

Demyelinating lesions behaving like aggressive tumours on advanced MRI techniques

Brainer Campos Barbosa¹ , Edson Marchiori², Caio Leal Leidersnaider³, Lara Brandao³ and Mauricio Castillo⁴

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Abstract

Tumefactive demyelinating lesions are a rare disorder in which inflammatory demyelination manifests as solitary or multiple focal brain lesions (greater than 2 cm in size), which can be mistaken for glioma, lymphoma, metastasis and in some cases even brain abscess. The symptomatology of tumefactive demyelinating lesions depends on the white matter area involved and includes quickly progressing neurological deterioration of motor, sensory and visual function, praxis, language and mood impairment, as well as seizures. Recognising the key imaging features in a patient with a prior history of demyelination may expedite appropriate management. Preoperative diagnosis or at least the consideration of a demyelinating process is important to avoid unnecessary surgery. We report three patients with demyelinating lesions who presented with findings suggestive of demyelination on conventional magnetic resonance imaging studies. However, in all patients the lesions showed high perfusion and in two high permeability, which are findings generally seen with high-grade neoplasias. In rare instances, tumefactive demyelinating lesions may show increased perfusion and high permeability, imaging findings more commonly seen in high-grade gliomas. We suggest that if white matter lesions on conventional magnetic resonance imaging are compatible with tumefactive demyelinating lesions, atypical findings of high perfusion/permeability should not dissuade the radiologist from suggesting the presence of tumefactive demyelinating lesions rather than high-grade gliomas.

Keywords

Tumefactive demyelinating lesions, high-grade gliomas, perfusion, permeability, MRI

Introduction

Tumefactive demyelinating lesions (TDLs) are a locally aggressive form of demyelination usually manifesting as a solitary lesion greater than 2 cm in size that may mimic a neoplasm on imaging studies^{1,2} and may pose a diagnostic challenge in patients without a pre-existing diagnosis of multiple sclerosis.³ These lesions more commonly occur in women with an average age of 37 years.⁴ However, they may occur at any age, including in children. TDLs may be a diagnostic dilemma and may be misinterpreted as tumours, with the correct diagnosis revealed only after biopsy.⁴ Thus, preoperative diagnosis or at least the consideration of a demyelinating process is important to avoid unnecessary surgery.⁴

The magnetic resonance imaging (MRI) appearance of these lesions may aid in the preoperative diagnosis and assist with the final pathological interpretation, potentially sparing patients unnecessary and possibly debilitating therapies. Here we report three patients with demyelinating lesions who presented with findings suggestive of demyelination on conventional MRI studies.⁵ However, in all patients the lesions showed high

perfusion and in two high permeability, which are findings generally seen with high grade neoplasias.⁶

Cases

Case 1

A 13-year-old boy presenting with hemiparesis on the right in the past 4 months. He had a history of chronic renal failure, treated with renal transplantation along with immunosuppression, which was discontinued a year earlier. He started on rituximab therapy

¹Department of Radiology, Pontifical Catholic University of Goiás School of Medicine, Goiânia, Brazil

²Department of Radiology, Federal University of Rio de Janeiro, Brazil

³Department of Radiology, Grupo Fleury Rio de Janeiro, Brazil

⁴Department of Radiology, University of North Carolina School of Medicine, Chapel Hill, USA

Corresponding author:

Brainer Campos Barbosa, Pontifícia Universidade Católica de Goiás Goiânia, GO 74605-010 Brazil.

Email: brainnerc@gmail.com

6 months ago, which was also discontinued one month after he became symptomatic with right side hemiparesis. MRI was performed and showed a large left frontal-parietal lesion (Figure 1), hypointense on T1 and hyperintense on T2 and fluid-attenuated inversion recovery (FLAIR). No blood products are demonstrated on the gradient echo image. The lesion is located adjacent to the left lateral ventricle and there is no midline shift despite the large lesion volume. A peripheral rim of restricted diffusion and very high permeability is demonstrated in the medial aspect of the lesion. Spectra from the lesion show reduced *N*-acetylaspartate (NAA), high choline and a very high lipid peak. There is also a very high blood volume in the lesion (M-relative cerebral blood volume (rCBV) map, N-perfusion curve). Biopsy showed inflammation and demyelination.

