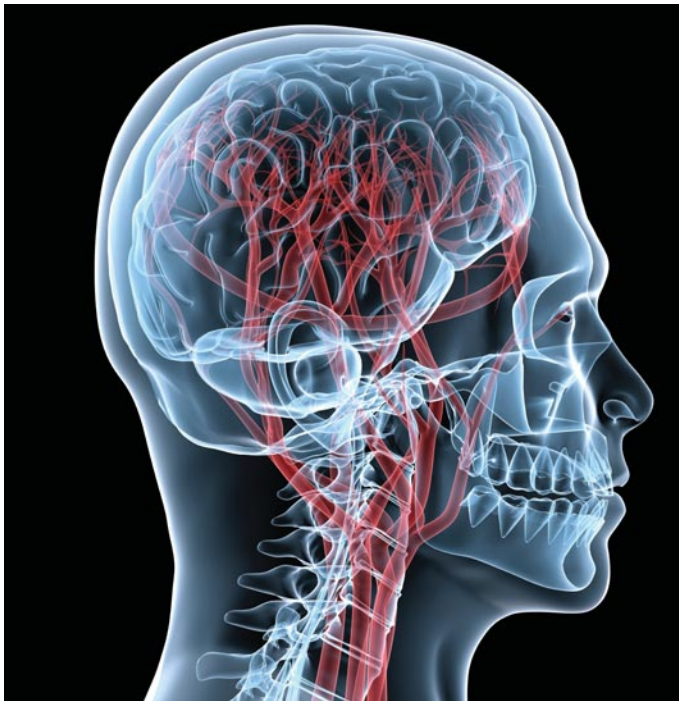
Ring-enhancing tumefactive multiple sclerosis



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Multiple sclerosis (MS) is an inflammatory disorder characterised by the demyelination of axons producing plaques in the brain and spinal cord.[1] The pattern of inflammation follows a relapsing course punctuated by periods of remyelination, with symptoms of neurodegeneration that correspond to the site and onset of inflammatory lesions.[1] MS lesions are disseminated in time and space, in that new lesions occur over time in different areas of the central nervous system (CNS). The disease is triggered in genetically predisposed individuals by poorly understood environmental factors.[1] While the aetiology of the disease remains elusive, there is growing evidence that viruses trigger the disease.[1,2] Of note, the regional prevalence of MS is proportional to the distance from the equator.[1]

MS is diagnosed using a combination of clinical evidence, and laboratory and radiographic findings.[1,3] Typical MS plaques appear on MRI as well demarcated, homogenous, ovoid lesions with no mass effect.[4] However, atypical features on MRI, such as solitary lesions larger than 2cm with mass effect and/or ring enhancement, have been described.[5,6] Such lesions fall under the category of CNS inflammatory demyelinating disease or tumefactive MS.[5] Because of its relative rarity (one to two cases per 1,000 MS cases), tumefactive MS is often mistaken for other conditions, such as brain tumour or cerebral abscess.[6,7] The clinical presentation of tumefactive MS varies based on the site of the lesion, but can include cognitive abnormalities, mental confusion, aphasia, apraxia and/or seizures.[5]

Case

A 27-year-old woman with no pre-existing medical conditions initially reported to her GP that she was feeling 'slow' and was having difficulty typing messages at work. Specifically, she reported difficulty with spelling, and could no longer remember how to spell correctly. She compared the feeling to 'being drunk', and reported that her 32-year-old sister had been

Table 1: Microbiology and toxicology screen.

