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TUMEFACTIVE MULTIPLE SCLEROSIS: THE LETHAL CHAMELEON

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ABSTRACT

Tumefactive multiple sclerosis (TMS) is a rare variant of multiple sclerosis that presents with a large demyelinating lesion in the central nervous system, accompanied by peripheral ring-like enhancement, perilesional oedema and mass effect.

We report a case of a 59-year-old woman who was admitted to the hospital with a four-day history of somnolence, muscle weakness in her left extremities and ultimately, loss of consciousness. Over the following 48 hours, the patient's condition worsened with progressive consciousness impairment. Although the results of the initial head computed tomography (CT) scan supported the diagnosis of a multifocal ischaemic stroke, toxoplasmosis was proposed as the most credible diagnostic hypothesis by brain magnetic resonance imaging (MRI). Due to the adverse clinical progression following the initiation of targeted therapy and inconclusive investigation, a brain biopsy was performed, which was indicative of active TMS in a subacute phase. The patient was started on plasmapheresis and natalizumab along with corticosteroids, with a very good response.

In conclusion, we report a biopsy-proven TMS diagnosis in a patient that clinically mimicked an acute stroke and was radiographically confounded with intracranial toxoplasmosis. It highlights that TMS is an uncommon neurological demyelinating disease that is often misdiagnosed. It also emphasises the importance of establishing an accurate differential diagnosis to promptly initiate aggressive immunosuppressive treatment, which may result in a more favourable prognosis.

KEYWORDS

Tumefactive demyelinating lesions, tumefactive demyelination, pseudotumoral demyelinating lesions

LEARNING POINTS

- Tumefactive multiple sclerosis is an uncommon variant of multiple sclerosis that presents a substantial diagnostic challenge due to its potential to resemble the clinical and radiological characteristics of other central nervous system (CNS) pathologies, including neoplasms, granulomatous diseases, abscesses and vasculitis.
- Despite the fact that multimodal imaging studies may help narrow the differential diagnosis, a biopsy is often required to reach a definitive diagnosis and should not be delayed.
- Awareness of this condition among non-neurologists is critical since a timely and accurate diagnosis prompts aggressive immunomodulatory treatments that may delay a second demyelinating event or progression to clinically definite multiple sclerosis.

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INTRODUCTION

Tumefactive multiple sclerosis (TMS) is an uncommon variant of multiple sclerosis (MS) that is distinguished by the presence of a large demyelinating lesion in the central nervous system (CNS) accompanied by peripheral ring-like enhancement, perilesional oedema and mass effect. It poses a significant diagnostic challenge since its presentation may mimic the clinical and radiological features of other CNS pathologies such as primary or secondary neoplasm, abscesses, vasculitis, granulomatous diseases and even other variants of MS[1].

We report a case of a biopsy-proven TMS diagnosis that mimicked stroke and intracranial toxoplasmosis, focusing on the diagnostic and therapeutic approach.

CASE DESCRIPTION

We report a case of a 59-year-old woman, with no significant medical history, who was admitted to the hospital with a four-day history of somnolence and non-specified headache. This was followed by muscle weakness in the left extremities, a progressive decline in ability to perform routine activities, subsequent falls, an increasing requirement for assistance from others and ultimately loss of consciousness, accompanied by loss of bladder control. She refuted previous occurrences of similar symptoms, fever or other indicative signs of infection, as well as any consumption of unpasteurised dairy products. She shares her home with an unvaccinated dog. Upon examination, the patient was haemodynamically stable, normoglycaemic and afebrile. Relevant neurological examination findings include left-sided visual extinction, limited ocular supraversion, inconstant ocular flutter, pronator drift test with a drop of less than 5 cm and pronation of the left upper limb. The Mingazzini test showed a 5 cm drop of the left lower limb, spasticity of the left limbs and decreased speed of finger to nose test on the left upper limb without associated dysmetria. Head computed tomography (CT) identified a right frontal subcortical hypodense area suggestive of ischaemic aetiology in the border region between the anterior cerebral artery (ACA) and middle cerebral artery (MCA). Head-and-neck CT angiography did not detect any signs of arterial stenosis or occlusion. The first diagnostic impression was that of a multifocal ischaemic stroke involving the brainstem and right MCA/ACA territory. The absence of a well-defined onset time and the presence of an established lesion on CT precluded the activation of the acute stroke pathway. Platelet anti-aggregation was started. Over the next two days the patient's condition worsened, with progressive consciousness impairment. Through this decline the patient reached a score of 7 on the Glasgow coma scale resulting in the need for intubation and transfer to the intensive care unit (ICU). The ICU's complementary examination yielded a number of notable findings.

