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Case Report

Radiology Section

MR Perfusion Imaging as a Problem-solving Tool for Differentiating High-grade Glioma and Tumefactive Demyelination: A Report of Two Cases

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ABSTRACT

Clinically, it is nearly impossible to differentiate between high-grade glioma, specifically Glioblastoma Multiforme (GBM), and Tumefactive Demyelination (TMD). Radiologically, distinguishing between GBM and TMD is challenging since they show similar findings on Computed Tomography (CT) and Magnetic Resonance Imaging (MRI). To avoid invasive procedures that may increase patient morbidity, the use of MR perfusion imaging is highlighted in these case reports. We present two cases of young adult females with neurological deficits. The first case involves an 18-year-old female who presented with a dull, intermittent, holocephalic headache for eight months, along with heaviness and recent onset of pain in the right upper limb. MR spectroscopy revealed an increased choline/creatinine ratio at the margins of the lesion, measuring approximately 2.4, with a decrease in N-Acetylaspartate (NAA) and NAA/Creatinine. Based on these findings, the possibility of either high-grade glioma or TMD was considered. Further evaluation using perfusion imaging showed a substantial increase in the mean relative Cerebral Blood Volume (rCBV) within the lesion, suggesting a higher likelihood of high-grade glioma rather than TMD. Biopsy confirmed the diagnosis as high-grade glioma (GBM), revealing marked mitotic changes with nuclear pleomorphism and multinucleated cells. The second case involves a 22-year-old female who presented with left upper limb and lower limb weakness for 10 days. MR spectroscopy showed reduced NAA values and an elevated choline peak with small lactate at a few places. A choline/creatine ratio of 1.9 was obtained. On perfusion imaging, the observed mean rCBV values were substantially low (rCBV measuring approximately 1.07). Consequently, a final radiological diagnosis of TMD was considered. A biopsy confirmed the presence of inflammatory demyelination.

