

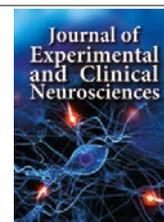


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Case Report

A Clinical Presentation of Tumefactive Multiple Sclerosis Mimicking Acute Ischemic Stroke on MRI

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Abstract

Tumefactive multiple sclerosis (MS) is characterized by a magnetic resonance imaging (MRI) finding of a large, inflammatory demyelinating lesion with or without contrast enhancement. The description of non-tumefactive MS lesions is well established for a variety of MRI sequences; however, explanation of MRI characteristics for tumefactive MS lesions is limited. The findings on diffusion weighted imaging and apparent diffusion coefficient in active MS plaques are well known, but little is known about these sequences in tumefactive MS. There is data to support the use of diffusion tensor imaging (DTI) in addition to basic MR sequences when differentiating tumefactive MS from other lesions such as non-tumefactive MS plaques. The patient in this case report presented with an acute right-sided hemiparesis with a discrete hypodensity on head computer tomography, which was thought to be an ischemic stroke. The initial MRI examination showed a finding that could be consistent with ischemic stroke having decreased apparent diffusion coefficient and increased diffusion restriction. However, a subsequent MRI examination clearly revealed a demyelinating process through development of other white matter lesions. The study attempts to underline that tumefactive demyelinating disease can mimic the clinical and imaging presentation of acute ischemic stroke; therefore, cautious interpretation with clinical correlation is required for correct diagnosis.

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Introduction

Tumefactive multiple sclerosis (MS) is thought to be a variant of MS that is characterized by atypical lesions shown on magnetic resonance imaging (MRI) that are inflammatory, demyelinating and with varying degree of axonal injury. The tumefactive lesions are frequently solitary, greater than 2 cm in diameter, associated with peri-lesional mass effect, edema and with or without contrast enhancement [1]. Clinical presentation varies by the location and size of the lesion, and it can mimic other clinical presentations such as stroke, lymphoma, abscess, or tumor. The accurate identification and diagnosis of tumefactive MS is challenging, and relies on clinical and radiographic findings. Differentiating tumefactive MS from other lesions such as acute non-tumefactive MS lesions, neoplasm and acute ischemic stroke may also be challenging, but also quite important when determining management and treatment. The clinical information is often telling, but may not be sufficient when diagnosing tumefactive MS. Several MRI characteristics such as open ring enhancement, peripheral restricted diffusion, venular enhancement, and proton magnetic resonance

spectroscopy may be useful when clinical information is insufficient [2].

Unlike MRI studies for non-tumefactive MS, there are limited studies that report the characteristics of tumefactive MS lesions using MRI. For example, previous studies have established that the vasogenic edema associated with the pathologic changes in the white matter of non-tumefactive MS can lead to increased diffusion restriction and increased apparent diffusion coefficient on MRI [3]. Although the data on tumefactive MS is sparse, there are reports that suggest a significant association between tumefactive lesion size and the presence of peri-lesional edema [1]. Furthermore, diffusion tensor imaging (DTI) techniques have shown that tumefactive lesions differ from typical MS lesions in a variety of sequences, including higher ADC and lower fractional anisotropy [4]. This is thought to be related to a greater degree of inflammatory response, which results in relatively severe micro-structural disruption. Nevertheless, DTI is not included in routine clinical sequences, so understanding the characteristics of tumefactive MS using other MR sequences is critical when making the

diagnosis of tumefactive MS and differentiating it from other lesions. In the present study, we report a case of a twenty-two year old female who presented with acute right-sided hemiparesis, a left thalamic hypodensity on head computer tomography (CT), and MRI findings suggestive of an acute ischemic stroke; however, the patient was subsequently diagnosed with MS.

