Tumefactive Multiple Sclerosis presenting as Acute Ischemic Stroke

Abstract

Background and Purpose: Multiple sclerosis (MS) plaques appear as well-demarcated, homogenous small ovoid lesions on magnetic resonance imaging (MRI). Atypical radiographic features of MS lesions include size greater than 2 cm, mass effect, and edema. Tumefactive MS lesions can radiographically mimic intra-cranial neoplasms, infarction, as well as infections. In atypical cases of tumefactive demyelinating lesions, brain biopsy may be required for the diagnosis.

Methods: The authors describe the case of a 43 year old woman who presented with worsening right-gaze preference and left side weakness and was initially diagnosed with acute ischemic stroke. The patient underwent laboratory investigation and brain contrast-enhanced MRI before undergoing brain biopsy.

Results: Fluid attenuation inversion recovery (FLAIR) MRI showed an increase in signal intensity in the right frontal lobe sub-cortical region. Diffusion-weighted imaging showed an area of restricted diffusion involving the white matter of the right-frontal lobe. Cerebrospinal fluid studies were normal except for the presence of oligo-clonal bands. Magnetic resonance spectroscopy (MRS) demonstrated an elevated choline (Cho)/creatine ratio, increase lactate, and normal N-acetylaspartate (NAA)/creatine ratio, findings suggestive of an inflammatory or a demyelinating disease. A brain biopsy of the right frontal lesion was performed and revealed well-demarcated foci of demyelination with axonal preservation. Peri-vascular and parenchymal CD3(+) T-cells were also identified within the demyelinated foci, findings that further supported the diagnosis of active multiple sclerosis.

Conclusion: Tumefactive MS can be radiographically misdiagnosed as one of several conditions, among which are infarction, infections, and tumors. Brain biopsy may be needed for diagnosing challenging cases of tumefactive MS.

Keywords: tumefactive, multiple sclerosis, stroke, tumor, demyelination.

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Introduction

Multiple sclerosis (MS) plaques appear as well-demarcated, homogenous small ovoid lesions on magnetic resonance imaging (MRI).[1] Atypical radiographic features of MS lesions include size greater than 2 cm, mass effect, and edema.[2] Tumefactive MS lesions can radiographically mimic intra-cranial neoplasms, infarction, and infections. In atypical cases of tumefactive demyelinating lesions, brain biopsy may be required for the diagnosis.

We report a case of a patient with tumefactive MS who presented with focal neurological deficits and challenging radiographic findings. Tumefactive demyelinating lesions may pose a considerable diagnostic challenge to both the neurologist and neuro-radiologist.

Case Description

A 43 year-old woman presented to our emergency room with worsening right-gaze preference and left side weakness that began one to two days prior to arrival. The patient was observed to have changes in behavior and episodes of being confused for the past three days. Three days after symptoms onset, she was observed to have right-gaze preference and left-sided weakness. One day before admission, the patients developed dizziness, confusion and a two-hour episode of right-sided numbness and was diagnosed with transient ischemic attack in a local hospital.

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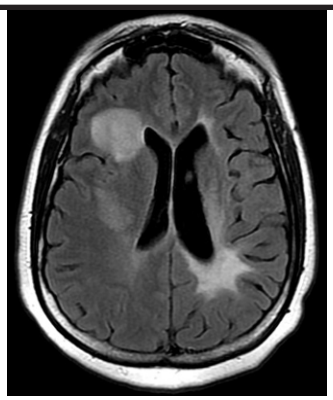

Figure 1: FLAIR MRI at the time of initial presentation showing an increase in signal intensity in the subcortical right frontal white matter.