Keywords: Choline/Creatinine ratio, Headache, Neurological deficits

CASE REPORT

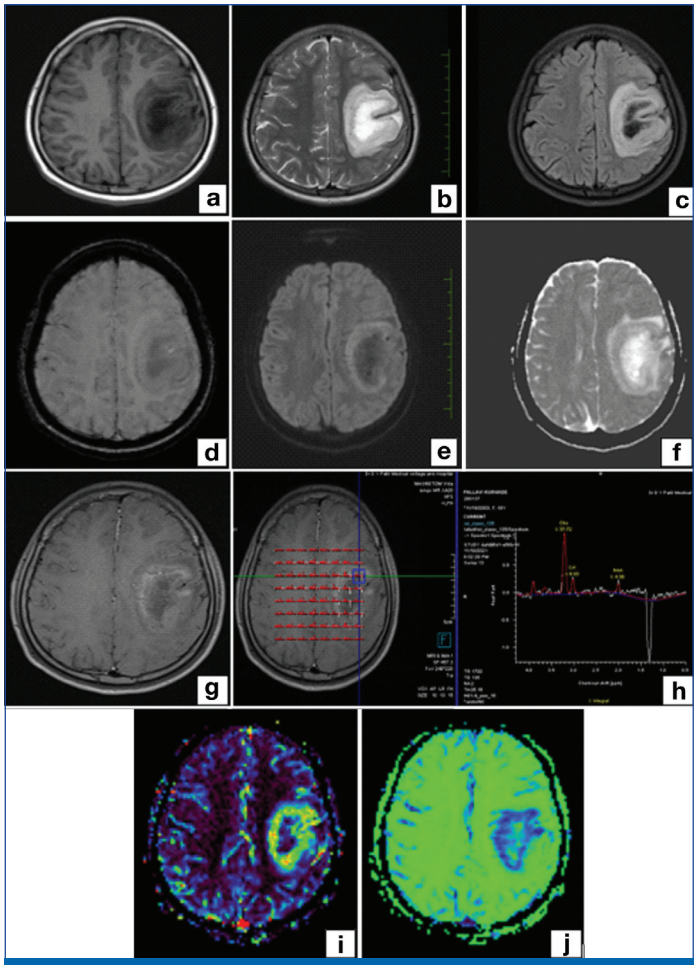
Case 1

An 18-year-old female presented with a dull, intermittent, holocephalic headache for eight months. She experienced heaviness and recent onset of pain in the right upper limb. There were no obvious relieving factors and no diurnal variations in symptoms. On the day of admission, she suddenly developed left-sided deviation of the mouth. She had no significant past medical or surgical history. The patient was referred for an MRI Brain for evaluation. The investigation revealed a well-defined heterogeneous mass with central necrosis in the left fronto-parietal region, involving subcortical and deep white matter while sparing the overlying cortex. The lesion measured 55×42×42 mm (APxTxCC). The solid component was predominantly located in the periphery and appeared iso-hypointense to grey matter on T1WI, hyperintense on T2WI and FLAIR [Table/Fig-1 a-c]. It showed mild diffusion restriction with corresponding low ADC values. There was no signal drop out on magnitude images and Susceptibility Weighted Imaging (SWI) images [Table/Fig-1 d-f]. The central cystic/necrotic component appeared hyperintense on T2WI, hypointense on T1WI, and was incompletely suppressed on FLAIR. Since the findings on plain MRI were inconclusive, a detailed MRI evaluation including intravenous contrast, MR spectroscopy, and perfusion imaging was advised.

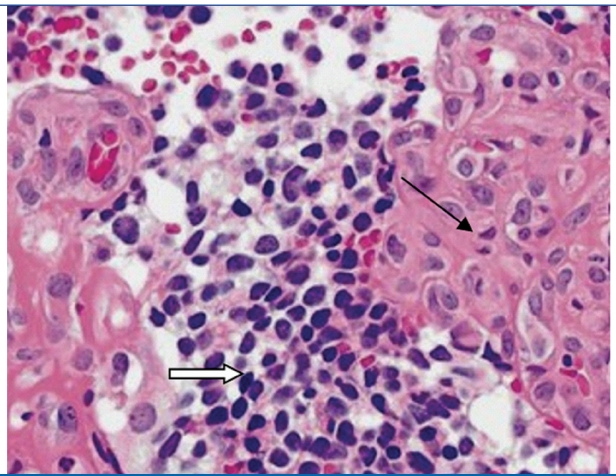
On post-contrast images, the peripheral solid component showed heterogeneous enhancement with a central non-enhancing necrotic area. An incomplete ring was noted towards the cortex [Table/Fig-1g]. Multiple linear vessels were seen as flow voids traversing through the lesion and coursing towards subependymal vessels along the lateral wall of the left lateral ventricle. Mild perifocal vasogenic oedema was noted, appearing hyperintense on T2WI and FLAIR. Mass effect was observed on the left lateral ventricle and third ventricle, with a mild shift of midline structures towards the right (2 mm). Adjoining sulcal spaces were effaced. MR spectroscopy revealed an increase in choline and an increased choline/creatinine ratio at the margins of the lesion, measuring approximately 2.4, with a decrease in NAA and NAA/Creatinine ratio compared to the normal brain parenchyma. Increased lactate was noted, which was inverted at an intermediate echo time of 1.3 ppm [Table/Fig-1 h]. In view of the above findings, the possibility of either high-grade glioma or TMD was considered. Further evaluation on perfusion imaging revealed a substantially increased mean relative cerebral blood volume within the lesion (rCBV measuring approx. 10.4) [Table/Fig-1i-j]. This finding suggested that the lesion was more likely a high-grade glioma than TMD. A biopsy confirmed the diagnosis as high-grade glioma (GBM) [Table/Fig-2].

Case 2

A 22-year-old female presented with left upper limb and lower limb weakness for 10 days. She had no other complaints, and there was no significant past medical or surgical history. She was referred for an MRI brain for evaluation. An area of altered signal intensity lesion was noted in the right temporoparietal subcortical and periventricular white matter, opercular and insular cortex, and the splenium. It appeared hypointense on T1, heterogeneously hyperintense on T2 and FLAIR [Table/Fig-3a-c]. There was minimal diffusion restriction at the periphery with no blooming on GRE [Table/Fig-3d-f]. Moderate perilesional edema was noted. The lesion



