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MR and Positron Emission Tomography with Fludeoxyglucose F 18 in Gliomatosis Cerebri

Mark A. Dexter, Geoffrey D. Parker, Michael Besser, Jonathan Ell, and Michael J. Fulham

Summary: A 16-year-old girl presented with a unilateral third nerve palsy and predominant gray matter involvement on MR and positron emission tomography with fludeoxyglucose F 18. These findings were manifestations of gliomatosis cerebri. The antemortem diagnosis was made by partial temporal lobectomy.

Index terms: Gliomatosis; Brain, neoplasms; Positron emission tomography

Reports that describe a diffuse overgrowth of the central nervous system with neoplastic glia have appeared in the literature since the turn of the century (1). Nevin in 1932 used the term *gliomatosis cerebri* for this condition (2). Early neuroradiologic investigations, namely cerebral angiography and pneumoencephalography, demonstrated only minor or nonspecific changes in the presence of a devastating clinical condition (3, 4). Computed tomography (CT) also often does not demonstrate specific morphologic changes in gliomatosis cerebri (5), and demyelinating and dysmyelinating conditions often cause confusion (6). Spagnoli et al (7) suggested that magnetic resonance (MR) imaging heralded the era of "unambiguous delineation and diagnosis" of gliomatosis cerebri when they demonstrated extensive lesions with high signal intensity on T2-weighted images at 1.5 T. We report the case of a 16-year-old girl who presented with a unilateral painless third nerve palsy as the first sign of biopsy-proved gliomatosis cerebri, and we discuss the role of MR imaging and positron emission tomography with fludeoxyglucose F 18 (FDG PET) in the preoperative diagnosis.

Case Report

A 16-year-old girl presented with diplopia in June 1992. On examination there was a right third nerve palsy with pupillary sparing. Cerebral computed tomography (CT) findings were normal. MR imaging was performed at 1.5 T and T1- and fast spin-echo T2-weighted pulse sequences and T1-weighted spin-echo pulse sequences after intravenous administration of gadopentetate dimeglumine were obtained. Focal areas of cortical thickening in lateral and mesial right frontal lobe and insula were seen, but underlying white matter was normal (Fig 1). The thickened cortex had slightly increased signal intensity on T2-weighted images but did not enhance with intravenous gadopentetate dimeglumine. Right internal carotid angiography was normal. The provisional radiologic diagnosis was focal polymicrogyria. MR studies performed 3 months later revealed a small but definite increase in the degree of gyral thickening in right frontal and temporal lobes together with mild uncal herniation and compression of the right third nerve. Again, white matter was not involved.

Nine months later diplopia and mild left-sided weakness developed. The patient was admitted to the hospital, where bilateral (worse on the right) third nerve palsies with pupillary sparing and a mild left hemiparesis were noted. MR showed increased cortical thickening and signal intensity in right frontal lobe and insula and hyperintensity in left mesial frontal cortex, right thalamus, and right striatum. White matter was normal (Fig 2). An FDG PET study was performed after the injection of 370 MBq of FDG. Blood sampling was not performed, and the eyes and ears were not patched. Marked reduction in FDG uptake in the right temporal and both frontal lobes was seen (Fig 3). Relative glucose hypometabolism also was noted in right thalamus and striatum when compared with the left. Focal areas of increased FDG uptake were not seen in the white matter. The patient deteriorated soon after admission with bilateral fourth nerve palsies, a right sixth nerve palsy, and drowsiness. Oral corticosteroids were commenced and an exploratory right temporal craniectomy was performed. At surgery the right temporal lobe was noted to be pale and swollen. The anterior 3 cm of the right temporal lobe were excised. After surgery the patient's drowsiness and the fourth and sixth cranial nerve palsies resolved, and there was marked improvement in the third nerve palsies.

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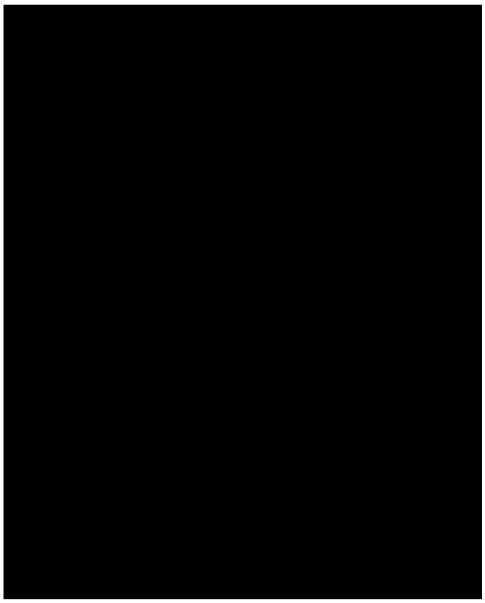


Fig 1. A 16-year-old girl with gliomatosis cerebri. Transaxial T2-weighted MR image at time of presentation shows marked thickening and hyperintensity in inferomesial right temporal cortex (*open arrows*).

