Case report

Tumefactive multiple sclerosis requiring emergency craniotomy: Case report and literature review

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A B S T R A C T

Multiple sclerosis (MS) is a demyelinating disease of the central nervous system, characterized by focal neurological dysfunction with a relapsing and remitting course. Tumor-like presentation of MS (or “tumefactive”/“pseudotumoral” presentation) has been described before with a certain frequency; it consists of a large single plaque (>2 cm) with presence of edema and mass effect and it is hard to distinguish from a brain tumor. However, we present a very rare case of a 53-year-old woman with a right temporal mass that turned out to be a MS plaque, who deteriorated within hours (brain herniation with loss of consciousness and unilateral mydriasis) and required an emergency craniotomy. We also present a review of the literature. It appears that only 4 cases of emergency craniotomy/craniectomy required in a patient with a tumor-like MS plaque have been reported before.

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E s c l e r o s i s múltiple pseudotumoral que precisa craneotomía urgente: caso clínico y revisión de la literatura

R E S U M E N

La Esclerosis Múltiple (EM) es una enfermedad desmielinizante del sistema nervioso central, que se caracteriza por déficits neurológicos con un curso recurrencia-remitente. La presentación pseudotumoral de la esclerosis múltiple ha sido descrita en la literatura con cierta frecuencia, se define como la presencia de una única placa desmielinizante grande (>2 cm) con edema asociado y efecto de masa, que puede confundirse fácilmente con un tumor cerebral entre otros diagnósticos alternativos. Presentamos el caso de una mujer de 53 años con una lesión en el lóbulo temporal derecho que resultó ser una placa de desmielinización aguda, la singularidad del caso reside en que la paciente deteriora neurológicamente en pocas horas (coma y midriasis ipsilateral) requiriendo una intervención quirúrgica urgente.

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Introduction

A large single MS plaque in the brain with surrounding edema and mass effect simulating a cerebral tumor is rare. When this occurs without other signs or symptoms, it often represents a diagnostic challenge.\textsuperscript{1,2} Typically, multiple sclerosis plaques do not produce mass effect. This feature has been used in the past to distinguish demyelinating processes from brain tumors.\textsuperscript{3}

There is no specific laboratory test available for multiple sclerosis diagnosis. Abnormal findings in the cerebrospinal fluid, the presence of oligoclonal bands and the results of electrophysiological studies are sensitive but not specific. Gadolinium-enhanced MRI studies may not clearly differentiate tumefactive MS from neoplasms in the acute stage.\textsuperscript{4} Lesions of both typical and tumefactive MS frequently enhance on MRI.

The occurrence of tumor-like demyelination is reportedly rare, being estimated at 1–2/1000 cases of multiple sclerosis.\textsuperscript{5} Rapid neurological status deterioration leading to emergent craniotomy is even rarer in this pseudotumoral form. To the best of our knowledge only four cases has been described before.\textsuperscript{6–9} In the present report we describe the clinical, radiological and pathological features of this infrequent course of tumefactive MS.

Case report

A 53-year-old Caucasian woman initially presented with a 2-week history of imbalance, unsteadiness with frequent falls. She had also had mild headache, not associated with nausea, vomiting, or other signs of intracranial hypertension. Her past medical history was only relevant for anxiety disorder, was family history was negative. Neurological examination disclosed no abnormalities except for bilateral papilledema.

A CT scan of the brain at that time revealed a space-occupying hypodense lesion in the right temporal lobe. Extensive edema surrounded the lesion associated with significant degree of mass effect, partially collapsing the lateral ventricle and producing a midline shift of few millimeters. MRI showed a 6.1 cm \times 3 cm \times 4.2 cm mass, hypointense on T1-weighted images and hyperintense, inhomogeneous, on T2-weighted images with digitiform areas of edema (Fig. 1). After injection of gadolinium subtle ring enhancement was present. MR spectroscopy showed a peak of choline, with increased choline/creatinine ratio (1.99), great decrease of N-acetyl-aspartate (NAA) peak, as well as a peak of lactate. The lesion showed peripheral restricted diffusion in diffusion-weighted imaging (DWI), especially in posterior and medial regions. Perfusion MR imaging revealed a mild increase of cerebral blood volume in the same regions.

