

Case report



TUMEFACTIVE MULTIPLE SCLEROSIS: A DIAGNOSTIC ENIGMA. A CASE REPORT

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ABSTRACT

Purpose: To present a clinical case of tumefactive multiple sclerosis (TMS), which is an inflammatory demyelinating disease of the central nervous system considered to be a rare form of multiple sclerosis (MS). It belongs to the group of borderline forms of MS – a collective term used to define a spectrum of demyelination-associated neurological conditions that share similar clinical, neuroimaging and histopathological features but vary widely in severity, clinical course and outcome.

Materials/Methods: We describe the case of a 31-year-old female who was admitted to the Neurology clinic of UMHAT “Dr Georgi Stranski” in Pleven, Bulgaria, with a rapid onset of neurological deficit including right-sided hemiparesis, dysarthria, imbalance, cognitive impairment and urinary incontinence. MRI of the brain showed several tumor-like concentric lesions of demyelination surrounded by moderate brain edema, consistent with the radiological criteria for the demyelinating disease.

Results: High-dosage corticosteroids were applied intravenously for this patient as acute therapy. A progressive improvement in the patient was achieved after the extended pulse corticosteroid therapy in combination with physiotherapy. Glatiramer acetate as a disease-modifying treatment was initiated within three months and had substantial efficacy.

Conclusions: The diagnosis of TMS is always difficult and requires not only complex clinical and neuroimaging investigations but also an extensive follow-up of the patient. It is believed that TMS usually has a progressive course and an unfavorable outcome, but a relapsing-remitting course of TMS, albeit rare, is also possible. Our case report confirms that such benign variants of TMS exist. We believe that highlighting such complex clinical cases will contribute to a better understanding of the mystery of MS.

Keywords: demyelinating disease, multiple sclerosis, tumefactive MS, magnetic resonance imaging,

INTRODUCTION

Tumefactive multiple sclerosis (TMS) is an inflammatory demyelinating disease of the central nervous system, considered a rare form of MS. It is characterized by the appearance of solitary or multiple space-occupying lesions associated with neuroimaging features mimicking

a neoplasm such as size >2 cm, mass effect, edema and ringlike or open-ring enhancement which is usually demonstrated by magnetic resonance imaging (MRI) [1]. It belongs to a group of borderline forms of MS – a collective term used to unify several demyelination-associated neurological conditions that share similar clinical, neuroimaging and histopathological features but vary widely in severity, clinical course and outcome [2]. Some notable disorders in this entity include Baló’s concentric sclerosis, Marburg disease, neuromyelitis optica and Schilder’s disease [3]. The existing overlap among their clinical and neuroimaging presentation raises the question of whether they manifest as separate diseases or co-exist together under the MS spectrum.

The incidence of TMS is from one to three of every 1,000 cases of MS [1]. It is extremely rare, and when encountered, it requires a carefully thought-out and structured diagnostic process. Before the era of MRI, TMS was considered an aggressive, rapidly progressive condition with predominantly fatal outcome [3]. Currently, no therapeutic guidelines for TMS exist, but a remarkable response to high-dosage corticosteroids has been reported in the literature [4]. Nevertheless, the specific MRI findings enable earlier diagnosis and treatment and, thus, a better prognosis of the disease [5].

MATERIALS AND METHODS:

A previously healthy 31-year-old female was admitted to the Neurology clinic of UMHAT “Dr Georgi Stranski” in Pleven, Bulgaria, with weakness of the right extremities, facial asymmetry, cognitive impairment and urinary incontinence. These symptoms appeared a month prior to her admission to the clinic and progressed considerably to the point where she could no longer walk on her own and had to use a wheelchair. The patient did not report any previous diseases or use of medications. She denied any febrile illness prior to the onset of these symptoms. When questioned about family history, the patient reported she had a sister with MS.

The neurological examination revealed severe right-sided spastic hemiparesis, right-sided facial and body hypoesthesia, asymmetrically brisk deep tendon reflexes (D>S), right central facial palsy, decreased visual acuity for the right eye, bladder incontinence, positive

Babinski, Hoffman and Troemner signs on the right.

The neuropsychological tests indicated cognitive disturbances, including dyslexia, dysgraphia, dyscalculia, amnesic aphasia and dysarthria.

