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Case reports

Tumefactive multiple sclerosis: an uncommon diagnostic challenge

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Abstract

Objective: This case report describes a rare presentation of multiple sclerosis (MS) that was initially diagnosed as a peripheral nerve lesion in the emergency department.

Clinical Features: A 30-year-old woman presented to a chiropractic teaching clinic with a complaint of a sudden right foot drop. Magnetic resonance imaging of the brain revealed a large mass in the left parietal lobe with additional white matter lesions. The mass and smaller lesions were consistent with a rare presentation of demyelinating disease, tumefactive MS.

Intervention and Outcome: The patient was referred to a neurologist for further evaluation and treatment. Her short-term clinical course was punctuated by recurrent myospasms and neurologic deficits.

Conclusion: Tumefactive MS may mimic the clinical and magnetic resonance imaging characteristics of glioma or a cerebral abscess. The clinical presentation, pathophysiology, differential diagnosis, role of diagnostic imaging, and treatment options of MS are described. This case report illustrates that the timely diagnosis and optimal treatment of MS require recognition of its varied, sometimes atypical, and often nonspecific clinical and imaging manifestations.

Introduction

Multiple sclerosis (MS) is the most common cause of progressive neurologic disability in adults aged 20 to 40 years in the developed world.[1] It presents as an

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inflammatory demyelinating and neurodegenerative disease.[2,3] The demyelination and/or axonal damage may produce varied and nonspecific clinical features. Demyelination causes slowing of conduction or complete failure, whereas axonal damage completely disrupts conduction.[3] The course of MS includes relapses and progression.[4-6] The relapses (exacerbations) occur on average once every other year[4] and correspond with new focal acute inflammatory lesions or reactivation of previous lesions. Progression is steady, with worsening of symptoms and signs over a 6- to 12-month period likely the result of chronic, progressive, diffuse central nervous system degeneration.[4] Remission phases are attributed to remyelination and resolution of inflammation. Recurrent exacerbations limit remyelination.[6]

Although the cause of MS is unknown, it is considered an autoimmune disease occurring in genetically susceptible individuals. Factors that impact the genetic susceptibility for MS are infectious, nutritional, climatic, or environmental.[7] Triggers for onset or relapse may include pregnancy, stress, trauma, anesthesia, surgery, or vaccinations.[4]

Multiple sclerosis affects 2 million people worldwide and more than 400 000 in the United States.[2] Lucchinetti et al[6] report a lower prevalence at 1 million adults worldwide and 300 000 cases in the United States. Tumor-like demyelination in tumefactive MS is rare and estimated at 1 to 2 per 1000 cases of MS or 3 cases per million per year in the general population.[5] Seventy-five percent of individuals with MS are female.[8] The distribution of onset is typically 10% before the age of 20 years, 70% between 20 and 40 years, and 20% after the age of 40 years.[4] Females have a slightly younger mean age of onset, and males have a worse prognosis.[4,8] Tumefactive MS also demonstrates a higher female prevalence with a median age at onset of 37 years.[5]

Multiple sclerosis poses a significant financial and social burden. In 1994, the mean total lifetime direct and indirect costs for a patient with MS was estimated at $2.2 million, with a national cost of $2.5 billion.[9] Multiple sclerosis in 43% of patients leads to job loss. Life expectancy is minimally reduced by MS.[4] Fifty percent of individuals with MS will die from other causes. Factors that influence survival include sex, age at onset, initial symptoms, and socioeconomic status.[10]

The purpose of this report is to emphasize the need for timely and accurate diagnosis of MS to optimize treatment. By using disease-modifying agents, a reduction in the frequency and severity of relapses as well as a decrease in brain lesion development can occur.[11] Unfortunately, the clinician often faces a nonspecific and/or atypical clinical presentation, particularly with the tumefactive form of this disease. This may result in diagnostic confusion and delayed treatment.

Case report

A 30-year-old woman presented to a chiropractic teaching clinic with a chief complaint of sudden right foot drop. The symptoms had been present for almost 2 weeks. Four days after the onset of foot drop, the patient presented to the emergency department (ED) dragging her right foot. Pressure and pain sensation in her right calf were preserved, but motor tone was reduced. She was diagnosed with right foot drop and peroneal nerve palsy. Electromyography (EMG) was ordered for the right leg and performed the following day; it yielded no evidence of mononeuropathy. Result of another EMG performed 3 days later was also normal. Three days after the second EMG, the patient reported to the same ED with a chief complaint of anterior right ankle pain subsequent to an inversion injury. The foot drop persisted. Result of radiography of the ankle was normal, and she was diagnosed with a right foot sprain. The patient was referred to her primary care physician for follow-up.

