
Neuroimaging Highlight

Editors: Mark Hudon, Richard Farb

Concurrence of glioma and multiple sclerosis

Submitted by: Shah-Naz Hayat Khan, Joseph E. Buwembo, Q. Li

Can. J. Neurol. Sci. 2005; 32: 349-351

A 29-year-old Caucasian female diagnosed with multiple sclerosis (MS) for seven years, presented with a history of headaches and a single episode of new onset seizures. Her physical examination was unremarkable and she was placed on anti-seizure medications. A computed tomography (CT) scan showed a right frontal brain lesion causing minimal mass effect (Figure 1). Magnetic resonance imaging (MRI) revealed a large nonenhancing space occupying lesion in the right frontal lobe, in addition to numerous smaller lesions which were characteristic of MS plaques (Figures 2 & 3). The large lesion was causing mass effect with right to left midline shift (Figures 2, 3A & B).

Given the patient's history, the appearance and unusually large size of the frontal lesion, it was unclear whether it was a demyelinating MS plaque, or an intra-axial tumour.

A stereotactic-guided biopsy was performed, targeting the right frontal lesion. The resultant tissue specimen was consistent with glioma. Therefore, the patient underwent an elective, frameless, stereotactic-guided craniotomy to effect gross total resection of the tumour. Final pathology returned as oligoastrocytoma (WHO grade II). Postoperatively, the patient continued to remain neurologically intact. She was discharged home with plans for observation and serial MRI examinations.

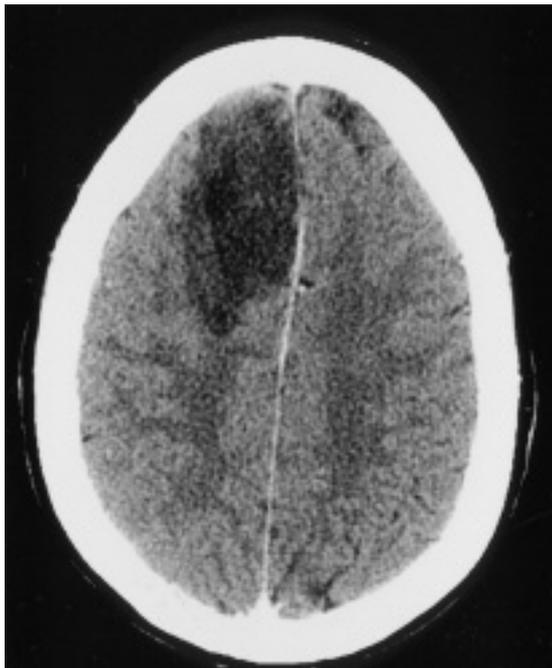


Figure 1: Computed tomography scan (enhanced) axial section, showing a low-density nonenhancing lesion primarily in the white matter of right frontal region which is causing minimal mass effect. This appearance is consistent with a low-grade glioma.

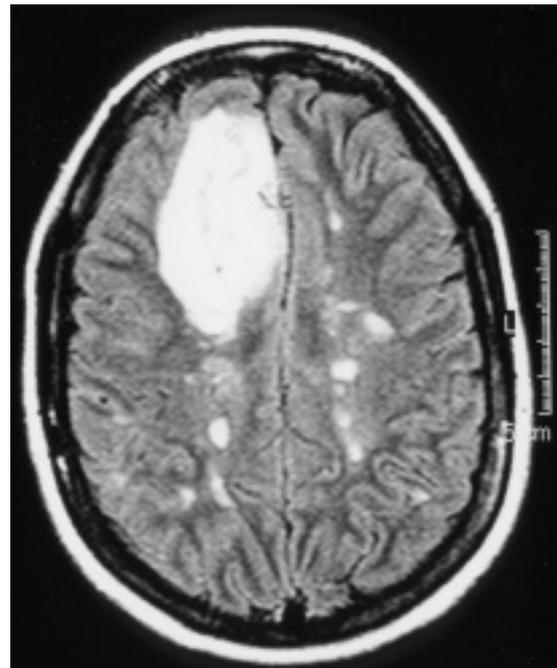


Figure 2: Fluid attenuated inversion recovery (FLAIR) magnetic resonance imaging (MRI) axial section, depicting the large 6 X 5 X 4 cm right frontal lesion. Numerous smaller lesions typical of MS plaques can also be visualized.

From the Division of Neurosurgery, Department of Surgery, University of Saskatchewan, Saskatoon, Saskatchewan, (SHK); Section of Neurosurgery, Department of Surgery, (JEB); Department of Pathology, (QL); Regina General Hospital, Regina, Saskatchewan, Canada.

RECEIVED DECEMBER 31, 2003. ACCEPTED IN FINAL FORM DECEMBER 22, 2004.

Reprint requests to: S.H. Khan, Division of Neurosurgery, Department of Surgery, 103 Hospital Drive, Royal University Hospital, Saskatoon, Saskatchewan, S7N 0W8, Canada.