The initial MRI demonstrated multiple well-defined concentric lesions that were hypointense on T1-weighted images and hyperintense on T2-weighted and FLAIR images, localized in the subcortical, deep and periventricular white matter bilaterally frontal, temporal, parietal and left occipital, the basal ganglia and the cerebellum.

Fig. 1. Brain MRI (sagittal) documenting hyperintense tumefactive lesions of demyelination in the brain parenchyma in the fronto-parietal region and the basal ganglia.

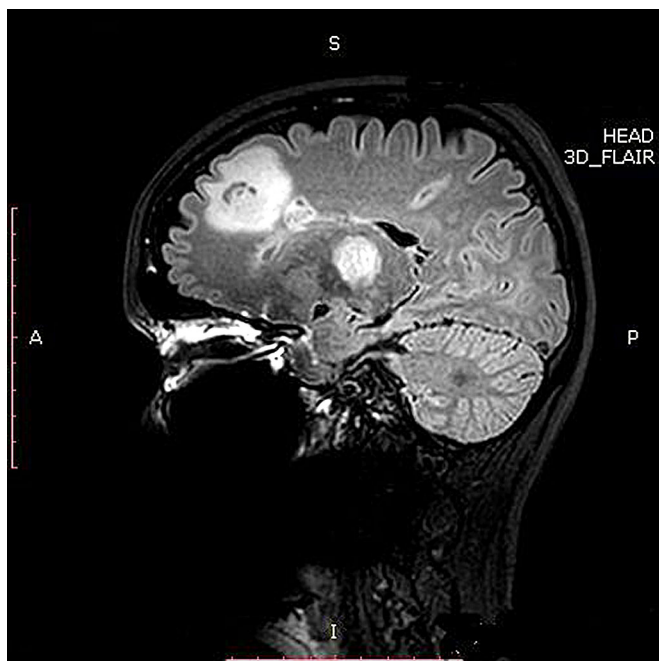


Fig 2. Brain MRI (axial) documenting hyperintense tumefactive lesions of demyelination in the brain parenchyma in the fronto-parietal region.

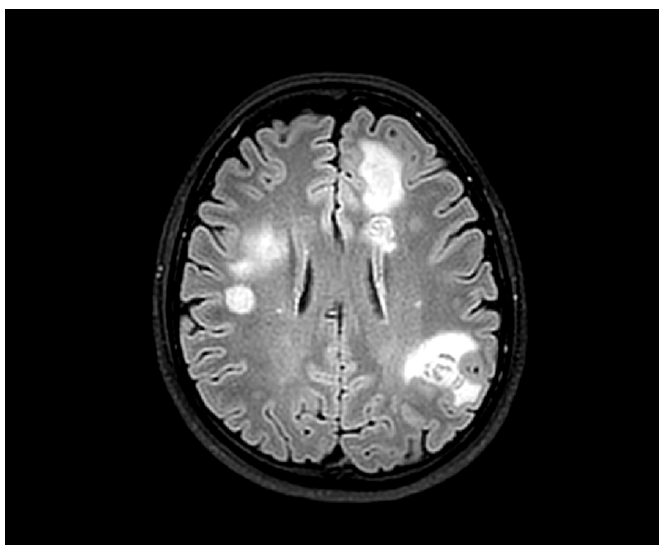
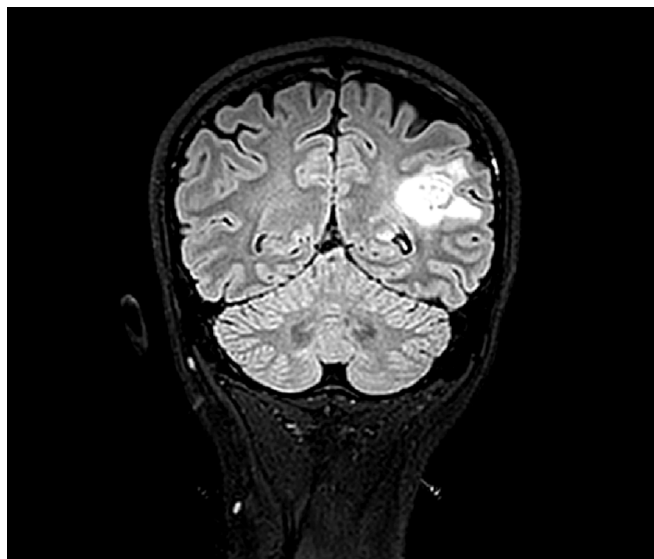


Fig 3. Brain MRI (coronal) documenting hyperintense tumefactive lesions of demyelination in the parietal lobe.