Basic metabolic panel	
Sodium	138 (ref: 135-147mEq/L)
Potassium	4 (ref: 3.5-5mEq/L)
Chloride	102 (95-105mEq/L)
CO_2	24 (ref: 33-44mmHg)
Glucose	145 (ref: 70-110mg/dL)
Urea nitrogen	10 (7-18mg/dL)
Creatinine	0.7 (0.6-1.2mg/dL)
Calcium	9.7 (ref: 8.4-10.2mg/dL)
GFR calculation	>60ml/min
Phosphorus	4.4 (ref: 3-4.5mg/dL)
Albumin	4.5 (ref: 3.5-5.5g/dL)
Total protein	7.4 (ref: 6-7.8g/dL)
Bilirubin total	0.7 (ref: 0.1-1mg/dL)
Bilirubin direct	0.2 (ref: 0-0.3mg/dL)
Alkaline phos.	55 (ref: 30-120IU/L)
SGOT (AST)	14 (ref: 10-40IU/L)
SGPT (ALT)	24 (ref: 9-60IU/L)
Urine drug screen	
Amphetamines	Negative
Barbiturates	Negative
Benzodiazepines	Negative
Cannabinoids	Negative
Cocaine	Negative
Opiates	Negative
Methadone	Negative
Phencyclidine	Negative
Oxycodone	Negative
CSF viral panel	
Fungal CSF culture	Negative
Cryptococc AG CSF	Negative
CMV by PCR-	Negative
CMV by PCR	Negative
HSV by PCR-	Negative
HSV by PCR	Negative
Bacteriology	
Blood culture	Negative
CSF culture	Negative
Urine culture	Negative
Bacterial Ag-CSF	
E. coli K1	Negative
H. influenzae T	Negative
S. pneumoniae	Negative
Group B strep.	Negative
N. meningitidis GR.B	Negative
N. meningitidis A/Y	Negative
N. meningitidis C/W135	Negative
Miscellaneous microbiology	
Syphilis screen	Negative

FIGURE 1: Axial CT head showing right frontal periventricular hypointensity.

diagnosed with MS. Her GP referred her to the emergency room at Montefiore Medical Center, New York, where she was subsequently referred to the neurological inpatient service.

At Montefiore, a neurological physical examination was conducted, and it was found that the patient had a slight right-sided facial droop with forehead sparing and partial right ptosis. The patient had difficulty performing the clock drawing test (a tool to assess cognitive function) and was visibly confused.[8] Differential diagnoses for encephalopathy, including bacterial and viral meningitis, metabolism-associated encephalopathy (hepatic encephalopathy, hypoglycaemia), and drug and alcohol abuse, were ruled out based on normal metabolic parameters, toxicology reports and negative cerebrospinal fluid (CSF), blood and urine cultures (**Table 1**).

The patient underwent a CT brain, which did not reveal any pathology. However, under close scrutiny, a right-sided frontal hypodensity in the periventricular area could be vaguely discerned, but the nature of the lesion, if any, was unclear (**Figure 1**).

Further investigations were ordered, including a lumbar puncture and an MRI of the brain. What was unclear in the CT scan became strikingly obvious in the MRI. It showed a large, arresting periventricular white matter lesion with concentric ring

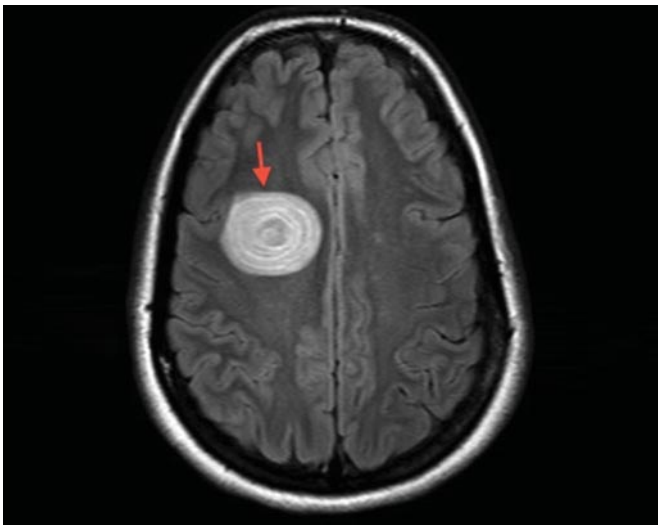

FIGURE 2: Axial T2-weighted fluid-suppressed MRI at the level of the anterior cingulate gyrus showing a large (>2cm) hyperintense ovoid lesion with ring enhancement and mass effect.