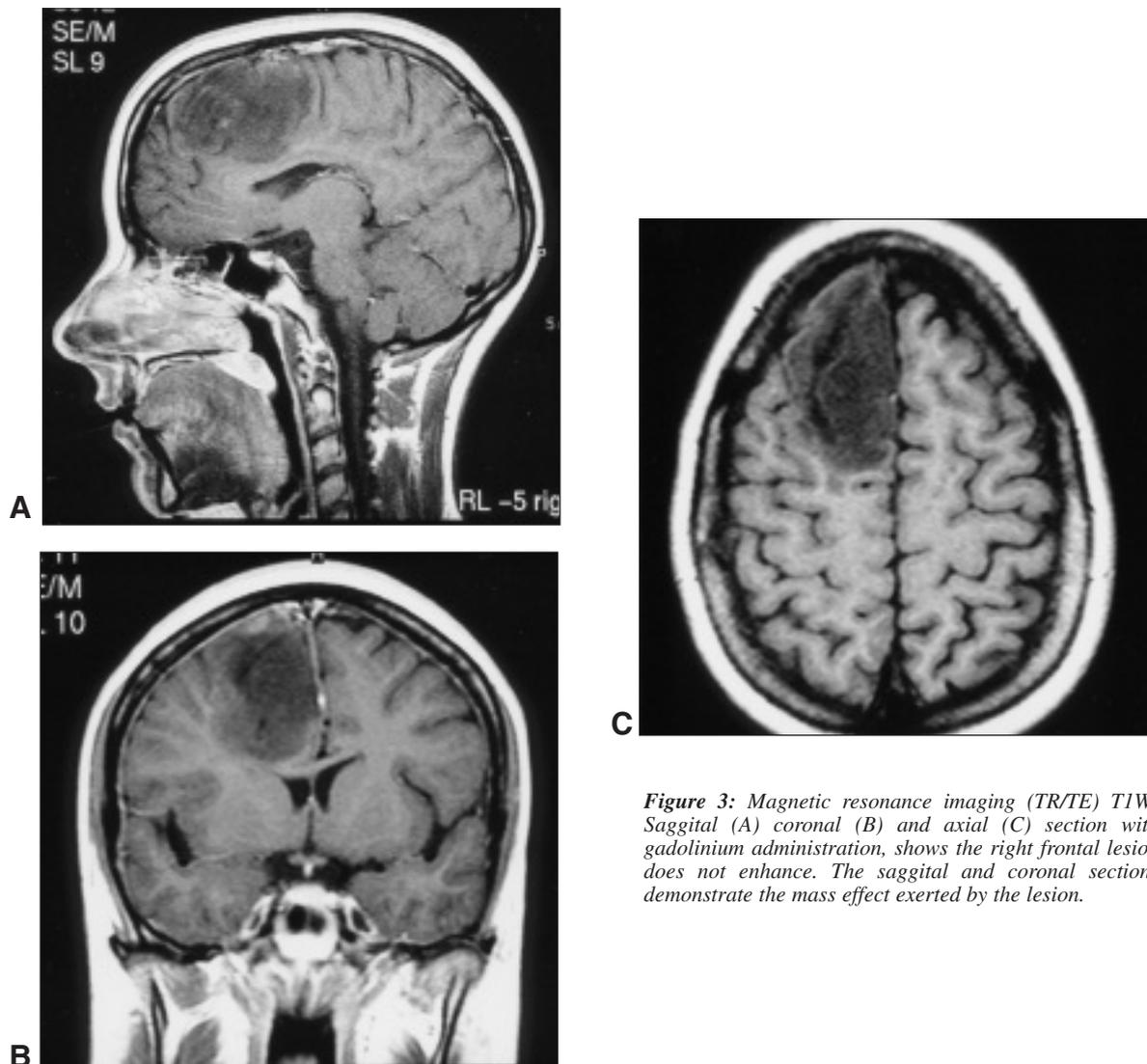


Figure 3: Magnetic resonance imaging (TR/TE) T1WI Saggital (A) coronal (B) and axial (C) section with gadolinium administration, shows the right frontal lesion does not enhance. The sagittal and coronal sections demonstrate the mass effect exerted by the lesion.