The lesions described were accompanied by moderately expressed surrounding edema. The visualized alterations resembled a malignant or atypical form of a demyelinating disease.

Biologically the patient presented no signs of inflammation, CRP was within normal ranges. An immunological profile was obtained in which the anti-nuclear antibodies, anti-cardiolipin antibodies, anti-beta glycoprotein antibodies were all negative. TSH, T3, T4 were all within normal ranges. CSF analysis showed normal protein value, and IgG did not reveal any oligoclonal bands.

Prior to her admission to the clinic, the patient had undergone a brain biopsy with a histopathological analysis excluding brain tumor and lymphoma.

Intravenous high-dosage corticosteroids were given to this patient as initial acute therapy. The patient was administered pulses of Methylprednisolone for eight days, followed by a taper of Prednisolone. While in the clinic, a slight reduction of her complaints was observed, and initial improvement was registered. On discharge from the clinic, the patient had a significant degree of disability and an Expanded Disability Status Score (EDSS) [6] of 7.0. It was recommended that the patient should undergo physical rehabilitation.

RESULTS:

At this stage, based on the patient history and clinical course, the diagnosis was suggestive of a demyelinating disorder. The typical neuroimaging findings led to the possibility of tumefactive MS (TMS).

A follow-up MRI, scheduled in three months, revealed partial radiological remission of the tumefactive lesions. No additional lesions were visualized. Clinically the patient showed moderate improvement. The patient remained with a degree of neurological deficit and the need for some assistance with every day activities, she was, however, able to walk with support. A positive response to the

combination of corticosteroid treatment and physiotherapy was observed overall. Another 5-day course with intravenous Methylprednisolone was applied, and over the next few months, the patient experienced gradual improvement and eventually, the neurological deficit was almost entirely resolved, thus achieving a considerable clinical remission.

Nonetheless, a relapse occurred approximately one year after the disease onset. This time the patient was admitted to the clinic with a sudden onset of blurred vision in the left eye. Neurological examination showed decreased visual acuity of the left eye. Residual deficits included mild right hemiparesis with an EDSS of 2.0. The third brain MRI demonstrated a consequent reduction in the mass-effect and volume of the lesions. No new lesions were detected. One of the previously described lesions had undergone complete radiological remission. Another treatment course with intravenous Methylprednisolone was initiated, followed by clinical improvement.

DISCUSSION:

This clinical case posed an extraordinary challenge in terms of diagnosis and therapeutic approach. Several diagnostic options were analyzed and discussed before reaching a consensus. Initially, the patient's history, clinical, CSF and neuroimaging investigations gave us reason to consider the following diagnostic possibilities:

1) Cerebral metastases: The described MRI lesions were to a certain extent similar to secondary disseminated lesions originating from a primary tumor. Given the fact that tumefactive MS may often mimic a tumor, the latter had to be excluded as a possible diagnosis [1, 7, 8]. For clinical correlation, a PET scan of the whole body was performed and showed no metabolically active extracerebral areas that could be considered malignancies. It was impossible to reliably identify a primary tumor focus. There were no detectable tumor masses and no areas of pathological uptake that could be considered malignant.

2) Acute disseminated encephalomyelitis (ADEM): There was no history of febrile illness, viral infection or recent vaccination, no disturbances in consciousness or behavior, the CSF analysis was normal, which rendered the diagnosis unlikely.

3) Demyelinating disease – TMS: The MRI findings were remarkably consistent with a demyelinating disorder. The patient's age and gender, the family history of a sister with MS, the rapid progression of neurological deficit, the clinical and radiological data, along with the positive response to intravenous corticosteroids gave us enough evidence to consider this diagnosis.

It may be argued that TMS may resemble classical MS in terms of disease course more than we think. This hypothesis is supported by the clinical remission of our patient, followed by an exacerbation of the symptoms a year later, indicative of a relapsing-remitting disease course [9]. In line with this theory, initiation of a disease-modifying treatment seemed reasonable [2, 10]. Treatment with Glatiramer acetate was started with impressive efficacy. The patient remains relapse-free to this day.