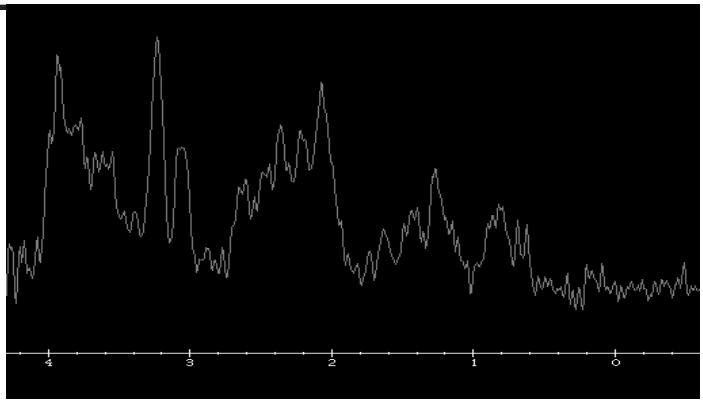

Figure 2: Single voxel MR spectroscopy placed within the right centrum semiovale posteriorly measures the NAA/creatine ratio of 1.23 and the Cho/creatine ratio of 1.43. Single voxel spectroscopy placed in the corresponding white matter demonstrated an NAA/creatine ratio of 1.31 and Cho/creatine ratio of 0.77. There is a lactate peak within the right frontal periventricular T2 hyperintense white matter.

She presented to a local hospital three years prior with right side weakness and was diagnosed with acute ischemic stroke, but eventually returned to baseline after rehabilitation.

Neurological exam revealed pronounced dysarthria, decreased blink to threat on the left side, right-gaze preference, and severe left-facial central weakness. Using the Medical Research Council scale for motor strength, motor exam revealed a 2-3 motor strength on her left side. Sensory exam revealed pronounced decrease in pain sensation on the left side. Reflexes were brisk and symmetrical.

Fluid attenuation inversion recovery (FLAIR) MRI showed an increase in signal intensity in the sub-cortical right frontal lobe region (Fig 1). Diffusion-weighted imaging showed an area of restricted diffusion involving the white matter of the right-frontal lobe. These findings were suspicious for a late-subacute infarction.

The patient's weakness progressed to 0/5 on the left side over the course of three days. An MRI with contrast revealed a minimal curvilinear enhancement in the deep white matter of the right frontal lobe (images not shown). Cerebrospinal fluid studies were normal except for the presence of oligo-clonal bands. Magnetic resonance spectroscopy (MRS) demonstrated an elevated choline (Cho)/creatine ratio, increase lactate, and normal N-acetylaspartate (NAA)/creatine ratio (Figure 2), findings suggestive of an inflammatory or a demyelinating disease. Neoplasm was thought to be less likely due to the normal NAA/Cho ratio.

A brain biopsy of the right frontal lesion was performed and revealed well-demarcated foci of demyelination (Figure 3) with relative axonal preservation (Figure 4A). Several CD68(+) macrophages were noted (Figure 4B) and PAS(+) material was identified within the macrophages (Figure 4C). Peri-vascular and parenchymal CD3(+) T-cells were also identified within the demyelinated foci (Figure 4D). These pathological findings were compatible with active multiple sclerosis.

The patient was started on intravenous dexa-methasone followed by a five-day course of intravenous cladribine with no clinical improvement. She was transferred to a rehabilitation facility with no further treatment. Nine months later, the patient's examination revealed dysarthria and right-gaze preference. Motor examination revealed a significant improvement in the left side strength to 3-4/5 with increased tone. A follow-up MRI showed a marked decrease in edema and mass-effect in the right fronto-parietal region (images not shown). The follow-up MRI also showed a significant expansion of confluent abnormal T2 prolongation within the left frontal and right parietal peri-ventricular white mater, findings that suggest interval demyelination.

Discussion

Multiple sclerosis can be usually diagnosed by demonstrating evidence of clinical and/or radiographic dissemination of disease in time and space.[3] MS lesions are usually small ovoid lesions that are often oriented perpendicularly to the long axis of the ventricular system.

The occurrence of neoplasm-like demyelination is very rare, reported in 1-2/1,000 cases of MS.[4]

Mass effect and edema of the central nervous system in tumefactive MS are reported to be proportionally minor relative to plaque size when compared to tumors and abscesses.[5-6] Previously published radiological series of biopsy-confirmed tumefactive MS suggest that the lack of mass effect differentiates lesions of MS from other space-occupying lesions such as neoplasm, abscess, or infarct.[7] However, a larger case series demonstrated that mass effect and edema can often be associated with tumefactive MS.[2] Our case report further supports the findings that atypical radiographic features of tumefactive inflammatory MS include both mass effect and edema.