Tumoral and inflammatory/infectious diseases were initially considered in a differential diagnosis; but the size of the lesion, mass effect, and contrast enhancement was felt to be more compatible with a low grade glioma. She had not had fever, leukocytosis, recent vaccinations, respiratory or gastrointestinal symptoms. Serologic findings for bacterial, viral, and fungal agents were all negative. She commenced corticosteroids and antiepileptic drugs.

Two days after admission, despite high doses of dexamethasone and mannitol, the patient presented increasing stupor and severe left-hemiparesis. Within hours, consciousness deterioration progressed (Glasgow Coma Scale of 7/15) with unilateral right-sided dilated but reactive pupil. Emergent craniotomy revealed a yellowish, poorly-defined subcortical lesion; an extensive resection was carried out.

Histopathologic examination revealed a confined white matter lesion with degeneration of myelin and relative preservation of axons. Foamy macrophages with vacuolated cytoplasm, loss of oligodendrocytes, reactive gliosis, and focal lymphocytic perivascular cuffs were present in degenerating myelin (Fig. 2). The histological diagnosis was acute demyelinating disease.

She then underwent examination of CSF, which evidenced unspecific postsurgical parameters and absence of oligoclonal bands. She received high doses of corticosteroids. The patient’s symptoms and signs rapidly improved following surgery. A repeat MRI examination 6 months later demonstrated absence of the temporal lobe lesion and no other new lesions (Fig. 3). Clinically, the patient was asymptomatic. At last clinical and radiological follow-up, one year after surgery, the picture remained unmodified.

Discussion

Multiple sclerosis (MS) may present as a wide variety of clinical symptoms and neurological manifestations, but the clinical diagnosis depends primarily on a remitting and relapsing course. At first, the recovery from relapses is almost complete, but then neurological disabilities gradually accumulate. For a definite diagnosis of multiple sclerosis, dissemination in time (at least two separate symptomatic events or changes on MRI over time) and in anatomical space (at least two separate locations within the central nervous system, which can be demonstrated by MRI or neurological exam) must be demonstrated. The following are classical MRI characteristics suggestive of MS: multiple white matter lesions (especially in the periventricular or centrum semiovale areas), occurrence of both infratentorial and supratentorial lesions, minimal surrounding edema and relatively little mass effect compared to the overall size of the white matter lesion.

Symptoms like headache, cognitive abnormalities, aphasia or seizures are uncommon in patients with multiple
Fig. 1 – Axial (1) and coronal (2) T2-weighted MR images showing a large expanding subcortical lesion in the right temporal lobe, with associated edema and mass effect. Gadolinium-enhanced sequence (3) reveals slight enhancement at the periphery of the lesion. Sagittal T1-weighted image (4) shows the large hypointense temporal MS plaque. MR spectroscopy (5) shows a peak of choline, with increased choline/creatine ratio (1.99), great decrease of N-acetyl-aspartate (NAA) peak, as well as a peak of lactate. Perfusion-weighted MRI (6) demonstrated mild increase of cerebral blood volume in posterior and medial regions. The ROI selected (with number “2”, in the posterior margin of the lesion) showed an elevated ratio of maximum relative blood volume (rCBV) with a value of 2.56.

Fig. 2 – Well-demarcated demyelinating lesion (7, HE) with preserved gray matter. Foamy macrophages (8, HE) with occasional focal collections surrounding blood vessels. Reactive astrocytosis (9, GFAP). Axon-specific staining (10) reveals dissociation between preferential loss of myelin relative to axons (11), anti-Myelin Basic Protein antibody. CD3-immunostaining (12) shows perivascular, lymphocytic cuffs, predominantly T.
sclerosis. When they are present and accompanied by a single lesion with mass effect it can be difficult or impossible to distinguish a multiple sclerosis plaque from a cerebral neoplasm, cerebral abscess, vascular disease or other inflammatory disorders.\textsuperscript{1,3,10} The definition of ‘tumefactive lesions’ is not consistent in the literature, and may refer to various combinations of the following: large size (>2 cm),\textsuperscript{1} presence of mass effect or edema and/or atypical enhancement patterns. These diagnostic difficulties are further compounded by reported cases of gliomas appearing concurrently with multiple sclerosis.\textsuperscript{11,12} On the other hand, oligoclonal band positivity is found less frequently in patients with pseudo-tumoral onset.\textsuperscript{10} Important information for differentiating diagnosis can be obtained by spectroscopy which can show the pattern usually observed in the demyelinating areas, characterized by an increase of the peak of choline, a decrease of N-acetyl-aspartate (NAA), and lactate peaks, as in our case.