CONCLUSIONS:

The reported clinical case accentuates on atypical and malignant forms of MS that manifest unconventionally both in terms of clinical and MRI findings [11]. The extensive in-depth diagnostic work-up proved no other likely diagnosis than tumefactive MS. Naturally, histopathological verification would render the diagnosis even more precise, but unfortunately, such an investigation was not done.

Follow-up neuroimaging proved to be essential in our steps of achieving a particular diagnosis. Undoubtedly, the role of MRI happens to be crucial in providing clinicians with an earlier diagnostic confirmation and specific treatment.

We strongly believe that highlighting such complicated cases will contribute to a better understanding of the immune pathophysiology and clinical course of rare MS forms. The satisfactory clinical response achieved in our patient demonstrates the spectacular efficacy of high-dosage corticosteroids against demyelination-associated neurological deficits.

Though the lack of data concerning the effect of disease-modifying treatment in patients with atypical MS variants, in our clinical case, the Glatiramer acetate proved to be beneficial for our patient.

REFERENCES:

1. Stourac P, Kolcava J, Kerkovsky M, Koprivova T, Kren L, Bednarik J. Progressive Tumefactive Demyelination as the Only Result of Extensive Diagnostic Work-Up: A Case Report. *Front Neurol.* 2021 Jul 8;12:701663. [[PubMed](#)]
2. Kaeser MA, Scali F, Lanzisera FP, Bub GA, Kettner NW. Tumefactive multiple sclerosis: an uncommon diagnostic challenge. *J Chiropr Med.* 2011 Mar;10(1):29-35. [[PubMed](#)]
3. Ayrignac X, Carra-Dallière C, Labauge P. Atypical inflammatory demyelinating lesions and atypical multiple sclerosis. *Rev Neurol (Paris).* 2018 Jun;174(6):408-418. [[PubMed](#)]
4. Mando R, Muallem E, Meka SG, Berghea R. A Blind Spot in the Diagnostic Field: The Challenging Diagnosis of Tumefactive Multiple Sclerosis. *Case Rep Neurol Med.* 2018 Jun 27;2018:6841291. [[PubMed](#)]
5. Lucchinetti CF, Gavrilova RH, Metz I, Parisi JE, Scheithauer BW, Weigand S, et al. Clinical and radiographic spectrum of pathologically confirmed tumefactive multiple sclerosis. *Brain.* 2008 Jul;131(Pt 7):1759-75. [[PubMed](#)]
6. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology.* 1983 Nov;33(11):1444-52 [[PubMed](#)]
7. Dolic K, Bilic I, Buca A, Radovic D, Titlic M. Differentiation of Tumefactive Demyelinating Lesions from Metastatic Brain Disease

with FDG PET-CT: A Case Report. *J Mult Scler*. 2014; 1(1):108. [[Crossref](#)]

8. Vakrakou AG, Tzanetakos D, Argyrakos T, Koutsis G, Evangelopoulos ME, Andreadou E, et al. Recurrent Fulminant Tumefactive Demyelination With Marburg-Like Features and Atypical Presentation: Therapeutic Dilemmas and Review of Literature. *Front Neurol*. 2020 Jun 30; 11:536. [[PubMed](#)]

9. Wadhwa A, Chatterjee A,

Chaudhry N, Laskar S, Chandan S. A Case of Relapsing-Remitting Tumefactive Demyelination. *Ann Indian Acad Neurol*. 2019 Jan-Mar;22(1): 124-126. [[PubMed](#)]

10. Hardy TA, Chataway J. Tumefactive demyelination: an approach to diagnosis and management. *J Neurol Neurosurg Psychiatry*. 2013 Sep; 84(9):1047-53. [[PubMed](#)]

11. Zaheer K, Ajmeri AN, Singh M, Suliman MS, Teka S. Tumefactive

Multiple Sclerosis, A Rare Variant Presenting as Multiple Ring-enhancing Lesions in an Immunocompetent Patient: A Case Report. *Cureus*. 2018 Dec 17;10(12):e3738. [[PubMed](#)]

12. Brod SA, Lindsey JW, Nelson F. Tumefactive demyelination: Clinical outcomes, lesion evolution and treatments. *Mult Scler J Exp Transl Clin*. 2019 Jun 18;5(2):2055217319 855755. [[PubMed](#)]

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