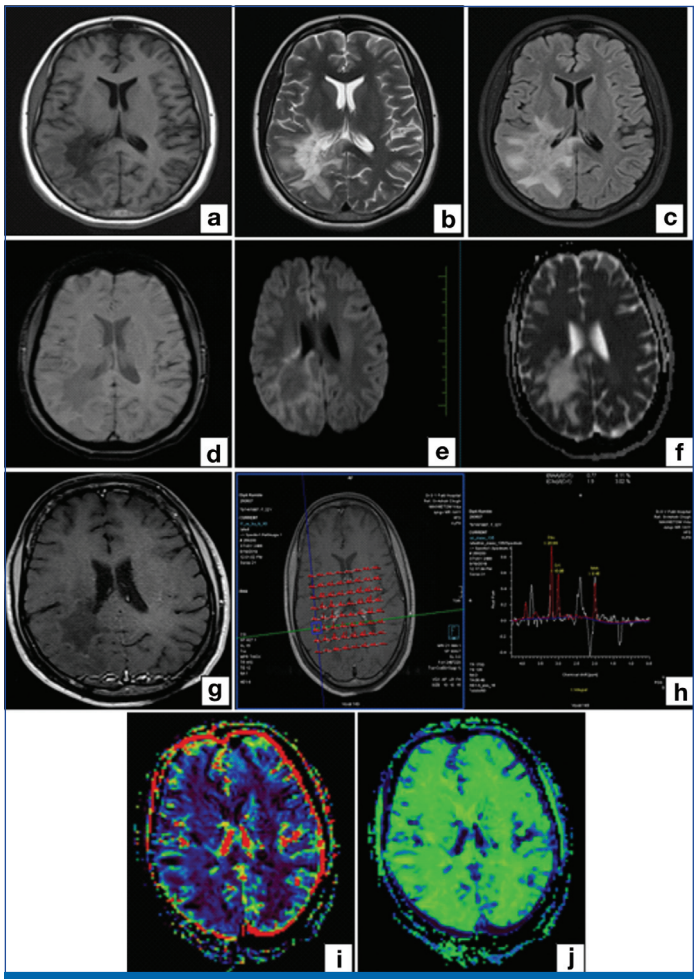
[Table/Fig-1]: Axial MR images of Brain: (a) T1WI showing heterogeneously hypointense space-occupying lesion in left frontoparietal lobe; (b) T2WI showing hyperintense lesion with high fluid signal centrally; (c) FLAIR images show peripherally hyperintense lesion with central suppression of fluid signal; (d) SWI images shows no obvious foci of susceptibility blooming; (e,f) DWI images, mild peripheral diffusion restriction with low ADC values is seen; (g) Post contrast images show peripheral open ring type of enhancement with open ring towards the cerebral cortex; (h) MR spectroscopy at 135 TE, shows a high Choline peak, high Choline: Creatine ratio, with an inverted large lactate peak; (i) and (j) show perfusion images, with high rCBF and rCBV in the peripheral component of the lesion.



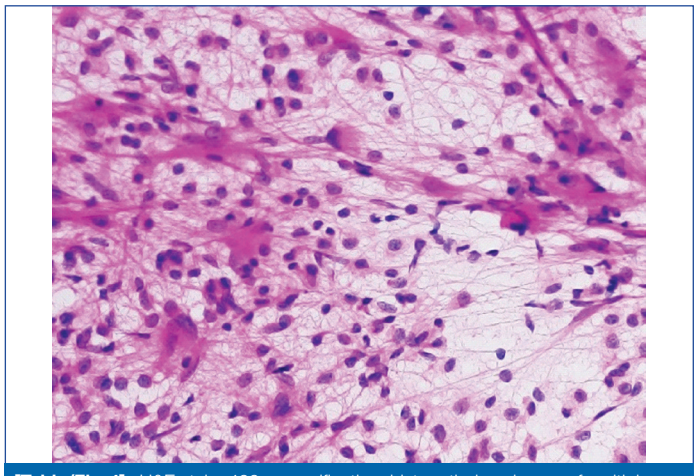
[Table/Fig-2]: H&E stain, 400x magnification, histopathology image of high-grade glioma showing marked mitotic changes (white arrow) with nuclear pleomorphism and multinucleated cells (black arrow).

measured approximately 5×3.4×4.8 cm (APxTRxCC). It resulted in effacement and compression of the body and temporal horn of the right lateral ventricle, but no significant midline shift was observed. Since the findings on plain MRI were inconclusive, a detailed MRI evaluation, including intravenous contrast, MR spectroscopy, and perfusion imaging, was advised.

On post-contrast images, mild peripheral enhancement was noted [Table/Fig-3g]. There was no clear incomplete ring observed in the periphery of the lesion. MR spectroscopy revealed reduced NAA values and an elevated choline peak with small lactate at a few places. A choline/creatine ratio of 1.9 was obtained [Table/Fig-3h]. On perfusion imaging, the mean rCBV values were substantially low (rCBV measuring approximately 1.07) [Table/Fig-3i-j]. Hence, a final radiological diagnosis of TMD was considered. The patient underwent a biopsy for confirmation of the radiological diagnosis, which revealed inflammatory demyelination [Table/Fig-4]. The patient received methylprednisolone at a dose of 800 mg/day for five days, which was effective, and the patient's condition improved.



