The Role of Multiparametric MRI in Diagnosing and Grading Glioma

Sir,

We write to share insights from a recent case that underscores the evolving role of multiparametric MRI in diagnosing and grading gliomas, particularly considering the WHO's 2021 classification prioritizing molecular markers over histological features.[1]

Our patient is a 42-year-old man with a history of tobacco and alcohol use who presented with new-onset seizures preceded by isolated right arm shaking, malaise, and anomic aphasia. The neurological examination was unremarkable, and the EEG showed several subclinical seizures originating in the left parasagittal region. Brain CT [Figure 1a] and non-contrast MRI demonstrated a subcortical, infiltrative lesion in the left parasagittal frontal region with a possible differential of progressive multifocal leukoencephalopathy (PML), tumefactive demyelination, or glioma. Subsequent contrast-enhanced MRI [Figure 1b-e] with perfusion [Figure 1f] and MR spectroscopy [Figure 1g-i] revealed predominant hypoperfusion, elevated choline levels, and an inverted lactate doublet peak. Following a left frontal craniotomy with submaximal resection [Figure 1j], histopathologic examination and molecular analysis confirmed a diagnosis of astrocytoma, IDH-mutant, 1p/19q intact, grade 3.

The T2/FLAIR mismatch sign ("mismatch sign") is highly specific, with a 2021 meta-analysis showing 100% pooled specificity but only 42% sensitivity for astrocytoma.[2] The sign appears as homogenous hyperintensity on T2 images but is more hypointense on FLAIR images with a hyperintense signal halo. Despite its specificity, Corell *et al*.[3] found no association between the sign's appearance and the patient's clinical presentation, outcome, or survival. Accurate application of the mismatch sign requires meeting certain prerequisites outlined in Table 1. In our case, the mismatch sign was present only in the central portion of the lesion, indicating IDH-mutant, 1p/19q-non-codeleted status [Figure 1c].

Table 1: Requirements for applying the T2/FLAIR mismatch sign for IDH-mutant, 1p/19q-codeleted astrocytoma

Case requirements	Adult patient
	Supra-tentorial lesion
Radiologic features	Homogenous T2 hyperintensity
	FLAIR hypointensity with hyperintense halo
	Minimal to no contrast enhancement
	No increased perfusion
	No diffusion restriction

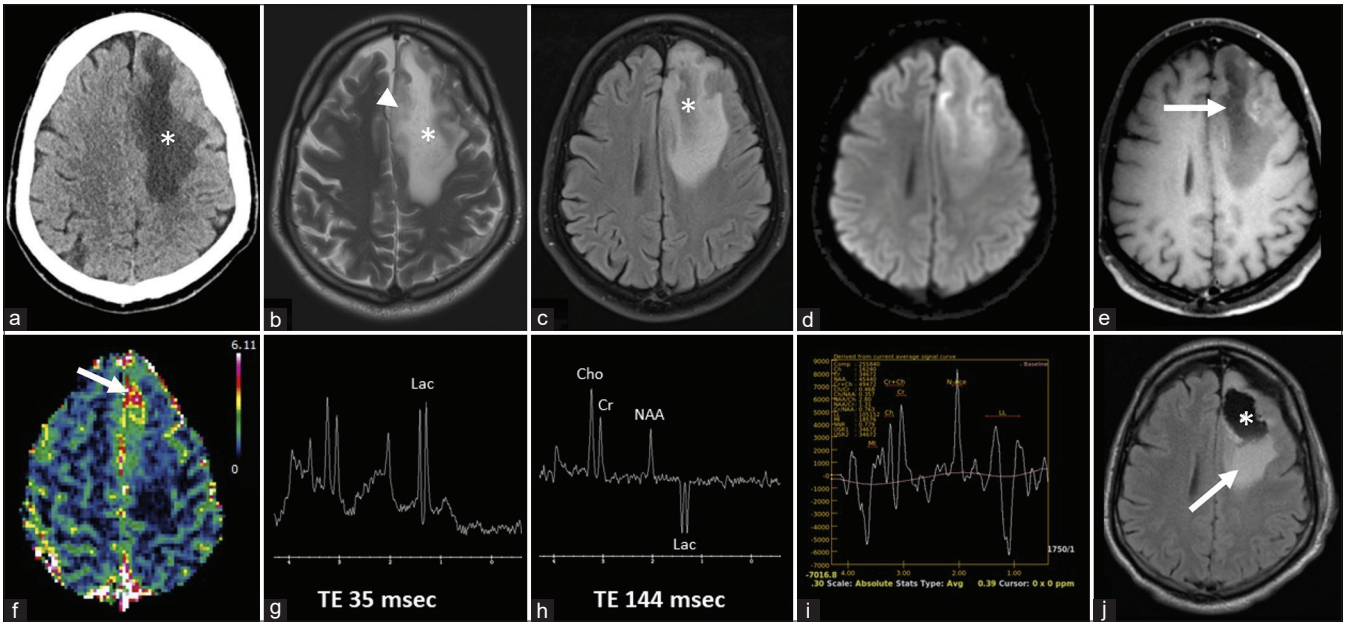

Figure 1: Axial CT (a) demonstrates subcortical hypoattenuation (*) in the left parasagittal frontal lobe. T2 (b) shows homogeneous hyperintensity (*) with cortical thickening (arrowhead). T2-FLAIR (c) exhibits a central hypointensity (*) corresponding to the mismatch sign. DWI (d) demonstrates patch peripheral diffusion hyperintensity. Post-contrast (e) reveals predominantly non-enhancing lesion with focal curvilinear enhancement (arrow). (f) Perfusion-weighted imaging shows mild rCBV increase (arrow). (g-h) Single-voxel MRS displays an inverted lactate doublet peak, increased choline, choline/creatine ratio, and decreased NAA. Multi-voxel MRS (i) reveals combined lipid-lactate inversion, elevated choline, and decreased NAA. (j) T2-FLAIR post-resection shows a fluid-filled cavity (*) with postsurgical changes (arrow)

Furthermore, the case underscores the potential of quantifying the apparent diffusion coefficient (ADC) for glioma grading. Higher ADC values have been linked to IDH-mutant astrocytomas, with a cutoff ADC value of 1.01 × 10^{-3} mm^2/s demonstrating high sensitivity (76.9%), specificity (82.6%), and positive predictive value (91.2%) for distinguishing mutation status.[4]

Magnetic resonance spectroscopy (MRS) also played a crucial role in our case. MRS can non-invasively differentiate gliomas from other mimics and determine their grading using metabolites such as choline, creatinine, N-acetyl aspartate, lactate, myoinositol, glutamine, glutamate, lipids, and amino acids. In our case, a high choline/NAA ratio and lactate/NAA ratio were indicative of a high-grade tumor. A choline/NAA ratio >1.72 had 100% sensitivity and 87% specificity in distinguishing gliomas from tumefactive demyelinating lesions.[5]

In conclusion, while the diagnosis of gliomas now relies heavily on molecular markers, multiparametric physiologic and metabolic MRI remains a crucial tool in differentiating neoplasms from tumefactive demyelination. The T2/FLAIR mismatch sign, ADC quantification, and MRS are essential for making a confident diagnosis. Further research is needed to investigate the correlation between these radiographic findings, patient outcomes, and epidemiologic factors.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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