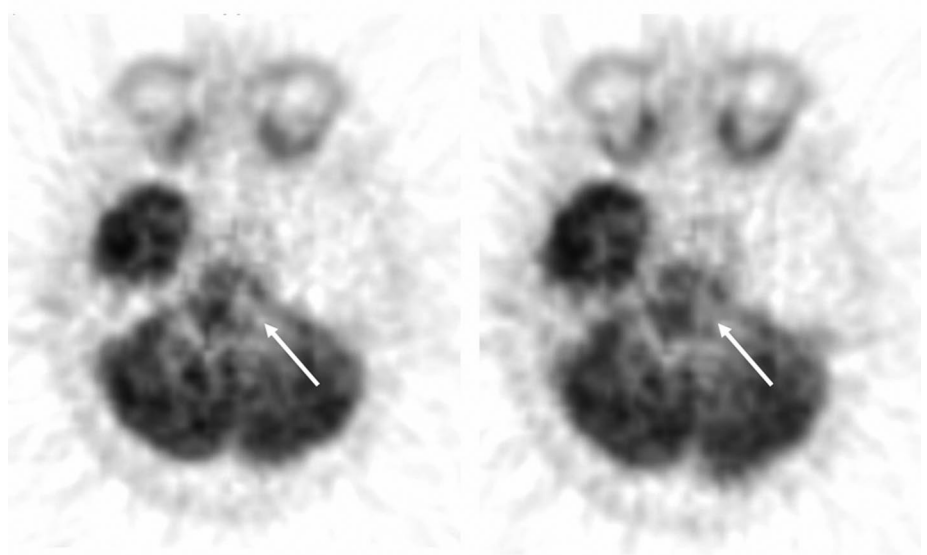
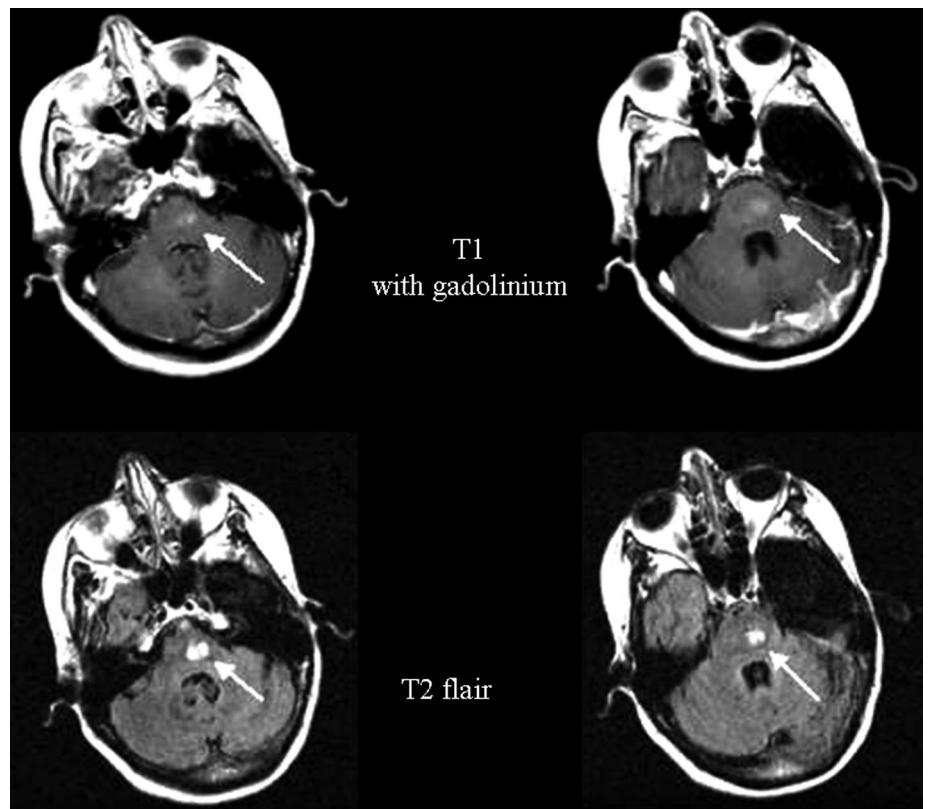


FIGURE 2. MR Spectroscopy centered over the left rim enhancing pontine lesion and over a normal appearing region in the right posterior temporal lobe is shown. The spectrum centered over the left pontine lesion reveals a diminished NAA/choline ratio. The relative choline peak is increased relative to NAA, the pattern is nonspecific and not typical for tumor. The control spectrum over the normal right temporal lobe region is within normal limits.





**FIGURE 3.** FDG PET shows decreased F-18 FDG uptake in the location of the enhancing lesion seen on the MRI in the pons region with no evidence of viable tumor.



**FIGURE 4.** The most recent follow-up MRI with gadolinium shows marked diminution of the size and the intensity of the signal in the previously noted abnormal area of enhancement in the brain stem (arrow), further supporting radiation-induced infarction rather than tumor recurrence.

such circumstances before an invasive procedure is contemplated and could often circumvent a risky course of action. In the case presented, a new lesion appeared farther away from the original tumor site more than a decade after the initial radiation. The lack of uptake on F-18 FDG PET corresponding to the area of abnormal signal on MRI confirmed that the brain stem lesion was long-term radiation-induced vasculopathy and not tumor

recurrence, which correctly precluded the patient from having a preventable invasive procedure.

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