Case Report

Magnetic Resonance Spectroscopy of Adult Thalamic Glioblastoma Multiforme

Ping Li, MD, MSc;[1]* Yingru Liu, MD, PhD;[2] Rachael Rowswell-Turner, PhD;[2] Fraydoon Esfahani, MD[3]

[1] *Department of Neurology, State University of New York at Buffalo, Buffalo, NY*
[2] *Department of Microbiology and Immunology, State University of New York at Buffalo, Buffalo, NY*
[3] *Department of Radiology, State University of New York at Buffalo, Buffalo, NY*

Thalamic glioblastoma multiforme (GBM) is a rare malignant primary central nervous system (CNS) tumor. Here we report a case of adult unilateral GBM involving the right thalamus. The diagnosis of GBM was first indicated by a region of irregular enhancement with central necrosis in the thalamus, visualized with traditional magnetic resonance imaging (MRI) with contrast. Magnetic resonance spectroscopy (MRS), showing elevated lipid and lactate peaks, provided further evidence of GBM while rendering primary CNS lymphoma (PCNSL), anaplastic glioma, or metastasis less likely. The final diagnosis of GBM was confirmed by pathological examination of the tumor specimen. This report highlights the utility of combining MRS with other imaging modalities to facilitate the diagnosis of CNS lesions.
[N A J Med Sci. 2012;5(1):51-54.]

Key Words: *magnetic resonance spectroscopy (MRS), magnetic resonance imaging (MRI),glioblastoma multiforme*

INTRODUCTION

Glioblastoma multiforme (GBM), the most malignant type of brain tumor, typically arises in the cerebral hemisphere; involvement of deep structures, such as the thalamus, is relatively rare. To date, magnetic resonance imaging (MRI) is the best modality for anatomic localization of central nervous system (CNS) lesions.[1] Diffusion-weighted sequence and the addition of contrast enhanced MRI aid clinicians in distinguishing abscess from tumor as well as differentiating between high-grade and low-grade tumors. Radiologic literature has shown that gliomas are frequently located in the cerebral hemisphere, while primary central nervous system lymphomas (PCNSL) more frequently occur within deep brain structures (thalamus, brain stem, cerebellum) and metastases typically present at the gray-white matter junction.

Magnetic resonance spectroscopy (MRS) was first introduced by Moon and Richards in 1973.[2] It allows noninvasive *in vivo* exploration of the molecular composition of tissue. MRS is useful for evaluating disorders of metabolism, tumors and certain inflammatory and ischemic diseases. MRS has further been used to determine the degree of malignancy of brain tumors. As a general rule, N-acetyl aspartate (NAA) and creatine (Cr) decrease, and choline (Cho), lactate, and lipids increase with malignancy.[3] When utilizing MRS, the selected area, or spectroscopic voxel, should be placed over an enhancing region of the lesion to maximize the accuracy of this diagnostic tool.

Received 06/20/2011; Revised 09/29/2011; Accepted 11/03/2011
***Corresponding Author:** Department of Neurology, State University of New York at Buffalo, 100 High Street, Buffalo, NY, USA.
(Email: pli6@buffalo.edu)

In this article, we report a rare case of adult thalamic GBM that was diagnosed by the combination of MRI and MRS and was subsequently confirmed by histopathology.

CASE REPORT

A 62-year-old man, with no significant past medical history, complained of both light-headedness and headache for approximately 2 weeks duration. His initial neurological evaluation revealed a normal sensory exam and no deficits in cranial nerve function or muscle strength. MRI of the brain demonstrated a large lesion centered in the right thalamus with extension to the ipsilateral lateral ventricle. The lesion was hypointense on T1-weighted images with peripheral irregular gadolinium enhancement, hyperintense on T2-weighted and fluid-attenuated-inversion recovery (FLAIR) images, hypointense in the center with a hyperintense border on diffusion-weighted images (DWI), and hyperintense on apparent diffusion coefficients (ADC) map (**Figure 1**). The differential diagnosis following MRI included neoplasm, either primary or metastatic, and cerebral abscess. Computed tomography (CT) with contrast of the torso did not reveal any neoplasms.

