Diagnostic uncertainty of tumefactive cystic demyelinating lesions

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Multiple sclerosis (MS) is an inflammatory demyelinating disease that affects the CNS. The typical MS lesions appear as asymmetric and multifocal, T2-weighted and fluid attenuation inversion recovery (FLAIR) hyperintense lesions with a tendency for the periventricular and subcortical white matter.[1] When their size exceeds 2 cm in size, they are defined as tumefactive demyelinating lesions (TDLs) or tumefactive multiple sclerosis (TMS). The TMS lesions may occur in prototypic MS as well as the acute fulminant variants of CNS idiopathic inflammatory demyelinating disease. The TMS lesions are well-demarcated, hypodense on CT, and hyperintense on T2-, and relatively hypointense on T1-weighted MRI. Ring enhancement is a characteristic feature of TDLs. Tumefactive MS is rare and estimated at 1-2 per 1000 cases of MS, or 3 cases per million per year in the general population.[2] Lucchinetti et al[3] reported a lower prevalence at one million adults worldwide and 300,000 cases in the United States.

The TMS lesions pose considerable diagnostic uncertainty due to the atypical neurologic symptoms that can be observed as a consequence of the size, location, and potential for associated mass effect and edema. Common presentations in biopsy-proven TMS include motor, cognitive, cerebellar, and brainstem dysfunction.[2] It can also present with seizures, headache, sensory loss, psychosis or aphasia. Two-thirds of patients with TMS lesions subsequently developed a relapsing-remitting disease course with a median time to the second relapse of 4.8 years. The remaining one third of patients has a monophasic illness at last follow-up. The aim of this report is to raise the index of suspicion regarding TMS, especially in the pediatric age group, as early diagnosis and optimal treatment that can prevent further deterioration.

A 10-year-old Saudi girl presented with history of headache and projectile vomiting for 4 weeks, and then developed left side limbs weakness and facial deviation to the right side. Her medical history was unremarkable. When evaluated, she was alert, cooperative and with normal speech. Her vital signs were stable. Fundoscopy revealed bilateral papilledema grade 3. Left facial nerve palsy of the upper motor neuron type, and left upper and lower limbs weakness with power of 4/5 were evident. Deep tendon reflexes were exaggerated on the left side limbs, and Babinski sign was positive on the same side. Her speech and sensory examination were normal. Her initial CT scan brain revealed diffuse right cerebral hemispheric vasogenic edema with significant subfalcine herniation and evolving right uncal herniation. The brain MRI (**Figure 1**) showed

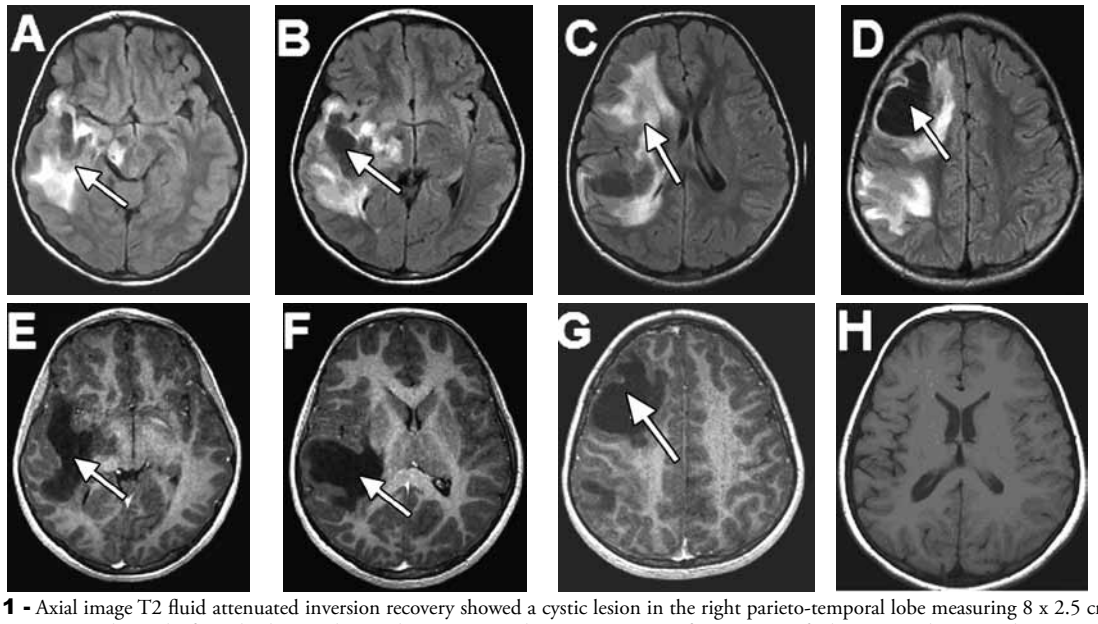

Figure 1 - Axial image T2 fluid attenuated inversion recovery showed a cystic lesion in the right parieto-temporal lobe measuring 8 x 2.5 cm (**A, B, C**). Another right frontal subcortical cystic lesion measured 5 x 3 cm (**D**). Different stages of edema were also noticed (**E, F, G**) with no contrast enhancement. (**H**) Disappearance of lesions on follow-up MRI 4 months later.