Concurrence of MS and glioma is extremely rare.^{1,2} Magnetic resonance imaging performed on this patient eight years earlier (images not available) had shown a smaller right frontal lesion (2.0 X 3.2 cm) and the possibility of low grade glioma was raised. However, no further diagnostic work up for a possible tumour was performed. Correct diagnosis of the two entities is essential, as they are treated differently. An MS patient with an unusual appearing lesion poses a diagnostic dilemma because it could be a plaque or, a primary intracranial glioma.¹⁻³

The demyelinating MS plaques are usually found in the periventricular white matter, optic tracts, cerebellum, brainstem and spinal cord. On MRI or CT, these plaques may show contrast enhancement and usually lack mass effect.⁴ Exceptionally, they enhance and show mass effect, raising the possibility of an intracranial neoplasm.^{3,5} The size of MS plaques usually varies from 3 to 16 mm. Larger plaques are unusual, the largest reported thus far being 7.2 cm.⁵

Low grade gliomas are usually hyperintense on T2-weighted MR images, do not enhance with contrast administration on T1-weighted images,⁶ and may manifest mass effect. Infrequently, tumours may not show these characteristics. Magnetic resonance spectroscopy (MRS) can differentiate between astrocytic tumours and demyelinating lesions. The distinction is made by the pattern generated from proton MRS image data. The resonance intensity values are determined for five metabolites namely, choline, creatinine, N-acetyl aspartate (NAA), lactate and myo-inositol. Analysis of all five metabolites is required for accurately identifying patterns of low grade astrocytoma from an acute demyelinating disease. Compared to the MRS spectra of a normal cortex voxel, that of an acute demyelinating lesion or low grade glioma demonstrate elevated levels of choline, lactate and lipid, with reduced NAA. Unlike glioma, the abovementioned MRS findings for an acute plaque disappear in a few months. A chronic MS plaque shows persistent reduction in NAA, with a

normalization of choline, creatinine, lactate and lipid. The above MRS findings also hold true for an atypical MS plaque e.g., a tumefactive demyelinating lesion which by its large size, position, mass effect and surrounding vasogenic edema, mimic intracerebral tumours. A low grade astrocytoma may be misclassified as a chronic demyelinating disease.⁷ A biopsy is usually necessary for definitive diagnosis.

A common aetiology for multiple sclerosis and gliomas is not established.^{1,8} The obvious common link is the oligodendrocyte. Oligodendrogliomas arise consequent to the neoplastic transformation of oligodendrocytes. Multiple sclerosis is an autoimmune, inflammatory, demyelinating disorder, where the oligodendrocyte is the principle target of attack.¹ Glutamate excess has been implicated in conversion of plaque to glioma.⁸ The apparent overrepresentation of benign MS with oligodendroglioma may be due to effective remyelination by mitotically active oligodendrocytes, or secretion of immunosuppressive cytokines by tumour tissue.¹

Treatment for MS is conservative, including steroid pulse therapy. Management of low grade gliomas includes stereotactic biopsy and resection of surgically accessible or symptomatic lesions.⁹ High grade gliomas require cytoreduction to the maximum extent consistent with preservation of neurological function followed by adjuvant therapy, usually radiation. The concurrence of MS and oligodendroglioma poses additional management problems e.g., the impact of administering radiation to an individual already suffering from a demyelinating disorder. Chemotherapy, in preference to radiation, may be a consideration in such patients as oligodendrogliomas are chemosensitive, particularly those demonstrating allelic loss of chromosome arms 1p and 19q.¹⁰

This case highlights the importance of rigorously investigating uncharacteristic lesions in patients with MS.

REFERENCES

1. Green AJ, Bollen AW, Berger MS, Oksenberg JR, Hauser SL. Multiple sclerosis and oligodendroglioma. *Mult Scler* 2001;7:269-273.
2. Paydarfar D, de la Monte SM. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 12-1997. A 50-year-old woman with multiple sclerosis and an enlarging frontal-lobe mass. *N Engl J Med* 1997;336:1163-1171.
3. Kumar K, Toth C, Jay V. Focal plaque of demyelination mimicking cerebral brain tumor in a pediatric patient. *Pediatr Neurosurg* 1998;29:60-63.
4. Barkhof F, Filippi M, Miller D, et al. Comparison of MRI criteria at first presentation to predict conversion to clinically definite multiple sclerosis. *Brain* 1997;120:2059-2069.
5. Hershey LA, Gado MH, Trotter JL. Computed tomography in diagnostic evaluation of multiple sclerosis. *Ann Neurol* 1979;5:32-39.
6. Brant-Zawadzki M, Berry I, Osaki L, et al. Gd-DTPA in clinical MR of the brain: 1. Intraaxial lesions. *AJR Am J Roentgenol* 1986;147:1223-1230.
7. Butteriss DJ, Ismail A, Ellison DW, Birchall D. Use of serial proton magnetic resonance spectroscopy to differentiate low grade glioma from tumefactive plaque in a patient with multiple sclerosis. *Br J Radiol* 2003;76:662-665.
8. Takano T, Lin JH, Arcuino G, et al. Glutamate release promotes growth of malignant gliomas. *Nat Med* 2001;7:1010-1015.
9. Kaye AH, Walker DG. Low-grade glial neoplasms. In: Batjer HH, Loftus CM (Eds). *Textbook of Neurological Surgery*. Philadelphia: Lippincott Williams & Wilkins, 2003:1257-1270.
10. Fortin D, Cairncross GJ, Hammond RR. Oligodendroglioma: an appraisal of recent data pertaining to diagnosis and treatment. *Neurosurgery* 1999;45:1279-1291.