Laboratory tests showed leukocytes 15.7 × 10^9 (RV 4–10), neutrophils 82% (RV 40–80) and C-reactive protein 3.06 mg/dl (RV<0.5). There were negative results for comprehensive infectious and autoimmune tests including human immunodeficiency virus and hepatitis serologies, Venereal Disease Research Laboratory and Rose Bengal tests, and negative antibodies against aquaporin-4 and myelin oligodendrocyte glycoprotein. Tests were positive for toxoplasmosis immunoglobulin (Ig) G but negative for IgM; there was an absence of monoclonal component in serum immunofixation, and normal levels of immunoglobulins. Cerebrospinal fluid analysis showed five cells with no predominance, negative mycological and bacteriological cultures (including mycobacteria), absence of neoplastic cells in pathological examination, an absence of oligoclonal bands, normal IgG index and negative beta-2-microglobulin. Continuous electroencephalogram monitoring revealed no paroxysmal activity, and a re-evaluation head CT scan showed ischaemic infarction in a subacute phase.

Brain magnetic resonance imaging (MRI) *(Fig. 1)* shows countless predominantly right-sided peripherally enhancing encephalic lesions measuring less than 15 mm located in the semiovale centres, radial crowns, white matter surrounding the temporal horns and lateral ventricles. The largest lesions, located in the right oval centre, are associated with adjacent vasogenic oedema. These findings were interpreted as probably attributable to toxoplasmosis.

A spectroscopy study showed elevated concentrations of lipids, lactates and choline; fundoscopy was unremarkable. A transoesophageal echocardiogram indicated no evidence of vegetation, and 24-hour Holter monitoring was unremarkable. A cervical-thoracic-abdominal-pelvic CT scan showed no suspicious lesions or lymphadenopathies. However, a positron emission tomography scan showed metabolic anomalies in the CNS, particularly in the cerebellum and left parietal cortex, but no focal uptake changes suggestive of metabolically active neoplastic disease. There was an absence of lesions in the spinal cord on the spine MRI.

The diagnostic hypothesis of cerebral toxoplasmosis was considered the most plausible, and therapy with sulfadiazine and pyrimethamine was initiated. The patient also received methylprednisolone pulses (1 g/day) for 5 days, followed by a maintenance dose of 1 mg/kg/day.

Following the discontinuation of sedation and anti-epileptic medications, there was no alteration in the patient's neurological condition, remaining at a Glasgow coma scale score of 6T, with eye-opening in response to vigorous stimulation, but no speech production or motor response, consistent with decortication. Due to the unfavourable clinical progression and inconclusive investigation, approximately seven weeks after admission, a brain biopsy of one of the white matter lesions was performed, revealing demyelinating lesions that may correspond to active TMS in a subacute phase.

The final diagnosis was assumed to be fulminant TMS. The patient was started on plasmapheresis and completed eight sessions with a very good response. A control MRI showed a disappearance of the previously observed lesion

