Electronic Physician (ISSN: 2008-5842) http://www.ephysician.ir
August 2018, Volume: 10, Issue: 8, Pages: 7180-7184, DOI: http://dx.doi.org/10.19082/7180

Tumefactive multiple sclerosis masquerade as a central nervous system tumor: a case report

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Type of article: Case report

Abstract

Introduction: Tumefactive multiple sclerosis is a demyelinating disorder that appears tumor-like on MRI. To most physicians, diagnosing tumefactive MS by applying clinical, radiological, or laboratory examination like Cerebrospinal fluid (CSF) analysis, can be challenging and ultimately biopsy is necessary to confirm the diagnosis.

Case presentation: This paper reports a case of a 37-year-old woman who presented with progressive headache and a strong family history of cancer and was misdiagnosed as having a CNS glioma. After considering the MRI features, CSF analysis results and observing improvement with IV steroids, the diagnosis of tumefactive MS was made. The patient refused biopsy to rule out the possibility of tumor or abscess. Nine months later, she presented with another relapse and an injectable disease modifying treatment (DMT) was initiated, and her course has been stable in follow up.

Take-away lesson: The overall clinical importance of this case report is to highlight the real possibility of being forced to decide between Tumefactive demyelinating lesions (TDLs) and brain tumors in clinical practice, in order to avoid unnecessary biopsy.

Keywords: Tumevactive demyelinating lesions (TDLs), CSF, OCB, MRI, CNS tumors

Note: This case report is prepared using the CARE Checklist (2013) of information to include when writing a case report (https://www.care-statement.org). The CARE guidelines for case reports help reduce bias, increase transparency, and provide early signals of what works, for which patients, and under which circumstance.

1. Introduction

The tumefactive form of the central nervous system (CNS) demyelinating disorder multiple sclerosis is a rare variant which presents similar to an intracranial neoplasm. It can mimic intra cerebral tumors as well as CNS infections and abscesses as it presents as large demyelinating lesions on magnetic resonance imaging (MRI), representing a space-occupying lesion (SOL) which may cause a diagnostic conundrum among physicians and radiologists. The incidence of tumefactive multiple sclerosis (TMS) is reported to be rare and occurs more commonly amongst young adults and women (1). Individuals who develop TMS usually present with symptoms related to pressure effect of the mass such as headache, and they often lack typical symptoms of MS relapses like numbness or visual symptoms. Nowadays, the diagnosis is made by MRI, Positron Emission Tomography scan (PET) and cerebral spinal fluid (CSF) analysis without an invasive procedure like brain biopsy, which can carry significant morbidity especially if it has the typical MRI features of TMS (2). MRI features of TMS include lesion size more than two cm and incomplete ring enhancement lesion surrounded by vasogenic edema. The literature has reported different cases of TMS that have been diagnosed without brain biopsy, depending only on radiological and CSF results. However, in some cases, brain biopsy was an essential procedure to confirm the diagnosis and to avoid mismanagement (3), and others went

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Received: April 06, 2018, Accepted: July 12, 2018, Published: August 2018
iThenticate screening: July 25, 2018, English editing: August 10, 2018, Quality control: August 14, 2018
This article has been reviewed / commented by three experts

for gross total tumor excision (4). Thus, recognizing TMS from other space-occupying lesions such as abscesses and primary or secondary CNS tumors is essential for proper management of patients to avoid unneeded medical or surgical intervention. The acute presentation is likely to recover by giving high-dose intravenous methylprednisolone or other immunosuppressives (5). Therefore, TMS should be considered in the differential diagnosis of brain space-occupying lesions, and brain biopsy should be sought only if truly warranted. The objective of this case report study was to highlight the real possibility of being forced to decide between TMS and brain tumors in clinical practice, present a reasonable approach to help differentiate them and especially to focus on the possibility of TMS, in order to avoid unnecessary biopsy.

2. Case presentation

2.1. Patient information

A 37-year-old right handed, married Saudi female teacher with no known prior medical illness was referred on December 2014 to the neurology department of King Fahd University Hospital in Al-Khobar (Kingdom of Saudi Arabia) as a case of brain tumor for further neurosurgery evaluation and possible tumor resection.