MRS images, using the 1.5-tesla system and Point-RESolved Spectroscopy (PRESS) single-voxel technique with TE of 288 ms, revealed a large accumulation of lipid and lactate which peaked at 0.8-1.33 ppm. A marked decrease in the peak NAA at 2 ppm and an increase in the peak Cho at 3.2 ppm were also observed. In addition, a decrease in the peak of Cr and NAA/Cr (0.377) and an increase in the Cho/Cr peak (3.769) were found (**Figure 2**). Collectively, these changes were indicative of a high-grade glioma.[4,5] Based on this MRS analysis, the pre-operative diagnosis was determined to be GBM.

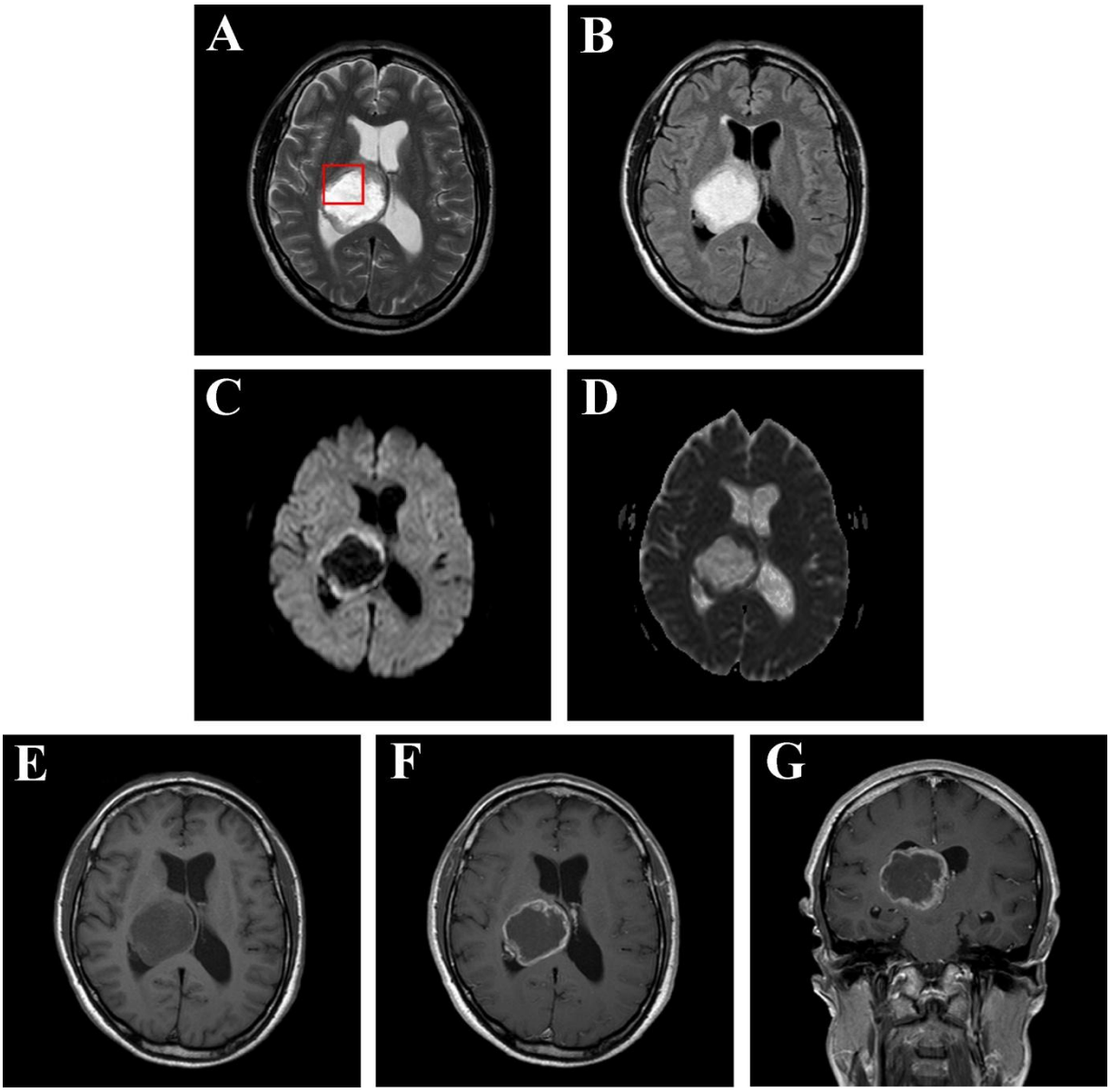

Figure 1. MRI of the brain demonstrating the irregularly-enhanced right thalamic mass, using the following sequences: (A) axial T2 image, (B) axial FLAIR image, (C) axial DWI image, (D) correlated ADC map, (E) axial T1 image, (F) post-contrast axial T1 image, and (G) post-contrast coronal T1 image.