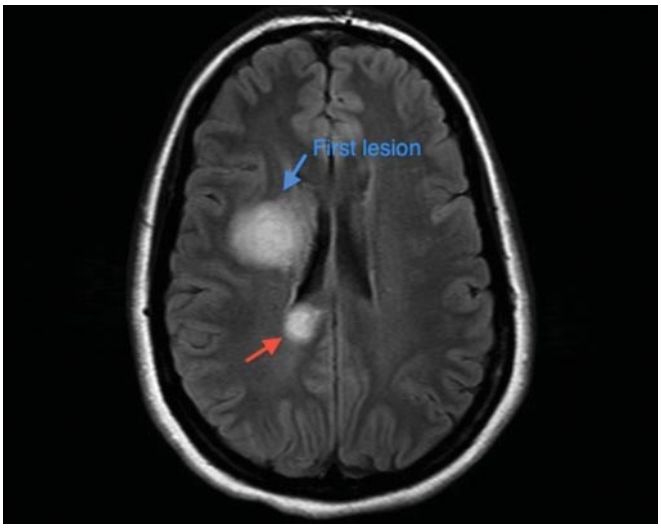

FIGURE 3: Axial T2-weighted fluid-suppressed MRI roughly at the level of dorsal caudate, splenium and genu of the corpus callosum, showing the inferior aspect of the large lesion and a small, hyperintense ovoid lesion in the splenium of the corpus callosum.

enhancement and mass effect, consistent with a number of cerebral pathologies, including tumefactive MS (**Figure 2**). Another smaller lesion was noted in the inferior sections (**Figure 3**). The lumbar puncture results supported the clinical suspicion of MS by demonstrating an elevated white cell count, a high protein level and a positive oligoclonal IgG band reading (**Table 2**). The patient was started on a course of intravenous methylprednisolone, which is useful in alleviating acute episodes of MS.[1] This treatment resolved the patient's cognitive symptoms and she was subsequently discharged. The patient was re-admitted to the hospital one week later with a similar attack of greater severity. She reported symptoms of worsening confusion, slurred speech and left hand weakness, which were consistent with a right-sided cerebral lesion. Another course of methylprednisolone was administered and the patient was discharged on oral steroids. A diagnosis of tumefactive MS was made based on a combination of clinical, laboratory and radiological criteria.

Discussion

The patient presented in an acute state of confusion and encephalopathy, both of which are common in tumefactive MS.[5] Positive CSF for oligoclonal bands and a large ovoid lesion with ring enhancement on MRI are also suggestive of tumefactive MS. Establishing a diagnosis of MS is challenging, as there are no pathognomonic clinical findings or tests.[2] In addition, imaging results and clinical signs can be confused with other conditions, specifically neoplasms and cerebral abscesses.[5,6]

The diagnosis of MS is facilitated by the McDonald diagnostic criteria.[3] The McDonald criteria use a combination of clinical, laboratory and radiological findings to standardise the diagnostic process and provide clinicians with a means to detect MS in its early stages with high specificity (**Table 3**).[3] These criteria reaffirm the need to demonstrate dissemination of clinical events and lesions in time and space.[5]

In this case, the patient met the McDonald criteria: firstly by demonstrating a clinical presentation of one acute event of cognitive decline; secondly, there was evidence for two or more clinical lesions disseminated in space; and, thirdly, dissemination in time was demonstrated by a second clinical episode one week after discharge. Typically, radiological findings of MS include multiple, well demarcated, homogenous, small ovoid lesions with no mass effect, often oriented perpendicular to the long axis of the lateral ventricles.[5] This patient was diagnosed with tumefactive MS based on the following MRI criteria: a solitary large lesion greater than 2cm in diameter; associated mass effect (mild sulcal effacement or moderate subfalcine or uncal herniation); and, perilesional oedema and/or the presence of ring enhancement.[5,6]

As tumefactive MS mimics other pathologies, it is sometimes necessary to confirm the diagnosis with a brain biopsy, although awareness of the clinical spectrum may obviate this need.[5] Based on this patient's clinical symptoms and findings, as well as her family history of MS, an invasive biopsy was deemed unnecessary. Close follow-up, including

Table 2: CSF parameters.