2.2. History

The patient had a 7-month history of progressive frontal headache, increasing in severity in the past 3 months. The headache would start when she first awakened and could last for the rest of the day, not improving with simple analgesia. It was associated with electrical-like sensations in both upper and lower limbs, which would last for seconds, along with vomiting many times during the day. There was no associated photophobia. There was no history of fever, neck rigidity, menstrual changes, visual symptoms, trauma, weakness, sensory symptoms, sphincter problems, joint pain, skin rash or recent weight change. She sought medical advice in another medical facility and was given the presumed diagnosis of migraine without aura, and treated with topiramate prophylaxis with no improvement. Family history was positive for seizure disorders and colonic cancer in two of her first-degree relatives. She was admitted to our hospital to rule out an SOL.

2.3. Clinical findings

Neurological examination showed visual acuity of 20/20 bilaterally, with no papilledema on fundoscopic examination. Motor exam was normal for tone, power and deep tendon reflexes were +2, with positive Babinski reflex bilaterally, and she had normal sensory, coordination and gait exam.

2.4. Diagnostic assessment

Laboratory investigations including metabolic profile coagulation profiles, autoimmune profile, tumor markers, Purified protein derivative (PPD) and Acid-fast bacilli (AFB) were all within normal values; Human immunodeficiency virus (HIV) screen was negative. Visual evoked potential (VEP) were abnormal, showing bilateral P100 wave latency prolongation. Brainstem auditory evoked potential (BAEP) were within normal limits. CSF examinations showed protein 29 mg/dL, White blood cells (WBC) 2 cells/µL, Red blood cells (RBC) 215 Cells/µL, Glucose 137 mg/dL (serum glucose 219 mg/dL). CSF specific oligoclonal bands were detected intrathecally with no corresponding bands seen in the serum. Brain MRI showed multiple periventricular, subcortical and infratentorial white matter lesions, which appear hypointense in T1 and hyperintense in both T2 and fluid-attenuated inversion recovery (FLAIR) with perilesional edema (Figure 1). One of these lesions, measuring 2.1 cm, showed an open ring enhanced lesion with a break in the ring toward the grey matter; enhanced venules were seen within the lesion (Figure 1). The ring wall shows restriction in DW/ADC. Spinal MRI was normal. Pan body CT including chest, abdomen and pelvis was done to exclude secondary metastasis, which was normal. Breast mammography as well, was unremarkable.

2.5. Therapeutic Intervention

The patient was admitted as a case of Tumefactive MS, and accordingly received a 5-day course of IV methylprednisolone with mild improvement of her symptoms. She was discharged and advised to start injectable disease modifying medication of Subcutaneous Interferon-β-1a (Rebif®) 44 mcg three times a week until her follow up time.

2.6. Follow-up and Outcomes

Follow up MRI for her two-month post discharge was arranged. Nine months later, she presented with another relapse in the form of right sided numbness and tremors, which was treated with pulse steroids for three days with

significant improvement of her sensory symptoms. Repeated brain MRI showed development of a new MS lesion, with significant improvement in the previous large tumorlike lesion (Figure 2).

2.7. Ethics of case report

In conformity with the ethics of publishing case reports, a signed consent form was taken from the patient to write this case report.