The next day, she reported to the chiropractic clinic for evaluation of her right foot drop. Her review of systems revealed muscle twitching in the lower left lumbar spine and left eyelid. She was also complaining of right buttock twitching. Lumbar spine and right ankle/foot examinations were completed. Inspection revealed abnormal gait, heel walk, toe walk, and pronation and supination of the right foot due to paresis of the right anterior compartment muscles. The right leg was cold to touch in comparison to the left. All distal pulses were normal bilaterally. The circumferential measurements of the patient's right leg 5 in distal to the right lower patellar pole was 1.5 cm smaller than the left. Neurologic examination revealed a Babinski response on the right without clonus. Motor testing of the right tibialis anterior and extensor hallucis longus elicited a grade 0/5. The L2, L3, L4, and L5 dermatomes revealed hypoesthesia on the right. Active range of motion in extension, dorsiflexion, toe extension, and inversion of the right foot could not be performed. Lumbar range of motion testing was within normal limits. Orthopedic tests were unremarkable except for Bechterew, as the patient could not elevate her right leg as high as the left.

Three-view radiography result of the lumbar spine was negative. Suspicion of intracranial neurologic disease prompted magnetic resonance imaging (MRI) of the brain with and without contrast (Figs 1 and 2). The examination revealed a 3.0-cm intraaxial mass in the superior aspect of the left parietal lobe with surrounding edema, mass effect, and a partial ring-like pattern of contrast enhancement. Two small, nonspecific foci of abnormal signal intensity were present in the white matter of the cerebellum and right temporal lobe. The differential diagnosis for the left parietal lobe mass and additional white matter lesions was consistent with tumefactive MS. However, the differential diagnosis included glioblastoma multiforme and cerebral abscess. The patient was referred to a neurologist for further evaluation and treatment.

Five days later, she was admitted to the hospital with right foot drop, paresthesias of the right trunk, and twitching of her right face. Result of a follow-up MRI of the brain was unchanged. The stable clinical presentation and the unchanged MRI examination result excluded glioblastoma multiforme and cerebral abscess from the differential diagnosis. No biopsy was performed. Hydrogen magnetic resonance spectroscopy (H-MRS) (Fig 3) demonstrated elevation in choline to creatine ratio. *N*-acetyl aspartate (NAA) was decreased. Magnetic resonance spectra from the contralateral hemisphere were normal. An electroencephalogram demonstrated no abnormality. Laboratory examination revealed elevation of the mean red cell volume, leukocytosis with neutrophilia, and elevated glucose. The patient was discharged from the hospital and referred to a neurologist for follow-up. She subsequently underwent echocardiography to evaluate spasms arising from a suspected stroke of cardiogenic origin. The result of the study was normal.

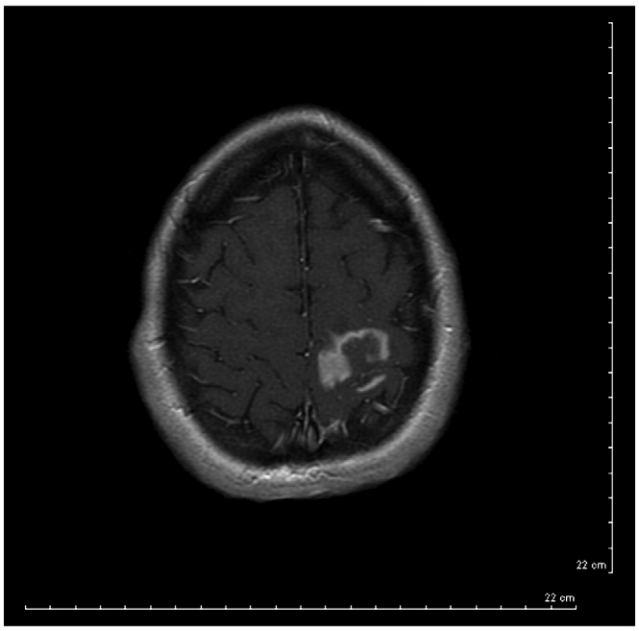

Fig 1. Contrast T1-weighted axial MRI examination of the brain demonstrated a 3.0-cm intraaxial mass in the left parietal lobe with an open-ring enhancement pattern directed toward the cortical surface. This pattern is frequently encountered with tumefactive MS. There was minimal mass effect.