This patient experienced worsening headache and difficulty walking in the following week. His neurological examination showed continued normal cranial nerve and sensory function, but revealed a left hemiparesis. Due to his worsening symptoms, he was treated with high-dose steroid. Following the review of all treatment options, he was then brought to surgery for resection of the tumor.

A biparietal craniotomy and interhemispheric transcallosal approach for excision of the tumor were performed. There was some fluid within the tumor, but the lesion was largely solid. It was internally decompressed with suction and tumor forceps. Samples were sent for pathological testing which confirmed the tumor to be GBM with features suggestive of oligodendroglial differentiation (**Figure 3**).

After craniotomy while still on high-dose steriod, the patient's condition had improved significantly although the left hemiparesis remained. On post-operative day 6, however, the patient went into asystole followed by pulseless electrical activity. He could not be revived despite one hour of resuscitation. The option of an autopsy was refused by the family.

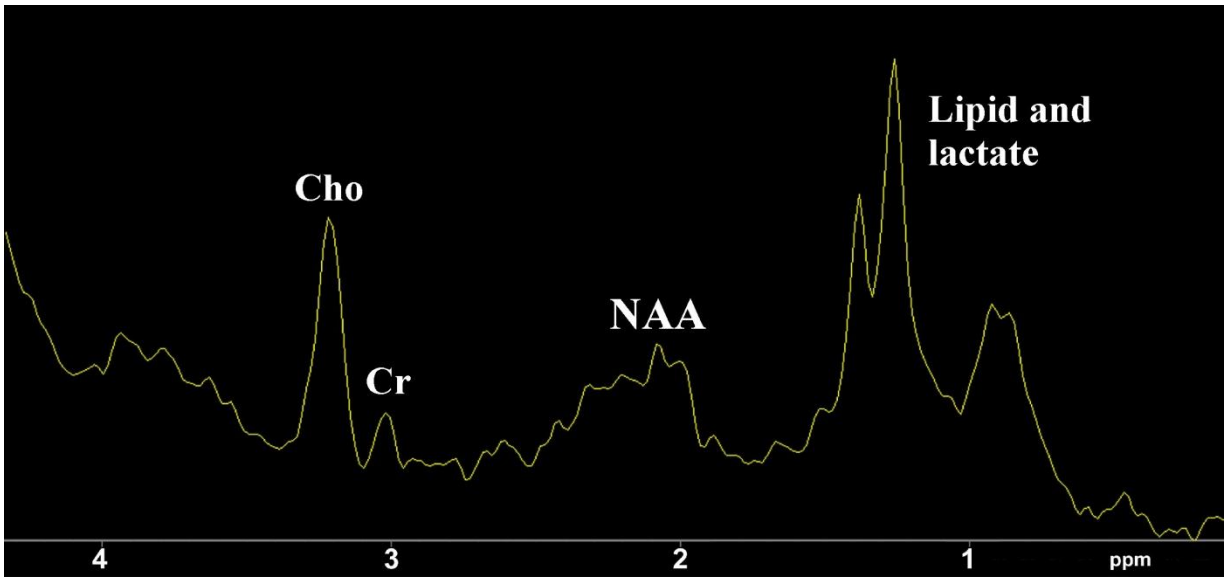

Figure 2. MRS of the right thalamic mass, which revealed large accumulation of lipid and lactate (peaked at 0.8-1.33 ppm), marked decrease in peak NAA at 2 ppm, marked increase in the peak of Cho at 3.2 ppm, and decrease in the peak of Cr. MRS results were from the single voxel square area that is labeled in **Figure 1 (A)**.