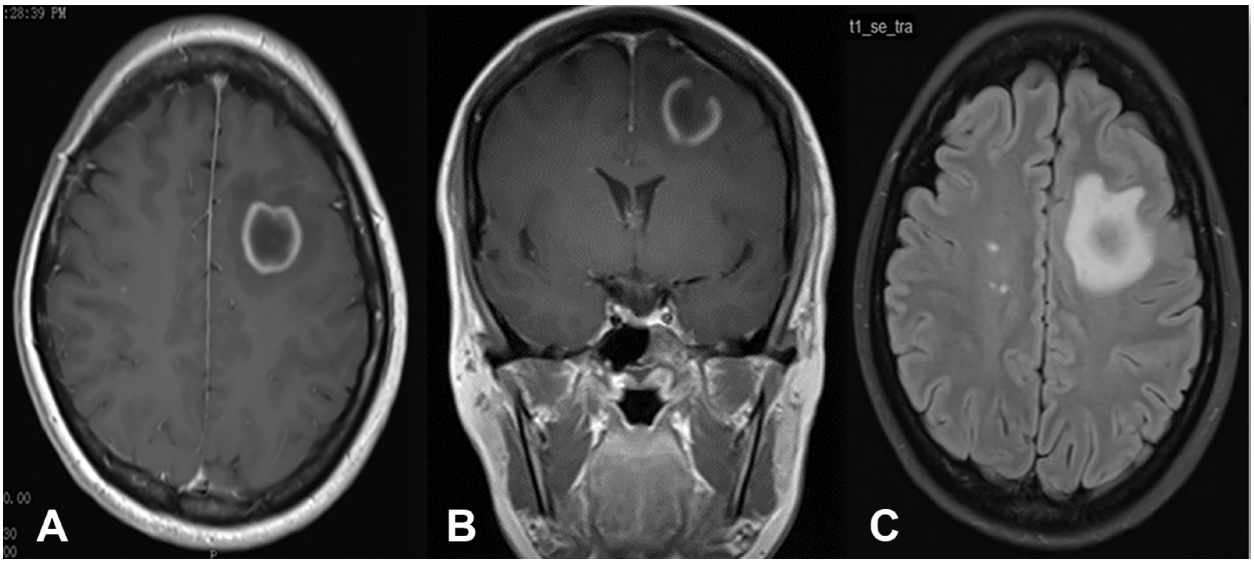

Figure 1. A) MRI T1 with contrast axial image showed left frontal ring enhancement lesion with enhanced venules, B) MRI T1 with contrast coronal image showed incomplete ring enhancement of the same lesion with open ring toward the cortex, C) MRI FLAIR axial image showed hyperintense lesion in left frontal lobe with surrounding vasogenic edema.

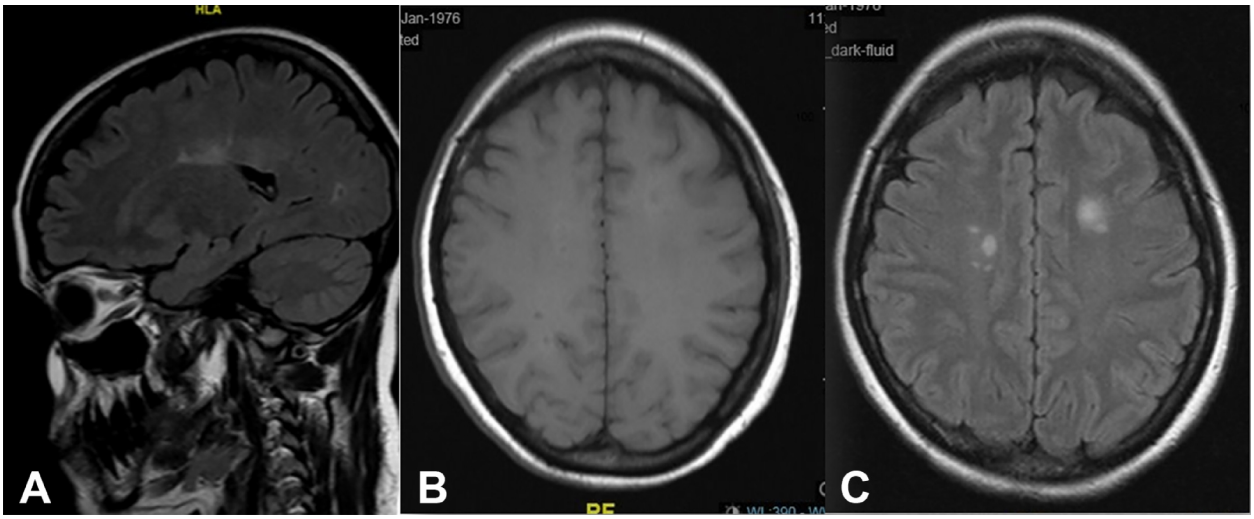

Figure 2. Follow up image A) sagittal FLAIR, B & C) axial MRI T1 and FLAIR showed significant improvement in the previous tumorlike MS lesion, and development of new periventricular MS lesions.