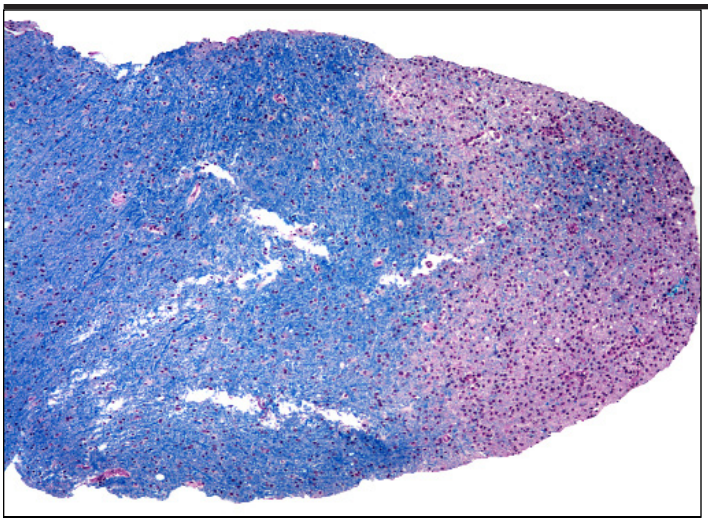

Figure 3: LFB/PAS 100X Sharply-demarcated area of demyelination with increased cellularity.white matter.

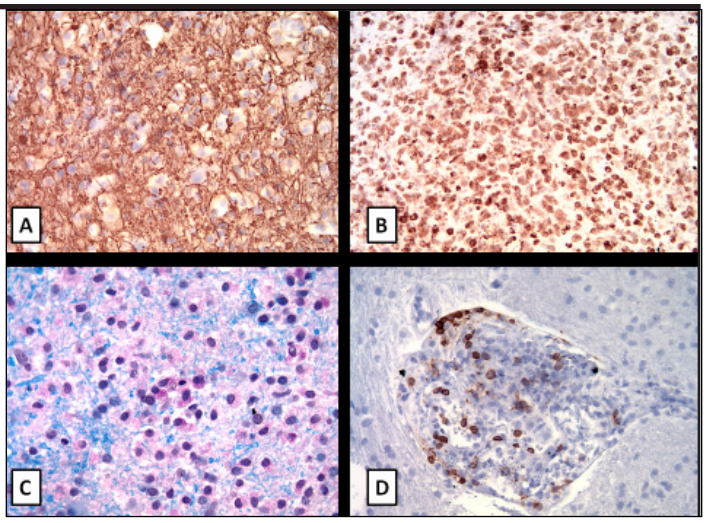

Figure 4: A) Neurofilament (IHC) 400x Relative preservation of axons B) KP-1 (IHC) 200x Macrophages (same area as in C) C) LFB/PAS 630x Macrophages containing PAS (+) material D) CD3 (IHC) 400X Perivascular CD3(+) T-cells.

Lesions of both typical and tumefactive MS frequently enhance on MRI. Different patterns of enhancement have been described in tumefactive MS including open-ring and multiple closed-ring enhancing lesions. In few cases, the demyelinating lesions may not enhance.[2,8] These studies undoubtedly reveal that lack of enhancement does not rule out an inflammatory demyelinating lesion of the central nervous system. Lack of significant enhancement is another feature that should be taken into consideration when facing a challenging case of tumefactive MS.

The natural course of tumefactive MS without treatment has been described as monophasic with a possible consequent conversion to typical relapsing-remitting MS (RRMS).[9-10] The risk of developing and the prognosis of RRMS after tumefactive MS are not well defined in the literature. According to one case series, the majority of patients (25/28) diagnosed with tumefactive MS did not develop typical RRMS, and those who did were reported to have typical radiographic appearance of MS plaques with future clinical exacerbations.[9] Radiographically, the majority of patients with tumefactive MS showed an improvement in the demyelinating lesions.[9] In a smaller case series of five patients, none of the patients with tumefactive MS developed typical RRMS after a median follow up of 44 months.[11] In contrast, a more recent retrospective review study discussed that the majority (70%) of patients with tumefactive inflammatory demyelinating disease ultimately developed clinically definite MS.[9]

Clinical and radiological follow-up in our case report are very crucial in supporting the diagnosis of tumefactive MS. The clinical and radiographic improvement without any long-term treatment is not a typical course of other central nervous system lesions such as most malignancies. This natural course of progression instead best fits and further supports the diagnosis of tumefactive MS. The lesions disseminated in time and space, the presence of oligo-clonal bands in the cerebrospinal fluid, and the pathological findings on brain biopsy all support the diagnosis of MS. Our patient was followed up only once after the initial presentation and further follow-up is warranted.

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