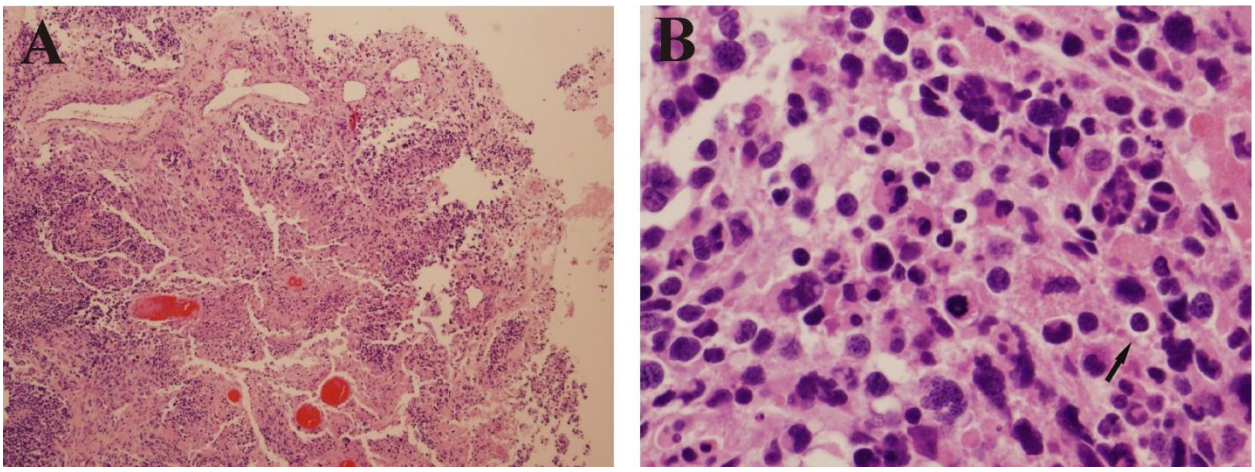

Figure 3. Pathology of the surgically resected mass. The low power image (A) showed pseudopalisading necrosis. The high power image (B) showed mitosis and a neoplastic oligodendrocyte with a round nucleus and perinuclear halo (arrow).

DISCUSSION

In the case discussed above, the patient was afflicted by a rare thalamic GBM with an oligodendroglial component. Because the thalamus is relatively small and constitutes less than 2% of the neuraxis, only 1% to 5% of all brain tumors arise primarily in this region.[6-9] Although GBM is the most common adult CNS tumor, the likelihood of thalamic involvement is rare. The standard of care for patients with GBM is surgery followed by standard radiotherapy with concomitant adjuvant chemotherapy (temozolomide). Despite all of these efforts, the prognosis following a GBM diagnosis remains poor, with a median survival of 14.6 months.[10] Due to rapid tumor growth, early diagnosis and timely initiation of radiation and chemotherapy are critical to the management of GBM. Histological diagnosis is also important for prognosis as the presence of an oligodendroglial component is considered a favorable factor.[11]

MRI has been widely used in identifying and locating brain lesions. In this case, MRI guided our diagnosis by revealing a right thalamic ring-enhancing lesion, which made PCNSL unlikely since PCNSL tends to enhance homogeneously. DWI and ADC map aid diagnosis by differentiating between cerebral abscess and tumors. In this instance, DWI showed a hypointense center which correlated with hyperintensity on ADC map, a finding inconsistent with a cerebral abscess. The lack of extensive cerebral edema around the mass lesion

suggested a low-grade tumor. However, the location of the lesion and the extension of the lesion to the lateral and third ventricles may have obscured the mass effect and the surrounding edema. Therefore, before MRS analysis was applied to this case, the malignant grade of the lesion remained unclear.

MRS adds to our diagnostic capabilities by measuring metabolic activities and detecting tissue characterization. There has been increasing data describing the use of MRS to improve tissue characterization,[4,5] particularly in brain tumors. Multiple single volume MRS methods have been proposed, including PRESS. MRS can be incorporated into routine brain imaging protocols or added to any unresolved MRI examination. Although proton MRS may be obtained with most modern MRI systems, it is still not a widely used technique. This case report again demonstrates that MRS may be used to characterize a deep brain lesion that cannot be biopsied. Specifically, it can aid in the differential between neoplasm and inflammatory lesion. MRS can also be utilized to distinguish PCNSL from high grade glioma or to separate GBM progression from pseudoprogression. The combination of MRI and MRS allows for a more accurate diagnosis than MRI alone. The information it provides can be critical for the formation of an appropriate treatment plan. Although this case study clearly shows the effectiveness of combined MRS and MRI we recognize that the neuropathological examination of tissue remains the gold standard for any brain lesion diagnosis.