Case presentation

A twenty-two year old female patient, Gravida 2, Parus 1, and 34-weeks pregnant, was admitted to the Emergency Room (ER) at Hennepin County Medical Center (HCMC), in Minneapolis, MN, with an acute onset of right face, arm, and leg weakness. The patient was in her usual state of health the night before her presentation but woke up the following morning with the reported neurological symptoms. The patient's pregnancy was uncomplicated, and she had no significant prior medical history. Upon arrival, her initial National Institute of Health Stroke Scale (NIHSS) score was a 7 (face 1, right arm 3, right leg 1, sensory 1, and dysarthria 1). After the initial evaluation, a noncontrast head CT was obtained, which showed a small area of hypodensity located within the left thalamus (shown by the arrow in Figure 1) with initial impression of lacunar infarction. The patient did not receive a thrombolytic due to ongoing pregnancy and unknown time of symptom onset. The patient was admitted to the Neurology Stroke Service at HCMC to undergo further evaluation. At 24 hours after arrival, the patient underwent further imaging examinations including a brain MRI, a transthoracic echocardiogram (TTE) and a bilateral lower extremity ultrasound to rule out deep vein thrombosis. In addition, multiple laboratory tests were performed, including coagulation screening. Excluding the MRI, all other diagnostic tests were normal. Of note, about 45 days prior to this presentation, the patient visited the same ER due to slurred speech lasting longer than 24 hours, but her speech deficit resolved. She was discharged from the ER without neurological evaluation as the symptom was attributed to mild hypokalemia, and she received potassium replacement before discharge.

Noncontrast brain MRI showed a 0.8 x 1.1 cm solitary lesion with increased signal in diffusion weighted imaging (DWI) and corresponding reduced diffusivity (dark signal) on the apparent diffusion coefficient (ADC) map along the periphery; there was increased signal on ADC map at the center, in the location of the thalamic hypodensity noted on the head CT (Figure 2). Fluid attenuated inverse recovery (FLAIR) sequence demonstrated that the hyperintense lesion was well circumscribed, without significant edema or mass effect. Based on the MRI finding, the differential diagnosis of tumefactive MS was reported by the radiologist. Over the course of a three-day hospitalization, the patient exhibited clinical improvement without treatment intervention; however, the patient exhibited a minor loss of dexterity of the right hand. A lumbar puncture was performed (results shown in Table 1), and the patient was discharged to home with a follow-up in the Neurology Clinic.

At her follow up Neurology Clinic visit, the patient reported deterioration in her neurological symptoms, and her examination showed 1/5 strength in her right arm and 3/5 strength in her right leg. A follow up brain MRI was performed 10 days after the initial MRI. The thalamic lesion was shown to have enlarged to 1.8 x 1.5 cm, while the MRI also depicted multiple other, new, subtle punctuate T2-hyperintense lesions in the left posterior frontal lobe and atrium of the right lateral ventricle (Figure 3). The lesion continued to have reduced diffusion, but the ADC signal had increased by this follow up MRI, having a heterogeneous signal at the center.

Based on the clinical and radiographic deterioration, the patient was treated with high-dose intravenous steroids. After five days of treatment, the patient had significant improvement in her motor function. On a subsequent clinic visit, the patient showed slight right hand and foot dexterity difficulty. The patient

delivered a healthy baby, without any complications, a few months later. The diagnosis of MS was made on subsequent Neurology Clinic visits post-partum, based on revised 2010 McDonald criteria [5]. The patient was started on immunomodulatory therapy. Follow-up MRIs were performed at intervals of 2, 3, and 8 months from the initial presentation. The most recent MRI demonstrated that the left thalamic lesion continued to be hyperintense on FLAIR, but developed decreased signal intensity on DWI along the portion of the lesion that initially had reduced diffusion (see Figure 4).



Figure 1. Initial non-contrast head CT upon presentation with an acute right sided hemiparesis. A left thalamocapsular hypodensity is seen (arrow).