In the largest series reported to date of 168 patients with biopsy confirmed tumefactive demyelinating lesions, Lucchini et al.\textsuperscript{1} reported in a retrospective review that 70% of patients developed classical multiple sclerosis at follow-up, while 14% had an isolated episode. Former studies, on the contrary, suggested that the majority of patients with an isolated tumefactive demyelinating lesion did not seem to develop MS subsequently.\textsuperscript{7,13} Kepes\textsuperscript{2} described in a series of 31 patients with tumor-like multiple sclerosis that the great majority of cases (28 of them) behaved as a single episode in time. In the same way, Altintas et al.\textsuperscript{10} describe that only 16.7% in a series of 54 patients with a first attack with tumor-like MS developed new tumefactive lesions during follow-up. It is crucial to consider that median follow-up was 3.9 years in Lucchini’s study\textsuperscript{1} and median time to second attack was 4.8 years; while median follow-up was 38.12 months in Altintas et al.\textsuperscript{10} and not specified in Kepes’ study.\textsuperscript{2} Lucchini et al.\textsuperscript{1} also conclude that the majority of patients have a clinical and radiographic course as well as prognosis similar to prototypic multiple sclerosis, instead of a more benign course previously suggested by most authors that reported a “single-episode” entity.\textsuperscript{2,10,13} Nevertheless, the biological and clinical behavior of these patients appears to be distinct from the usually acutely progressive monophasic malignant form of MS known as Marburg’s disease that typically kills within a year. As stated by Walid and Sanoufa,\textsuperscript{14} the diagnosis of the Marburg variant of multiple sclerosis should be made based on disease course.

Treatment of pseudotumoral forms of multiple sclerosis is not well-defined. Corticosteroid therapy is most commonly used in literature reported cases. In addition to steroids some of the authors performed surgical procedure (brain biopsy or mass resection), while others opted for steroids only and clinical and radiological follow-up.\textsuperscript{15} In the vast majority of cases, the patients showed further improvement or disappearance of the mass lesion with treatment in both surgical and non-surgical treated patients, making multiple sclerosis the most likely diagnosis in cases without pathological confirmation. Therefore, some of the authors recommend a conservative approach with careful clinical and radiological follow-up avoiding a brain biopsy. Serial magnetic resonance imaging performed during steroid treatment, together with other paraclinical data, may be sufficient for the diagnosis.\textsuperscript{15}

We analyzed the other reported cases of tumefactive MS requiring emergent craniotomy or craniectomy,\textsuperscript{5-9} looking for similarities. These five cases consist of four women and one man, between 20 and 55 years old. None of them had previous neurologic symptoms, being their first episode. Four of them presented with an isolated large lesion, while one patient showed two small subcortical lesions in the contralateral white matter. Complete neurological recovery was achieved in three patients, in two of them only mild neurological deficits remained. None of them suffered a second episode, but follow-up was less than 2 years in four cases.

\textbf{Conclusion}

The appearance of a large solitary mass lesion may present considerable diagnostic difficulties in the acute stage of MS, and may be misinterpreted as a brain tumor, abscess or vascular lesion. Many of these patients are eventually operated on (biopsy or mass resection) even though other authors defend a conservative approach with steroid therapy and clinical and radiological follow-up. Uncommon clinical course with consciousness deterioration, uncal herniation and mydriasis that requires emergent surgical intervention is anecdotic.
Contributions

Dr. Castaño-Leon has helped with the initial composition of the paper. Dr. Martinez-Perez has helped with data gathering. Dr. Hernandez-Lain has helped with the description of the pathological findings. Dr. Ramos has helped with the description of the radiological findings. Dr. Lagares has helped with the final composition of the paper.

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Conflict of interest statement

The authors have no conflict of interest to declare.

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