3. Discussion

Tumefactive demyelinating lesions (TDLs) are not an uncommon manifestation of demyelinating disease, with incidence of 2.8% of MS cases, but can pose diagnostic challenges in patients without a pre-existing diagnosis of multiple sclerosis (MS) as well as in known MS patients (6). Brain tumors can also arise in MS patients, and can be seen in chronic MS patients as co-morbidities. Tumefactive MS displays as a large solitary intracerebral lesion, more than two cm in diameter surrounded by mass effect and perilesional edema. Clinically, patients can present with headache, cognitive abnormalities, mental confusion, aphasia, apraxia, motor symptoms, or seizure. In

radiological images such as MRI, TMS appears as primary or secondary intracranial tumors mimicking malignant gliomas and abscesses (7, 8). It is important that other pathologies such as vasculitis, granuloma, infection, abscess and malignancy are excluded as far as possible before reaching the point where TMS is considered vs. tumor. Vigilant monitoring of patients after corticosteroid therapy is crucial in avoiding misdiagnosis of TDLs with other CNS tumors. Neoplastic lesions such as glioblastoma multiforme (GBM) and brain lymphoma are often initially responsive to corticosteroids due an effect at reducing perilesional edema. This early dramatic response is however, only temporary and lesions will rebound in a few weeks or months.

Diagnosis of MS depends mainly on the clinical presentation in association with radiological findings or CSF analysis. In reviewing the literature, diagnosed cases of TMS without histopathological examination showing the typical inflammation with loss of myelination were rare. MRI and PET scan can be helpful (1, 9). Although the diagnosis of typical MS does not need a surgical intervention, in some cases of TMS, brain biopsy was required, as the large demyelinated lesions resemble brain tumors. Some MRI features are more suggestive of TMS. These include incomplete ring enhancement, mixed T2-weighted iso-and hyper-intensity of enhanced regions, and absence of cortical involvement (10). An open ring enhancement that is directed toward the cortical surface of the brain has been reported in association with demyelinating lesions. Conventional MRI using magnetic resonance spectroscopy may help in differentiation of tumefactive demyelination from tumors showing decreased N-ACETYL CYSTEINE (NAA) (11), but its role in aiding the diagnosis of TMS is not yet established.

Our case presented with severe progressive headache and strong family history of cancer that did not improve with painkillers. Since biopsy was refused by the patient, which is a big challenge to us, we decided to manage the patient depending on her clinical manifestations in correlation to her MRI radiological finding and CSF analysis. MRI images demonstrated periventricular, subcortical and infratentorial white matter lesions, one of which measured greater than 2 cm with open ring enhancement, and specific oligoclonal bands were detected intrathecally in CSF analysis. Thereby, we started a short course of intravenous steroids as trial therapy. Fortunately, the rapid improvement of symptoms suggested that we were dealing with a TMS, and this was confirmed by clinical and MRI follow-up of the patient. As compared to what is seen in the literature, which shows that the TMS is responding partially to treatment, our patient showed significant improvement and resolution of her tumefactive lesion on follow-up MRI.

Careful and close follow up is warranted for those cases that did not go through lesion biopsy to confirm the diagnosis. Closely repeated MRI imaging is advised in order not to miss any new lesion or deterioration of the patient. If the diagnosis is still questionable, lesion biopsy should be done in certain patients presenting with a fulminant course, or if the oligoclonal bands are not detected in CSF or in those with rapid lesion enlargement on subsequent MRI (12). An earlier decision for biopsy among those cases should be considered. Treatment of TMS relapse is with IV steroids, which is usually effective to alleviate the symptoms (13). Disease modifying therapy can reduce disease activity and delay MS disease progression.

4. Conclusions

We presented here a challenging case hoping to illustrate the dilemma in the diagnosis of TMS versus brain tumor. Although with early clinical presentation, imaging findings or other ancillary tests can help favor one diagnosis over the other, sometimes only follow-up visits or ultimately pathological diagnosis of biopsies can clarify the final diagnosis. In our case, clinical and imaging findings after a trial of high dose corticosteroid treatment were very helpful in reaching the final diagnosis of TMS and avoiding unnecessary biopsy of lesions. But, any red flags, clinically or radiologically, should warrant biopsy. If the patient declines biopsy, close imaging follow up is mandatory.

Acknowledgments:

Sincere appreciation is conveyed to Dr. Ibrahim Alghanimi (Department of Radiology, King Fahd University Hospital, Saudi Arabia), for his help in gaining access to image reports.

Conflict of Interest:

There is no conflict of interest to be declared.

Authors' contributions:

All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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