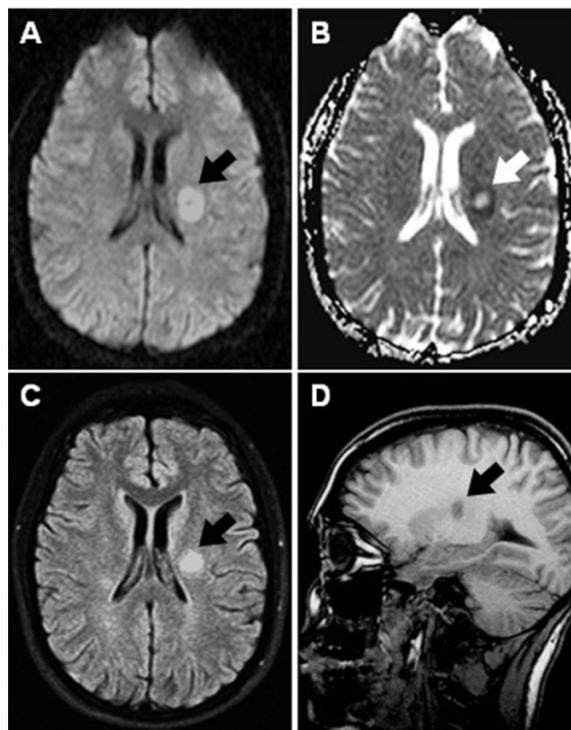


Figure 2. Non-contrast MRI acquired 24 hours post-presentation. (A) DWI-axial, (B) ADC-axial, (C) FLAIR-axial and (D) T1-sagittal. The lesion is 0.8 cm x 1.1 cm, has increased DWI, increased ADC centrally, decreased ADC peripherally, hyperintense on FLAIR, and hypodense on T1 (arrows).

Discussion

Tumefactive MS is an atypical radiographic presentation within the inflammatory demyelinating disease spectrum that frequently poses diagnostic dilemma. Lucchinetti et al. [1] reviewed 168 patients with confirmed diagnosis of tumefactive demyelinating disease via histological studies, characterized by hypercellularity with confluent demyelination, macrophages containing myelin debris, reactive astrogliosis, relative axonal preservation and variable perivascular and lymphocytic inflammation. According to their report, it is presumed to be more common in females with an average age of 37 years old [1]. In addition, they also reported that 51% had a relapsing remitting course, while 70% were diagnosed with multiple sclerosis using the Poser or McDonald's criteria during a median follow up time of 3.9 years.

In the setting of a solitary lesion presenting with contrast enhancement, it is difficult to differentiate tumefactive demyelinating lesions from an enhancing neoplasm, radiation necrosis, abscess or infarct, although an abscess typically would exhibit reduced diffusion centrally while a high grade neoplasm typically exhibits reduced diffusion peripherally [6]. MR spectroscopy has been studied to assist in diagnosis; however, except for difference in N-acetylaspartate and creatineratio seen only in center of lesions, no other metabolite ratio could be used to distinguish high gradeglioma from tumefactive demyelinating lesion, thus limiting its use [7]. More recently, Miron et al. [4] proposed that DTI could be used to detect tumefactive lesions with high sensitivity through quantifying the resulting microstructural changes from inflammation.

The few imaging clues to identify tumefactive demyelinating lesion include minimal mass effect and edema, enhancement, either closed or arc-like and large in size [8]. Often biopsy is undertaken to confirm the diagnosis, which shows histological findings of typical MS plaque encompassing myelin breakdown, reactive astrocytes, and macrophage infiltrates [8]. A clinical clue to support the diagnosis of tumefactive demyelinating disease is a highly favorable response to steroid treatment [8]. Also, if demyelinating disease is initially suspected, the utilization of thin slice (<2 mm thickness), sagittal FLAIR images may detect concomitant, tiny "striations" oriented perpendicular to the corpus callosum that could point to a demyelinating etiology [9].

It is well-established that an acute demyelinating lesion in patients with MS can exhibit increased signal in ADC and DWI sequences on MRI [3]. This finding is thought to be a result of vasogenic edema, unlike the cytotoxic edema of ischemic stroke that can result in decrease ADC and increased DWI signal. Balashov and colleagues [5] reported another patient with relapsing-remitting MS with an acute presentation that showed increased DWI and reduced ADC signal in an early lesion, which is a finding compatible with an ischemic stroke. However, subsequently the lesion's signal changed to show increased DWI and ADC signal, a finding which was more consistent with an MS lesion. Thus, it is thought that the presence of reduced diffusion (low ADC value) is related to the "acuity" of the demyelinating lesion, which likely increases (high ADC value) over time; hence, our patient likely suffered from an "acute" demyelinating lesion [5,10]. Thus, it should be noted that ischemic stroke can occur in MS patients and needs to be differentiated from tumefactive lesions, both of which can exhibit restricted diffusion and enhancement depending on acuity

[5,10]. Therefore, this case demonstrates that occasionally there may be difficulty in discriminating between these two entities (i.e., tumefactive MS and acute infarct) based on imaging, given their overlap in the acute phase.