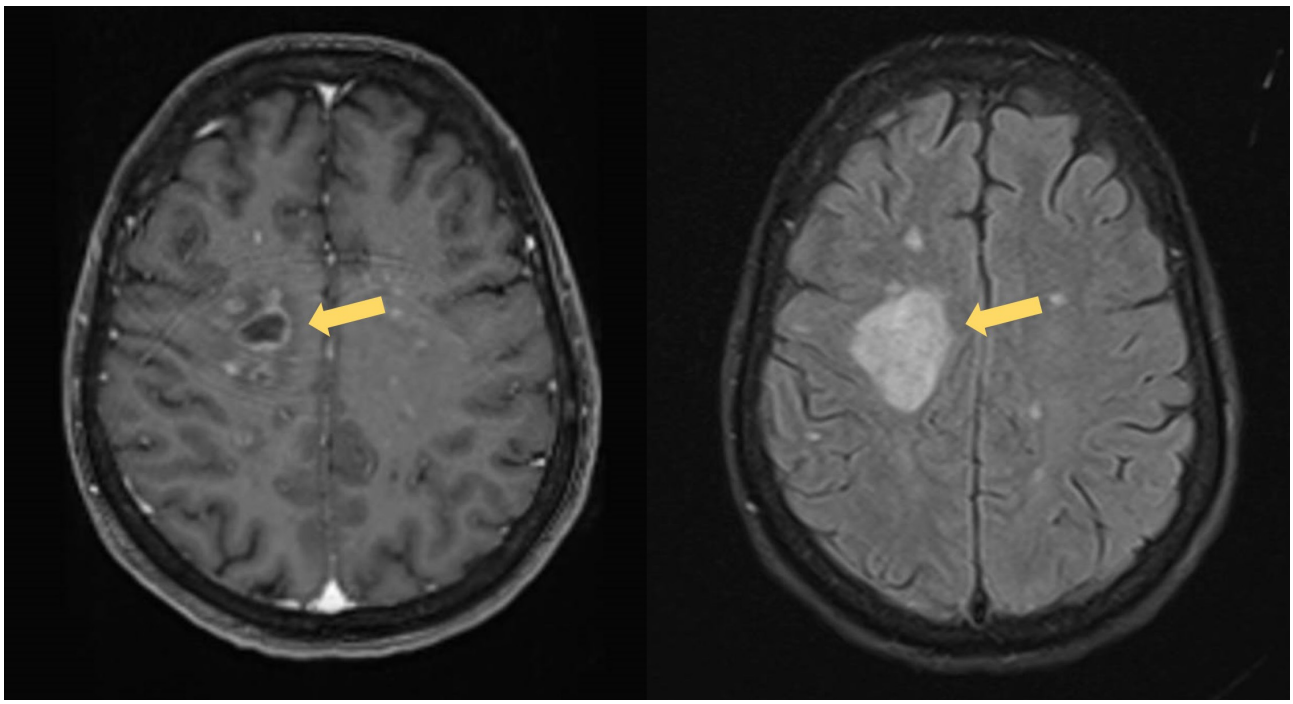

Figure 1. Brain MRI axial images. The T1-FS sequence (left) shows several small ring-enhancing parenchymal lesions, the largest one in the right centrum semiovale (arrow), also surrounded by a hypointense area. On the T2-FLAIR sequence (right), the lesions are hyperintense and have adjacent hyperintense areas of perilesional oedema (arrow).

enhancement. The patient was subsequently initiated on disease-modifying medication with natalizumab and protracted corticosteroid treatment for two and a half months. She was discharged from the hospital after three months with an expanded disability status scale score of 9 out of 10.

DISCUSSION

We report a case of TMS that posed a significant diagnostic challenge since its clinical and radiological findings were indistinguishable from other aetiologies.

The clinical presentation of TMS is diverse, including motor, cognitive, sensory, cerebellar and brainstem-related signs, usually developing over days or weeks[2]. Given the frequent supratentorial location of TMS lesions, they may present with focal neurological deficits that can be mistaken for an acute ischaemic stroke, as was observed in this case[2].

The preferred neuroimaging modality for TMS diagnosis is still MRI, even though TMS may have radiological features that can resemble features of other CNS pathologies, including primary or secondary neoplasms, granulomatous diseases, abscesses, vasculitis and other MS variants[3].

Cerebrospinal fluid (CSF) analysis has a lower negative predictive value in TMS cases that are the initial disease manifestation, as the reported case, since CSF oligoclonal bands occur less frequently compared to those that occur in the course of established MS[4]. Histopathological evaluation is critical to establishing the correct diagnosis, particularly in the presented case, which features severe and pronounced clinical deterioration, uncertain CSF and radiological findings, and a lack of response to treatment. The biopsy was performed seven weeks after hospital admission, which aligns with the average time reported in the literature, despite representing a substantial delay in diagnosis and subsequent initiation of targeted therapy[2].

TMS is typically difficult to treat, with partial recovery constituting the most common outcome[5]. Corticosteroids are the first-line treatment for acute symptomatic TMS; plasmapheresis is a plausible second-line option for patients where corticosteroids are ineffective or insufficient[4]. MS disease-modifying therapy should be considered in particularly severe, fulminant or disabling cases progressing under the previous treatments due to its potential to reduce long-term disability and delay the occurrence of a second demyelinating event and progression to MS[4,5].

CONCLUSION

In conclusion, non-neurologists must be aware of this uncommon and often misdiagnosed condition. We presented a biopsy-proven TMS diagnosis in a patient that clinically mimicked an acute stroke and was radiographically confounded with intracranial toxoplasmosis. This report underscores the importance of an accurate differential diagnosis, as it facilitates prompt and aggressive immunosuppression treatment, which may result in a more favourable prognosis.

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