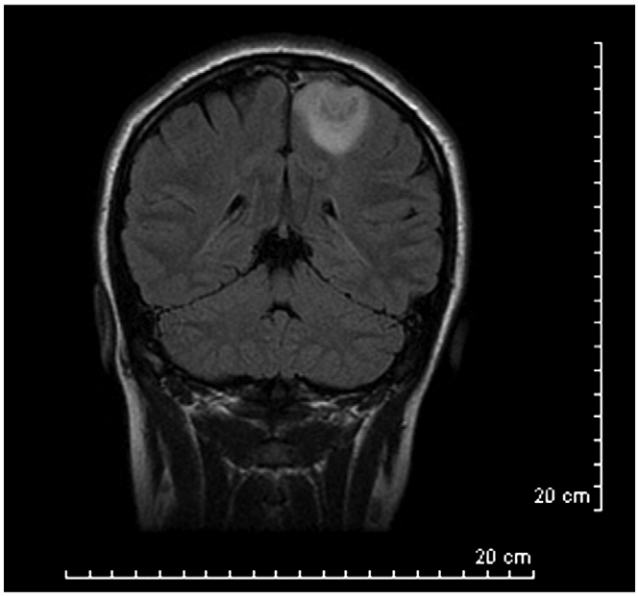

Fig 2. T2-weighted fluid-attenuated inversion recovery coronal MRI examination of the brain revealed a heterogeneous high-signal intraaxial lesion in the superior aspect of the left parietal lobe resulting in sulcal effacement.

Discussion

Multiple sclerosis is the most common inflammatory demyelinating disease classically presenting as multifocal plaques in the brain and spinal cord. The demyelinating plaques are commonly noted in the optic nerves, brainstem, spinal cord, cerebellum, and periventricular white matter.[6] Multiple sclerosis has been described as a 2-stage disease with an initial inflammatory component attacking the myelin or white matter. A second stage involving white and gray matter degeneration occurs later in the course. Steinman[12] reported gray matter degeneration early in the disease.

Tumefactive MS presents with a large intracranial lesion, greater than 2.0 cm in diameter with mass effect, perilesional edema, and/or ring enhancement with