Case 2

An 8-year-old boy presented with difficulty walking and pyramidal right-sided symptoms. MRI demonstrated bilateral high signal intensity lesions on the sagittal FLAIR (Figure 2) as well as in the pyramidal tracts in the pons with marginal enhancement. There is no

callosum compromise. Despite steroid administration the patient's condition worsened – he had bilateral pyramidal signs and symptoms characterised mainly by Babinski signal, hyperreflexia and hypertonia, and he could not speak anymore. He became hemiplegic on the right and paretic on the left. A new MRI study demonstrated that the lesions in the white matter and corpus callosum had increased in size (Figure 2). No blood products were demonstrated and there was restricted diffusion peripherally. High permeability and perfusion were present. Biopsy showed demyelination and inflammation and the patient died soon after surgery.

Case 3

A 16-year-old girl presented with 2 weeks of progressive left-sided weakness. MRI showed a non-contrast enhancing right frontal white matter lesion with significantly restricted diffusion and high perfusion (Figure 3). No treatment was given and one week later the patient's condition worsened and a repeat MRI showed that the lesion was larger but the perfusion was normal. The presumptive diagnosis of demyelination was made and high-dose steroids were given. Follow-up MRI one month later showed significant

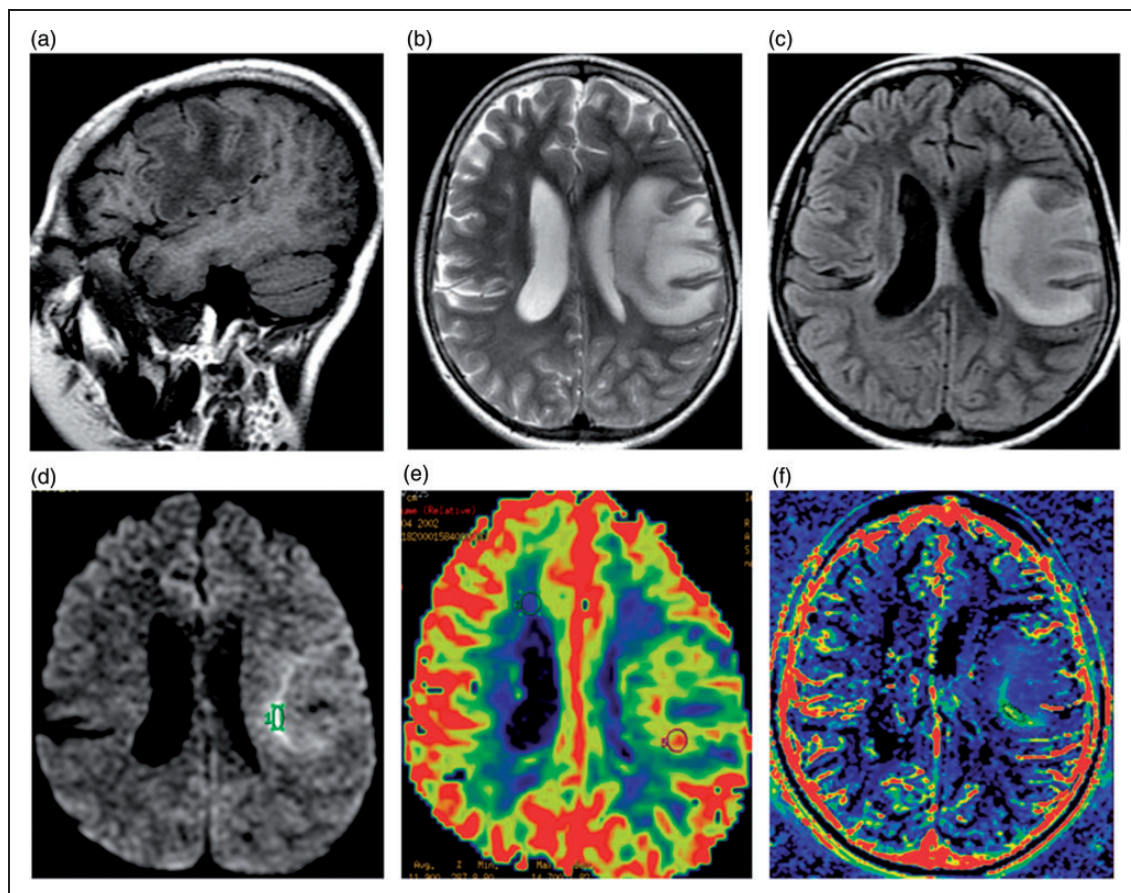


Figure 1. Case 1: (a) Magnetic resonance imaging demonstrates left frontal lobe lesion with mass effect hypointense on T1-weighted images and (b) hyperintense on T2-weighted images and (c) fluid-attenuated inversion recovery (FLAIR). An incomplete peripheral rim of restricted diffusion was demonstrated (d). The lesion showed increased perfusion – relative cerebral blood volume (rCBV) (e) and a peripheral rim of high permeability – *K*trans (f) consistent with high-grade glial neoplasm.

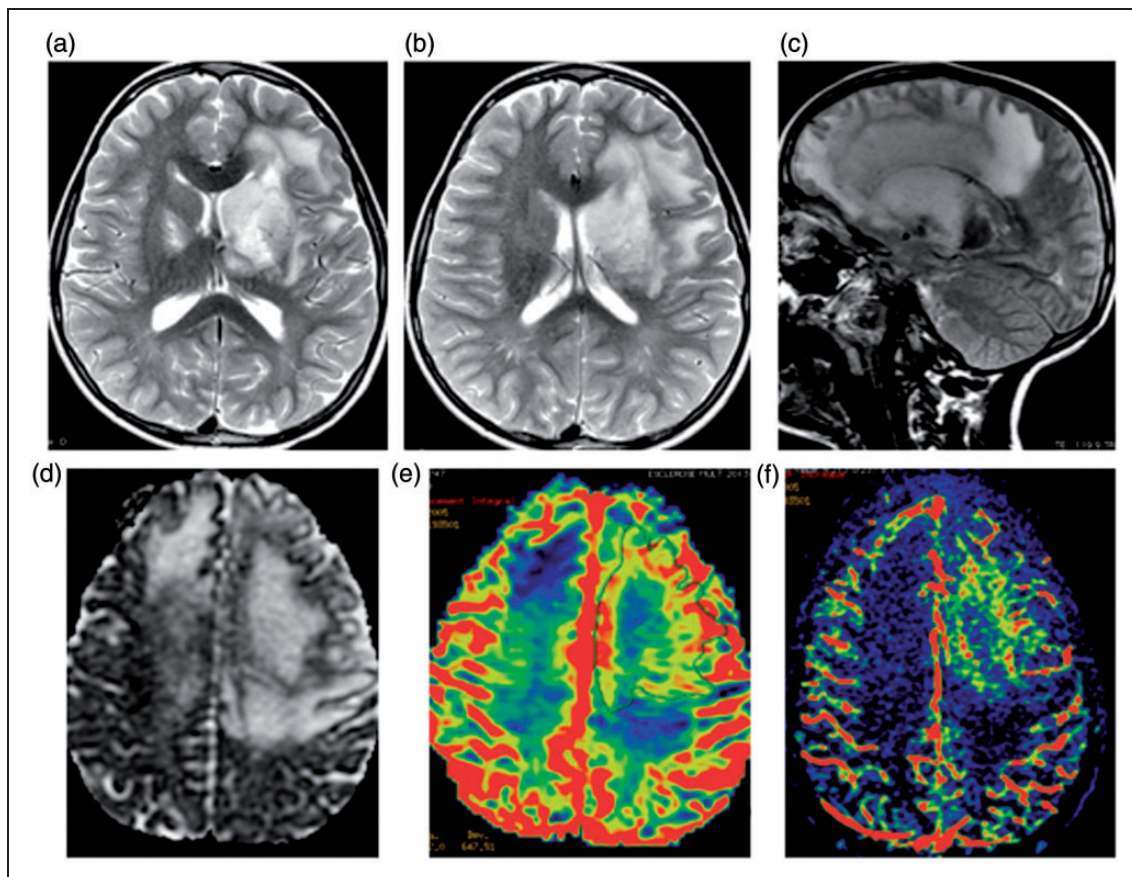


Figure 2. Case 2: Magnetic resonance imaging shows (a and b) high T2 signal intensity lesions in the frontal white matter and corpus callosum (c). An incomplete peripheral rim of restricted diffusion was demonstrated (d). The lesion showed increased perfusion (e) and a peripheral rim of high permeability on the maximum slope of increase map (f).