Due to the imaging and clinical similarities between an ischemic stroke and tumefactive MS, misdiagnosis between the two diseases is commonly encountered in the clinical setting. In order to obtain the correct diagnosis, accurate clinical and family history and ancillary testing, such as lumbar puncture, should be performed. However, recently with more reliance on the neuroimaging to diagnose a demyelinating disease such as MS, serial MRI maybe warranted to confirm the diagnosis, such as in our patient, who later developed other white matter lesions.

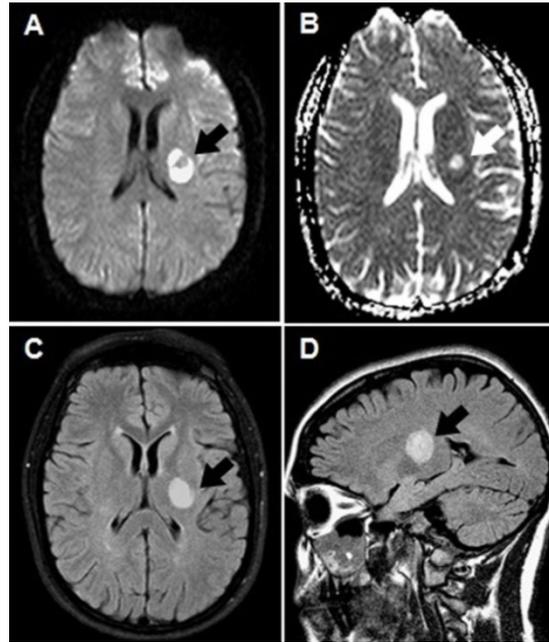


Figure 3. Follow up brain MRI acquired 10 days from the initial MRI due to worsening right-sided hemiparesis. The images reveal the development of right periventricular white matter lesions on FLAIR (arrows). (A) DWI-axial, (B) ADC-axial, (C) FLAIR-axial and (D) FLAIR-sagittal.

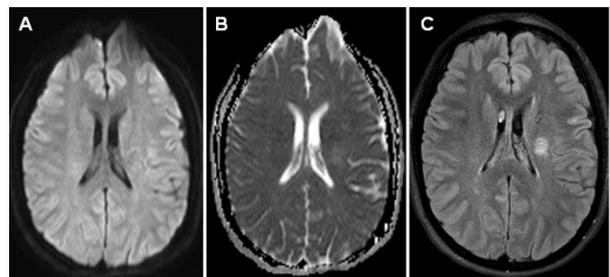


Figure 4. Follow up MRI study at 8 months that shows decreased conspicuity of the left thalamic lesion on DWI (A) and ADC (B), but the lesion continues to exhibit hyperintensity on FLAIR (C).

Table 1. Laboratory testing data.

Myelin basic protein	Lumbar Puncture			Serology		
	Oligoclonal bands	Nucleated cell	Glucose	Protein	TSH	Lyme
42	9	1	Normal	25	2.7	Negative

Conclusion

Demyelinating disease can have highly variable clinical presentation and can mimic other neurological entities, which translates into difficulty and challenge for the clinician in formulating differential diagnoses for patients with an abrupt neurological deficit. Tumefactive demyelination can present with various atypical clinical and imaging findings. These include hypodensity on head CT and increased DWI with reduced ADC signal on MRI (which is also seen in ischemic stroke) as illustrated in our patient. Further meticulous radiographic study of characteristic features of tumefactive lesion using different imaging techniques in conjunction with clinical and histopathologic correlation is warranted.

Conflict of interests: The authors declare no conflict of interest.

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