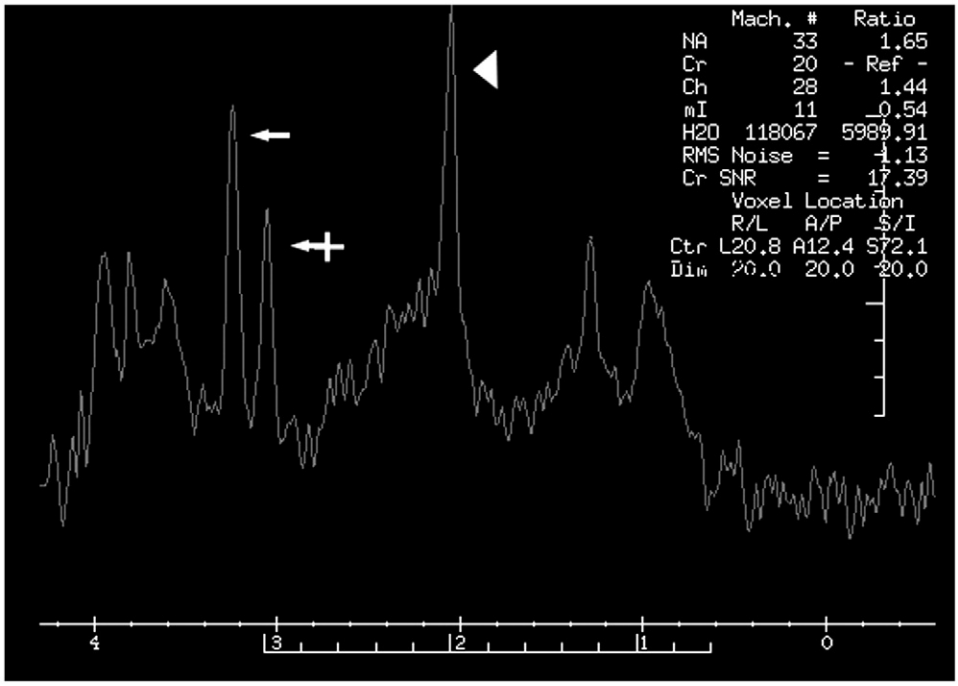

Fig 3. The H-MRS of the left parietal lobe lesion. It demonstrated elevation in the choline (arrow) and creatine (crossed arrow) peaks with a decrease in the NAA peak (arrowhead). An increased choline peak indicated elevated cell membrane destruction consistent with demyelination and inflammation. The reduction of the NAA concentration indicated neuronal and axonal damage.

gadolinium contrast. An open-ring enhancement directed toward the cortical surface has been associated with demyelinating lesions.[6] The intracranial mass may mimic a malignant glioma or cerebral abscess. Clinical presentation of tumefactive MS includes headache, cognitive abnormalities, mental confusion, aphasia, apraxia, and/or seizures.[5] A biopsy may mistakenly diagnose the lesion as a neoplasm given its hypercellularity, frequent identification of atypical reactive astrocytes, and numerous mitotic figures. In a study by Lucchinetti et al[5] 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%.

The clinical course of MS is varied.[3] Clinical manifestations of MS and patient symptoms are noted in Table 1.[1] The initial symptoms of MS are often confusing and difficult to diagnose because of their nonspecific character. Motor and sensory symptoms commonly occur with MS. The motor symptoms tend to develop first and are followed by sensory.[13] Patients with MS can display 4 clinical disease courses. Eighty-five percent initially present with relapsing-remitting MS.[2,9] This course is characterized by clear episodes of neurologic disability and recovery. Fifty percent of these individuals with relapsing-remitting MS will develop secondary progressive MS within 10 years and 90% within 25 years. Secondary progressive MS is characterized by steadily increasing permanent neurologic disability. A third clinical presentation is primary progressive MS seen in 10%. These patients demonstrate a steady decline in neurologic function from the onset of the disease without periods of recovery. The final clinical course of MS is progressive relapsing. Five percent of MS

Table 1 Clinical features of MS[1]

Signs	Symptoms
Optic neuritis	Blurred vision, eye pain, color loss, field defects
Myelitis	Numbness, pain, dysesthesias, pressure sensations, weakness, ataxia (sensory), gait dysfunction, neurogenic bladder, neurogenic bowel, sexual dysfunction, spasticity
Ocular, motor, vestibular	Double vision, oscillopsia, vertigo, nausea, vomiting, disorientation, gait disturbance
Paroxysms	Seizures, focal dystonias, tonic spasms, dysarthria, ataxia, speech arrest
Uhthoff phenomenon	Symptoms are exacerbated by infection, heat, prolonged exercise, or stress.
Cognitive	Slow processing speed, poor multitasking, reduced memory, rarely aphasic syndrome
Fatigue	Related to sleep disturbance, mood, altered properties of physical function (ie, biomechanics, spasticity)

cases will undergo steady progressive neurologic decline accentuated by clearly defined acute attacks.[2]

Diagnostic imaging plays an important role in assessing MS. Magnetic resonance imaging diagnosis is based on lesions that are disseminated in time and space. Dissemination in time refers to multiple episodes, whereas dissemination in space suggests involvement of more than one area of the central nervous system. Tintore et al[14] developed criteria (Table 2) for diagnosis, currently accepted by the National Multiple Sclerosis Society,[3] after modifying the criteria of Barkhof et al.[15]

Magnetic resonance imaging is the primary modality in the workup of the brain and spinal cord. Gadolinium enhanced T1-weighted imaging identifies new lesion activity. Brain and spinal cord MS lesions are best depicted on T2-weighted sequences. Inversion recovery sequence (fluid-attenuated inversion recovery) suppresses cerebrospinal fluid signal hyperintensity, leading to improved visualization of periventricular and juxtacortical lesions. Gadolinium-enhanced T1-weighted images demonstrate hyperintensity within blood vessels but will display hyperintensity within the brain parenchyma if the blood brain barrier is disrupted.[16] The barrier is disrupted by inflammation in active plaques.[17]