Histologic examination of the surgical specimen revealed diffuse infiltration and enlargement of the cerebral cortex by a population of relatively bland glial cells, resembling astrocytes. The abnormal glia extended into the subjacent white matter, although not to the degree seen in the cortex. Cortical structure was preserved, although some neuronal satellitosis and neuronophagia were noted. Small vessels were prominent and showed only limited cuffing. Necrosis and endothelial proliferation were absent. The appearances were regarded as characteristic of gliomatosis cerebri.

Discussion

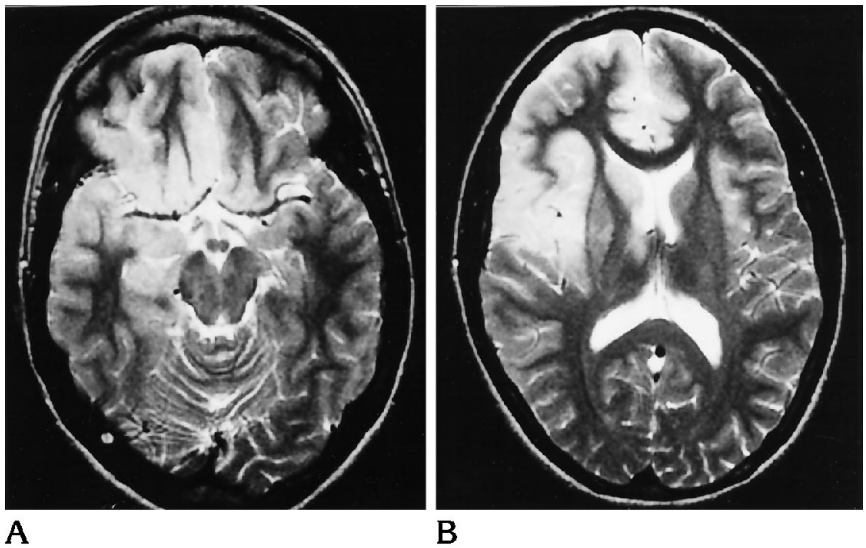
A third nerve palsy with pupillary sparing is a rare presentation of gliomatosis cerebri. Most patients with this condition present with vague or nonspecific findings. Behavioral changes, seizures, headache or weakness, and focal neurologic signs, if present, typically appear late in the course of the disease (4, 5, 8). Thus the diagnosis often is only made at autopsy (5). When our patient presented, external compression of the oculomotor nerve was suspected, because the pupil was not involved. Cerebral angiography excluded a posterior communicating artery aneurysm. The later appearance of multiple cranial nerve palsies and a hemiparesis suggests that there was neoplastic infiltration of the brain stem from the outset, and the third nerve lesion was nuclear in origin. Brain stem involvement was not detected with either MR imaging or FDG PET, however, abnormalities of signal intensity and glucose use in cerebral cortex and deep nuclei remote from the brain stem were seen with MR imaging and later FDG PET.

In gliomatosis cerebri, MR imaging may detect diffuse contiguous high-intensity mass lesions on T2-weighted images, loss of gray-white matter delineation, asymmetric changes in brain morphology, and, rarely, enhancement with paramagnetic contrast agents (7, 9–11). However, since the report of Spagnoli et al, it is apparent that MR studies may underestimate the extent of neoplastic infiltration. Koslow et al showed that in one patient, MR findings were normal in the brain stem where the density of

Fig 2. MR images 9 months after presentation and before partial right temporal lobectomy.

A, Transaxial T2-weighted MR image shows extensive thickening and hyperintensity in cortex of right temporal and orbitofrontal lobes. Midbrain appears normal.

B, Higher transaxial T2-weighted MR image shows signal hyperintensity and thickening in cortex of both mesial frontal lobes, right insula, and right lateral frontotemporal lobes. Signal hyperintensity is also seen in head of right caudate nucleus, right anterior thalamus, and, less marked, in right putamen.