Cerebrospinal fluid (CSF)	
Colour	colourless/clear
WBC count	25 cells/mm^3 (ref: 0-5 cells/mm^3)
RBC count	51 cells/mm^3 (ref: 0 cells/mm^3)
Glucose	70mg/dL (ref: 40-70mg/dL)
Total protein	42mg/dL (ref: <40mg/dL)
Oligoclonal IgG bands	Positive
IgG/pro	0.15 (ref: high nl is 0.14)
IgG CSF	6.2 (ref: 0.5-6mg/dL)

Table 3: The McDonald criteria: diagnostic criteria for multiple sclerosis.[5,7]

Clinical presentation	Additional data needed
Two or more attacks; objective clinical evidence of two or more lesions	None
Two or more attacks; objective clinical evidence of one lesion	Dissemination in space demonstrated by – MRI; – two or more MRI-detected lesions consistent with MS plus positive CSF; or, – await further attack implicating a different site
One attack; objective clinical evidence of two or more lesions	Dissemination in time demonstrated by: – MRI; or, – second clinical attack
One attack; objective clinical evidence of one lesion	Dissemination in space demonstrated by: – MRI; or, – two or more MRI-detected lesions consistent with MS plus positive CSF And, Dissemination in time demonstrated by: – MRI; or, – second clinical attack
Insidious neurological progression suggestive of MS	One year of disease progression (retrospectively or prospectively determined) and two of the following: – positive brain MRI (nine T2 lesions or four or more T2 lesions with positive VEP); – positive spinal cord MRI (two focal T2 lesions); or, – positive CSF

Attack: an episode of neurological disturbance caused by lesions that are inflammatory and demyelinating in nature.
MRI abnormality: three of the following:
1. At least one gadolinium-enhancing lesion or nine T2 hyperintense lesions if there is no gadolinium-enhancing lesion.
2. At least one infratentorial lesion.
3. At least one juxtacortical lesion.
4. At least three periventricular lesions.

MRI evidence of dissemination in time: either of the following:
1. Detection of gadolinium enhancement three months after onset of initial clinical event at a different site.
2. Detection of a new T2 lesion if it appears at any time compared with a reference scan done at least 30 days after the onset of the initial clinical event.

CSF: oligoclonal IgG bands in the CSF (and not serum) or increased IgG index.

repeat MRI scans to monitor lesion development and medical management in an outpatient setting, was determined to be the most appropriate coarse of action. Typical therapy for MS consists of three approaches, namely immune-modifying agents targeting the pathogenesis of MS, palliative treatments directed at individual symptoms, and disability/psychological management.[2] Immune-modifying agents include high-dose methylprednisolone, interferon and monoclonal antibodies. Intravenous methylprednisone is used to treat acute episodes and should not be administered more than twice a year since it has no impact on prognosis. Interferon decreases relapses and lesion accumulation by 30% and has little impact on degree of disability. Monoclonal antibodies (natalizumab) decrease relapse rate in relapsing-remitting MS and reduce MRI lesions. A multi-disciplinary approach towards the management of MS is necessary, and therefore physical and occupational therapists, neuropsychologists and social workers must be involved.

Conclusion

This report showcases an extremely rare variant of MS known as tumefactive MS and describes the clinical facets involved in its diagnosis. Tumefactive MS is estimated to account for one to two cases per 1,000 cases of MS, and can often confound the diagnostic process by presenting with atypical radiographic features mimicking other CNS pathology, such as tumours or cerebral abscesses.[5,6] Use of the McDonald criteria can assist the physician in making a diagnosis of MS, reducing unnecessary surgical and medical intervention.

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