Proton MR spectroscopy (H-MRS) detects biochemical changes in the brain, improving pathologic specificity, a limitation of structural MRI.[18] Metabolic products of neural tissue measured with MR spectroscopy include choline, creatine, NAA, mobile lipids, and lactic acid.[19] Increased choline from elevated cell membrane turnover is seen in MS during demyelination and inflammation. The ratio of NAA to creatine is an important biomarker, as NAA is found only in neurons. Reduction of the NAA concentration indicates neuronal or axonal dysfunction and loss.[18]

Treatment of MS includes nonpharmacologic and pharmacologic approaches. Fifty-seven percent of 3140 individuals with MS surveyed in the United States used one or more complementary and alternative medicine therapies.[20] Frequently used therapies included herbs (26.6%), chiropractic (25.5%), massage (23.3%), and acupuncture (19.9%). A case report regarding chiropractic treatment of MS described the complete absence of symptoms (lower extremity numbness, gastric distension, chronic daily fatigue, and cognition difficulties) after spinal adjusting procedures.[21] A small study of 14 individuals with secondary progressive MS demonstrated greater improvement in the Multiple Sclerosis Impact Scale 29 (a measure of the physical and psychologic impact of MS from the patient's perspective[22]) using acupuncture.[23] Other therapies included dietary supplementation with linoleic acid and its derivatives[13] and vitamin D supplementation. Vitamin D supplementation has been considered a treatment of MS because vitamin D affects the growth and differentiation of immune-modulator cells such as macrophages, T cells, and B cells.[24] Dosages varied in several small studies from 25 to 1000 μg (1000-40 000 IU) per day for 6 months.[25] Although vitamin D has been used therapeutically, individuals with the highest levels of vitamin D had a significantly lower risk of MS.[26] Geographic latitude as described by Kidd[13] correlates with MS. Exercise and MS have been discussed in the literature.[11,27,28] Limited physical activity was recommended by physicians before 2001 to minimize the risk of exacerbations and symptoms of fatigue.[27] Dalgas et al[28] completed a 12-week randomized control trial examining the relationship between progressive resistance training, muscle strength, and functional capacity in patients with MS. The study concluded that supervised and intense resistance training of the lower extremity improved muscle strength and functional capacity in individuals with moderate relapsing-remitting MS.

Pharmacologic approaches for MS include disease-modifying agents including immunomodulators and immunosuppressants. The immune-modulating therapies are used for individuals with relapsing-remitting

Table 2 MRI diagnostic criteria for MS[3]

Determination of dissemination in space*	Determination of dissemination in time
3 out of 4 of the following: At least 1 gadolinium-enhancing lesion or 9 T2-weighted hyperintense lesions At least 1 infratentorial lesion At least 1 juxtacortical lesion At least 3 periventricular lesions	Enhancing lesion at least 3 mo after onset of clinical symptoms at a site different from initial symptoms or In the absence of enhancing lesions at the 3-mo scan, follow-up scan after an additional 3 mo showing an enhancing lesion or new T2-weighted lesion

* A spinal cord lesion can replace any of the brain lesions, and immunoglobulin abnormalities in the cerebrospinal fluid are sufficient to relax the T2-weighted lesions to 2.

disease. These agents reduce the frequency and severity of relapses, reduce brain lesion development, and possibly reduce disability,[11] although the natural history is only modestly altered.[29] Adverse effects of these drugs include flu-like symptoms, nausea, fatigue, myalgia, menstrual disorders, sweating, liver toxicity, anemia, and depression. Kidd[13] reported that these drugs reduced relapse rates by 35%, but no studies have been conducted that assessed long-term benefits for quality and length of life. Medications are also used for MS patients who experience depression, chronic fatigue, bowel/bladder dysfunction, and spasticity.[11]

Patients with MS seek both pharmacologic and complementary and alternative treatment. Integrative chiropractic treatment including mobilization, therapeutic exercise, dietary/nutritional recommendations, and stress reduction may be beneficial in MS management. This approach awaits scientific investigation and validation.

Conclusion

Chiropractors often encounter patients with neurologic disorders. The recognition of the subtle and nonspecific manifestations of MS, as well as the role of imaging and paraclinical testing, will assist clinicians in arriving at a timely diagnosis and optimal treatment.

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No funding sources or conflicts of interest were reported for this study.

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