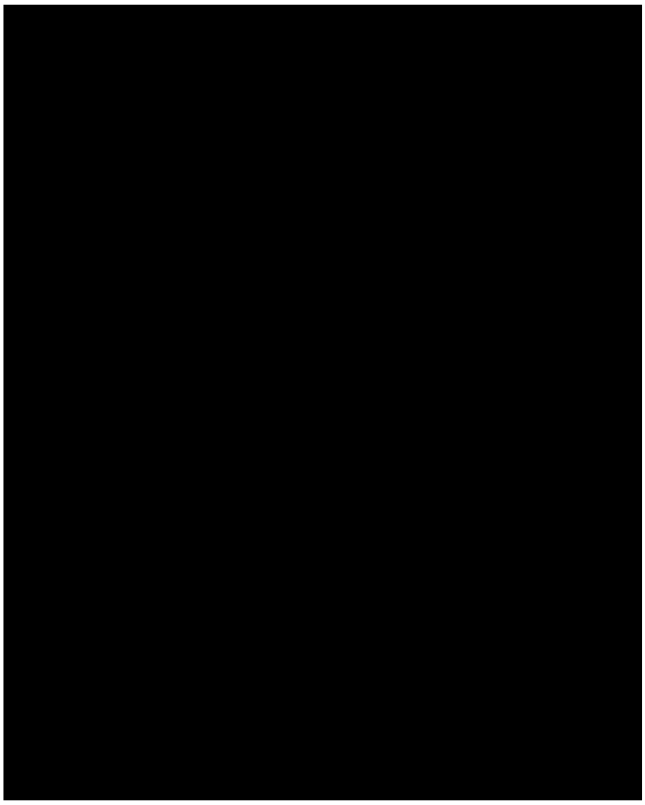


Fig 3. Transaxial FDG-PET image shows marked reduction in FDG uptake in cortex of right lateral frontotemporal lobes and left lateral frontal cortex (*open arrows*), both mesial frontal lobes, right insula cortex (*curved arrow*), right caudate and putamen (*horizontal solid arrows*), and anterior right thalamus (*curved arrow*). Areas of high FDG uptake are orange-yellow, and areas of low FDG uptake are green-blue.

neoplastic cells was the greatest (9). Gadopentetate dimeglumine–enhanced MR imaging showed a linear pattern of enhancement over the temporal lobe and cerebellum with leptomeningeal tumor dissemination in the patient reported by Rippe et al (10). Autopsy revealed that the leptomeninges were normal, but there was extensive infiltration of the underlying cortex. For our patient MR findings suggested that the process was limited to gray matter when there was involvement of the white matter but this involvement was microscopic rather than macroscopic. Computed tomography (CT) findings in our patient were normal, a finding in concordance with the literature. If CT findings are abnormal, there can be diffuse mass effect or marked hypodensity, and enhancement after intravenous iodinated contrast media is not usually seen (6, 12).

Most pathologic series described gliomatosis cerebri as a condition that affects mainly white matter, although uncommonly the disease may be largely confined to gray matter (2, 13). Histologic, immunohistologic, and ultrastructural findings now clearly demonstrate that gliomatosis cerebri is a neoplastic process in cells of astrocytic origin and that transitional forms of oligodendroglia and astroglia are frequently encountered (14). The cells have a proliferative potential similar to that of low-grade gliomas (15) and this similarity may explain why MR imaging may not show small areas of bland neoplastic glia. Gliomatosis cerebri shows no sex predilection. It is reported in all age groups, with a peak incidence in the fifth decade, and the duration of the illness varies from as short as 25 days to 22 years (5, 16).

FDG PET is used to measure cerebral glucose metabolism. Deoxyglucose, an analog of glucose, crosses the blood-brain barrier by facilitated transport, and it is phosphorylated by hexokinase (17). For methionine the mechanism of cerebral uptake is via carrier-mediated transport as for other amino acids (18). [^{11}C]-methionine PET measures amino acid uptake rather than protein synthesis (18, 19). In patients with brain tumors, using FDG PET, increased glucose use is seen in high-grade gliomas, and glucose hypometabolism is found in low-grade gliomas (20). There is increased [^{11}C]-methionine uptake in both high- and low-grade gliomas. Thus it is not as valuable as FDG PET in the evaluation of tumor grade. However, in low-grade gliomas [^{11}C]-methionine PET may better delineate tumor extent than FDG PET (18, 19).

In another report of PET findings in gliomatosis cerebri (21), [^{11}C]-methionine was used in a 32-year-old woman with extensive tumor infiltration of gray and white matter of both temporooccipital lobes. The authors reported that [^{11}C]-methionine-PET was better able to demarcate the extent of the tumor when compared with MR imaging; however, the images they show do not support their contention that MR imaging did not show gray matter involvement. In our case FDG PET depicted extensive hypometabolism of superficial and deep gray matter consistent with diffuse infiltration; however, the technique did not show any abnormality in the midbrain or white matter. Detection of white matter involvement by slow-growing infiltrative tumors is a difficult task with FDG PET, because of the poor contrast between normal hypometabolic white matter and the glucose hypometab-

olism typical of low-grade tumors (20). Further study will be necessary to document the spectrum of PET appearances in this condition.

Gliomatosis cerebri often arises in the differential diagnosis of patients in whom there is a diffuse process involving the central nervous system and it should also be considered in patients in whom the changes on neuroimaging are confined to gray matter. The concurrent use of MR and PET imaging aid in demonstrating the extent of the disease process and in directing surgical biopsy although in our patient both imaging modalities did not show involvement of the site responsible for the clinical presentation.

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