[Table/Fig-3]: Axial MR images of Brain; (a) T1WI showing heterogeneously hypointense space occupying lesion in right parieto-temporal lobe; (b) T2WI showing hyperintense lesion; (c) FLAIR images show heterogeneously hyperintense lesion; (d) SWI images shows no obvious foci of susceptibility blooming; (e,f) Mild peripheral restriction diffusion with low ADC values; is seen; (g) Postcontrast images, show minimal peripheral enhancement with no obvious open ring; (h) MR spectroscopy at 135 TE, shows high choline peak, high Choline:Creatine ratio; (i) and (j) shows perfusion images, with low rCBF and rCBV in the lesion.



[Table/Fig-4]: H&E stain; 400x magnification, histopathology image of multiple areas of reduced myelin that are well demarcated from adjacent white matter with intact myelin. There is no evidence of mitosis or polymorphonuclear morphology.

DISCUSSION

Clinically, it is nearly impossible to differentiate between high-grade glioma (such as GBM) and TMD. TMD is a rare variant of demyelinating disorder found in multiple sclerosis subtypes. It predominantly affects middle-aged women, with an average onset in the 3rd to 4th decade [1]. In contrast, high-grade glioma exhibits a slight male predominance and has its peak incidence in the 6th to 7th decade [2]. Radiologically, distinguishing between GBM and TMD is challenging since both show similar findings on CT and MRI scans. As a result, an invasive biopsy is necessary for a definitive diagnosis. The treatment for GBM involves surgical excision along with chemo-radiotherapy, while TMD can be managed with high-dose corticosteroids [3].

GBM is a common cerebral neoplastic lesion classified in the 5th edition of WHO as IDH wild type, which is now a separate entity from astrocytoma classified as IDH-mutant type [4]. The majority of GBMs are sporadic, with only a few related to a history of radiation, which may cause radiation-induced GBM [5]. Rarely, they occur secondary to genetic abnormalities, leading to inherited tumour syndromes such as neurofibromatosis Type I, p53 mutation, or Li-Fraumeni syndrome [6].

Clinically, both GBM and TMD-affected patients have similar presentations, such as focal neurological deficits, seizures, or headaches. Epidemiologically, both disorders are possibly seen in late adult life, with GBM peaking in the 6th decade. Radiologically, typical GBM shows extensive perilesional oedema with irregular, thick, and vivid peripheral enhancement [7]. Parks NE et al., showed that perfusion MRI rCBV was lower among TMD compared to GBM [8].

These present cases are unique as our patients were in early adult life, unlike those who typically present in late adulthood. Initially, contrast MRI findings suggested a diagnosis of TMD in the first case, as the reported radiological markers included less perilesional oedema and incomplete ring enhancement with an open ring towards the cerebral cortex. Other findings, such as mild restricted diffusion on DWI and absence of foci of blooming on SWI/MAG images, were not useful in differentiating between the two pathologies. Even on MR spectroscopy, both lesions can have a similar appearance, showing high choline peaks with low NAA and high lactate peaks. In the second case, contrast MRI findings also suggested a neoplastic lesion such as glioma. Further evaluation with perfusion imaging in both cases was a problem-solving tool, as the lesion in the first case showed high perfusion values (rCBV was 10.4), which is usually seen in GBM. Therefore, a radiological diagnosis of GBM was concluded for the first patient. Similarly, low perfusion values were seen in the second case (rCBV was 1.07), leading to the radiological diagnosis of TMD.

Law M et al., demonstrated that GBMs may reach very high max rCBV values of >3.0 or even >10.0, and a max rCBV of 1.75 has been set as the threshold value for differentiating high-grade gliomas [9]. TMDs are usually more than 20 mm in size and are usually associated with surrounding mass effect, perilesional oedema, and peripheral contrast enhancement [10,11]. Overall, MR perfusion rCBV is lower among TMD (0.88±0.46) when compared to intracranial malignancies (6.47±6.52) [12]. However, there are a few limitations for perfusion MRI as well. One such limitation is that there is no significant difference in differentiating TMD and low-grade glioma, as both lesions show reduced rCBV [13]. Another limitation is the requirement of contrast, hence it cannot be used in patients with renal failure.

CONCLUSION(S)

The radiological diagnosis of TMD should not rely solely on the type of ring enhancement or MR spectroscopy features, as it can lead to misdiagnosis between GBM and TMD. The specificity in differentiating GBM and TMD increases when perfusion imaging is used as an adjunct to routine MRI techniques.

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