reduction of lesion size and the patient was asymptomatic. On a 2-year follow up, the patient remains well and asymptomatic.

Discussion

TDLs are defined as lesions larger than 2 cm centered in the white matter that often have conventional MRI findings indistinguishable from those of high-grade gliomas (HGGs). Five pathological patterns are common to both demyelinating lesions and high-grade glial neoplasms: hypercellularity, pleomorphic reactive astrocytes with large hyperchromatic nuclei, mitotic figures, the presence of necrosis and areas of cystic degeneration and/or cavitation.⁷ TDLs are most frequently encountered in women, usually young to middle aged with an average disease onset at 37 years of age.³ Symptoms depend on location and usually include focal neurological deficits, seizures and aphasia.

MRI is the method of choice for imaging demyelinating lesions, tumefactive or not.⁸ In the three patients presented here, the findings on conventional MRI were suggestive of demyelination. TDLs usually appear as large ill-defined ring enhancing lesions with or without central necrosis, perilesional oedema and have less mass effect than expected for their size.⁹ Contrast

enhancement may be seen in the form of an open ring with the incomplete portion of the ring abutting the gray matter.⁸

In addition to conventional MRI techniques, advanced techniques including diffusion-weighted imaging, proton magnetic resonance spectroscopy (MRS), perfusion imaging and permeability studies may provide information that may help distinguish TDL from HGGs. Low apparent diffusion coefficient (ADC) values correlate with increased cellularity, increased grade and high Ki-67 cellular proliferation index in cerebral gliomas. A peripheral rim of restricted diffusion may be demonstrated in both gliomas and TDLs.¹⁰

MRS provides additional metabolic diagnostic indices beyond anatomical information, and has been extensively used to evaluate brain tumours. MRS may be helpful in the evaluation of acute demyelinating disease by identifying elevated Glx peaks (glutamate and glutamine).¹¹ A high Glx peak is more suggestive of a TDL than a HGG.¹² However, this finding is infrequent and more commonly MRS changes of low NAA, high lipids and high choline are found in both TDLs and HGGs.

rCBV maps can be generated from dynamic susceptibility contrast T2* gradient echo, echo planar sequences acquired during the first pass of a standard