The brain metabolites visualized utilizing intermediate to long echo time include NAA (marker of neuronal viability), Cho (marker of membrane turnover), Cr (related to the energy state of the cells), and lipids and lactate (observed in necrosis and other pathological processes). With TE 280 ms, the NAA/Cr ratio is lower in high-grade tumors (low grade 1.05 ± 0.51 and high grade 0.78 ± 0.28) compared to demyelinating lesions (0.95 ± 0.39). The Cho/Cr ratio is higher in tumors (2.68 ± 2.20) than non-neoplastic lesions.[12] The specificity of MRS detection of tumor is 97.6% with a *p*-value of 0.001 when the Cho/Cr ratio is greater than 1.97 and the NAA/Cr ratio is less than 1.12 with TE 110 ms.[4] Also, high grade oligodendrogliomas show large resonances of lipids plus lactate (24.7 ± 12.4), in contrast to low grade tumors (5.2 ± 2.4 in low grade oligodendrogliomas, and 3.9 ± 3.4 in low grade astrocytomas) with short echo time.[5]

CONCLUSION

In conclusion, we have described a patient who had a rare thalamic GBM that was first visualized by MRI, further characterized by MRS and later confirmed by histopathologic examination. Based on these findings, the potential of MRS to enhance diagnosis when combined with other imaging modalities is clear. Specifically, the addition of MRS to MRI analysis can effectively facilitate the diagnosis of brain lesions and should be emphasized more in clinical settings.

CONFLICT OF INTEREST
None.

REFERENCES

1. Zimmerman RA, Bilaniuk LT, Johnson MH, et al. MRI of central nervous system: early clinical results. AJNR Am J Neuroradiol. 1986;7(4):587-594.
2. Moon RB, Richards JH. Determination of intracellular pH by 31P magnetic resonance. J Biol Chem. 1973;248(20):7276-7278.
3. Hou BL, Hu J. MRI and MRS of human brain tumors. Methods Mol Biol. 2009;520:297-314.
4. Ferraz-Filho JR, Santana-Netto PV, Rocha-Filho JA, Sgnolf A, Mauad F, Sanches RA. Application of magnetic resonance spectroscopy in the differentiation of high-grade brain neoplasm and inflammatory brain lesions. Arq Neuropsiquiatr. 2009;67(2A):250-253.
5. Rijpkema M, Schuuring J, van der Meulen Y, et al. Characterization of oligodendrogliomas using short echo time 1H MR spectroscopic imaging. NMR Biomed. 2003;16(1):12-18.
6. Cheek WR, Taveras JM. Thalamic tumors. J Neurosurg. 1966;24(2):505-513.
7. Cuccia V, Monges J. Thalamic tumors in children. Childs Nerv Syst. 1997;13(10):514-520; discussion 521.
8. Puget S, Crimmins DW, Garnett MR, et al. Thalamic tumors in children: a reappraisal. J Neurosurg. 2007;106(5 Suppl):354-362.
9. Tovi D, Schisano G, Liljeqvist B. Primary tumors of the region of the thalamus. J Neurosurg. 1961;18:730-740.
10. Stupp R, Mason WP, van den Bent MJ, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med. 2005;352(10):987-996.
11. Park CK, Lee SH, Han JH, et al. Recursive partitioning analysis of prognostic factors in WHO grade III glioma patients treated with radiotherapy or radiotherapy plus chemotherapy. BMC Cancer. 2009;9(1):450.
12. Hourani R, Brant LJ, Rizk T, Weingart JD, Barker PB, Horska A. Can proton MR spectroscopic and perfusion imaging differentiate between neoplastic and nonneoplastic brain lesions in adults? AJNR Am J Neuroradiol. 2008;29(2):366-372.