2 intraparenchymal non-enhancing right cerebral hemisphere lesions with surrounding edema. The MRI spectroscopy and Diffusion Tensor Image strongly supported the diagnosis of TMS. The whole spinal cord MRI was normal. She received pulse therapy of methylprednisone (Depo-Medrol® IV, Pharmacia & Upjohn, Puurs, Belgium) for 5 days followed by tapering doses over 2 months. Gradual motor improvement and almost full recovery was obtained over 2 months. The CSF analysis for the usual tests in addition to cytology and polymerase chain reaction studies for different infectious etiologies was normal, but oligoclonal bands were positive and continued to be positive on follow-up CSF study carried out 4 months later. Follow-up brain MRI (**Figure 1**) after 4 months showed dramatic disappearance of the previous lesions. She was seen once in the clinic, and she was almost back to her normal health, with no neurological deficit.

Tumefactive multiple sclerosis presents with a large intracranial lesion, greater than 2.0 cm in diameter with mass effect, edema, or ring enhancement with gadolinium contrast, or both. An open-ring enhancement directed toward the cortical surface has been associated with demyelinating lesions.[4] The tumefactive lesion may resemble an abscess or malignant glioma. Clinical presentation includes headache, cognitive abnormalities, mental confusion, aphasia, apraxia, or seizures, or both.[2] Based on the pattern of clinical, biological, and radiological features of acute tumefactive lesions, the following favored tumefactive demyelination over malignancy and helped us rule out invasive brain biopsy in our patient: Clinical symptoms rapidly increasing over a relatively short period of time (usually less than one week); clinical features implicating involvement of more than one site in the CNS, even if brain imaging does not detect additional lesions; clinical, CSF, or serological evidence of recent viral infection; and a predilection to white matter regions. Although this feature alone does not exclude intracerebral lymphoma, which has a similar distribution, the latter is extremely rare in immunocompetent children; MRI results that display a "disproportion" featured by a smaller mass effect than expected for a true tumor when considering the large size of the lesion; and another factor is that in children with demyelination, corticosteroid therapy seems to be associated with rapid improvement in the MRI appearance of the lesion, a feature that is less conspicuous in CNS malignancies in childhood.

Published radiological series of biopsy-confirmed TMS suggest that the lack of mass effect differentiates lesions of MS from other space-occupying lesions such as neoplasm, abscess, or infarct. However, a larger case series demonstrated that mass effect and edema can often be associated with TMS as in our case.[2] Different patterns of enhancement have been described in TMS, including open-ring and multiple closed-ring enhancing lesions. In few cases, the demyelinating lesions may not enhance.[2] The histopathology of these lesions may resemble a neoplasm in the presence of reactive astrocytes, hypercellularity, and increased mitosis. In a study by Lucchinetti et al[2] of 168 cases characteristic of an inflammatory demyelinating disease, the most frequent misdiagnosis (39%) was a low-grade astrocytoma, followed by high grade in 15%. Without treatment, the natural course of TMS has been described as monophasic with a possible conversion to relapsing-remitting MS (RRMS). The prognosis and the risk of developing RRMS after TMS are not well defined in the literature.

The remarkable clinical improvement, the disappearance of the brain lesions on follow-up MRI, and the presence of CSF oligoclonal bands in our case are very crucial in supporting the diagnosis of TMS. The clinical and radiographic improvement without any long-term treatment is not a typical course of other CNS lesions such as most malignancies. This natural course of progression instead best fits and further supports the diagnosis of TMS. Our patient was followed up only once after the initial presentation and further follow-up is warranted.

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References

1. Dastgir J, DiMario FJ Jr. Acute tumefactive demyelinating lesions in a pediatric patient with known diagnosis of multiple sclerosis: review of the literature and treatment proposal. ***J Child Neurol*** 2009; 24: 431-437.
2. Lucchinetti CF, Gavrilova RH, Metz I, Parisi JE, Scheithauer BW, Weigand S. Clinical and radiographic spectrum of pathologically confirmed tumefactive multiple sclerosis. ***Brain*** 2008; 131: 1759-1775.
3. Lucchinetti CF, Parisi J, Bruck W. The pathology of multiple sclerosis. ***Neurol Clin*** 2005; 23: 77-105.
4. Coyle PK. Gender issues. ***Neurol Clin*** 2005; 23: 39-60.