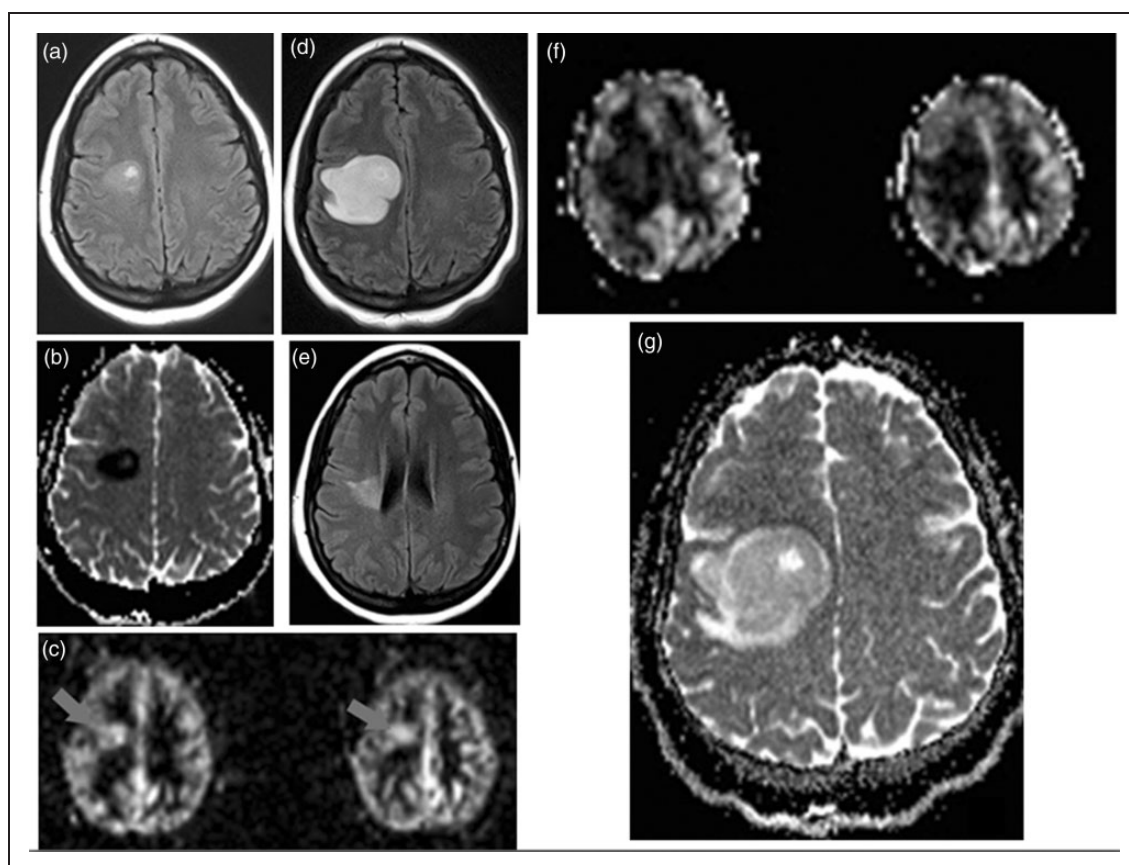


Figure 3. Case 3 – Axial FLAIR (A) shows a lesion in the right frontal white matter which shows marked restricted diffusion on an ADC map (B). The lesion showed no contrast enhancement (not shown) but ASL (C) shows high blood flow in the lesion (arrows). One week later, FLAIR shows marked increased lesion size (D) and ADC shows that restricted diffusion has basically normalized (E). ASL study (F) no longer shows high blood flow but decreased perfusion in the region of the lesion. Follow up at 2 years shows marked decreased in lesion size (G). ASL: arterial spin labelling.

dose of gadolinium-based contrast agent. Tumour blood volume correlates with vascularity and higher grade. Perfusion imaging may be useful to differentiate between TDLs and HGGs as rCBV in TDLs has been found to be substantially lower than that of HGGs and lymphomas.¹³ Perfusion may also be obtained without contrast administration with the use of arterial spin labelling techniques which produce only cerebral blood flow maps. High blood flow has the same implications as high rCBV with respect to cellularity. MRI dynamic contrast enhanced four studies allow estimation of brain tumour permeability. High permeability is typically demonstrated in HGGs, mainly glioblastoma and this finding may serve to differentiate HGGs from TDLs.

Here we present three patients with atypical TDLs which showed findings on advanced techniques (contrast enhanced rCBV, arterial spin labelled cerebral blood flow and contrast enhanced permeability) suggestive of HGGs. However, all lesions were proved by biopsy, follow-up, or treatment response to be TDLs. It has been proposed that higher white matter perfusion in demyelination may reflect inflammation, increased cellularity and vasodilation.^{14,15} Similar findings have been reported using arterial spin labelling.¹⁶ Thus, high

perfusion and increased permeability may rarely be seen in TDLs, as shown in our patients. Despite these findings, conventional and diffusion-weighted imaging findings suggested that the lesions were TDLs.

In conclusion, in rare instances, TDLs may show increased perfusion and high permeability, imaging findings more commonly seen in HGGs. We suggest that if white matter lesions on conventional MRI are compatible with TDLs, atypical findings of high perfusion/permeability should not dissuade the radiologist from suggesting the presence of TDLs rather than HGGs.

Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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ORCID iD

Brainer Campos Barbosa  <http://orcid.org/0000-0003-3434-7806>

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