CASE REPORT

Fulminant tumefactive multiple sclerosis in pregnancy

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SUMMARY

A 35-year-old pregnant woman was admitted with acute onset of paresthesias and word finding difficulty. Initial MRI scan of the brain was suggestive of ischaemic event. During hospitalisation, she had a rapid course with worsening of her neurological deficit that prompted additional testing. Further investigations were consistent with tumefactive multiple sclerosis. After a poor initial response to intravenous steroids and plasma exchange, and discussion of all available therapeutic options, the patient decided to proceed with elective termination. Introduction of physical, occupational, speech and disease-modifying therapy resulted in clinical improvement.

BACKGROUND

Tumefactive multiple sclerosis (TMS) is a rare variant of multiple sclerosis (MS), with a prevalence of 1–2 in 1000 cases of MS. It is defined by a single focal demyelinating lesion greater than 2 cm in size and multifocal symptoms caused by a variable degree of mass effect and oedema of the primary lesion, in addition to the demyelinating pathology.¹

Due to the immunological and hormonal changes during pregnancy, both diagnosis and MS relapses are rare and reported only in few case reports.^{2,3}

We report a unique case of a first MS attack with an unexpected course during pregnancy, which encompasses a number of diagnostic and therapeutic dilemmas.

CASE PRESENTATION

A 35-year-old woman, previously healthy, in her 14th week of second pregnancy, presented to a local hospital with right-sided paresthesias and word finding difficulty after a long road trip from Florida. On further questioning, she disclosed mild headache and attention difficulties during the trip, but both symptoms were attributed to travel and pregnancy-related fatigue. On admission, MRI scan of the brain without gadolinium, in diffusion-weighted images (DWI), showed a large area of diffusion restriction in the left parietal lobe measuring 4.5 cm, with low corresponding apparent diffusion coefficient (ADC) signal and periventricular white matter changes. She was diagnosed with ischaemic stroke (figures 1 and 2) and was referred to our hospital for further management.

Neurological examination on admission revealed anomia and decreased sensation to sharp and fine touch in the right face, upper and lower extremity. The remainder of the examination was normal. After reviewing her MRI scans, and taking into

consideration her age and the lack of risk factors for ischaemic event, TMS was included in the differential diagnosis. MRI scan of the cervical spine showed intramedullary signal changes (figure 3). Cerebrospinal fluid analysis showed 14 unique oligoclonal bands, high IgG index of 1.2 and high protein.

Shortly after her admission, her clinical condition worsened. She exhibited profound right-sided weakness and inability to speak. Neurological examination revealed right facial weakness, decreased light touch in the right face, arm and leg, and complete expressive aphasia. Repeat MRI scan of the brain without gadolinium showed interval progression with increase in the size of tumefactive demyelinating lesion (TDL) measuring 6 cm, with diffuse surrounding oedema and new periventricular signal changes (figure 4). Magnetic resonance spectroscopy demonstrated elevated choline to creatinine ratio, decreased N-acetyl aspartate, elevated myoinositol and elevated lactate, favouring an inflammatory demyelinating process. Autoimmune and infectious panels were unremarkable.

TREATMENT

The patient was treated with a 7-day course of high dose intravenous methylprednisolone, followed by plasma exchange with only minor improvement. Treatment options, such as interferons (pregnancy category C), glatiramer acetate (pregnancy category B) and natalizumab (pregnancy category C), were extensively discussed with the patient and her family with the help of a speech therapist through a communication board. Although there are limited data on disease-modifying therapies (DMTs) during pregnancy, the possible beneficial effect of DMTs was emphasised, taking into consideration her highly active disease.⁴ A small case series suggested that natalizumab is a therapeutic option throughout pregnancy for patients with highly active disease.⁵ The patient was extensively counselled about the protective effect of pregnancy on MS. Furthermore, she was advised that recent studies of a large registry cohort provide further evidence of long-term protective effect of pregnancy against disability accumulation.⁶ However, concerns about her health and her responsibility towards her existing and her potential child led the patient and her family to terminate her pregnancy at 17th week. This difficult decision was primarily made in order to lessen the physical and emotional burden of the disease, to start on DMT and intense physical therapy promptly, and to focus on her existing child instead of caring for two young children while having a chronic progressive

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Figure 1 Initial diffusion-weighted MRI scan showing diffusion restriction in the left parietal lobe suggestive of ischaemic lesion.

disease with uncertain recovery. Surprisingly, 10–12 hours after an uncomplicated dilatation and curettage, she started moving her right arm. The drastic improvement in the right upper extremity strength was followed by moderate improvement in her right lower extremity. The following weeks in the rehabilitation unit, she had a satisfying course with gradual improvement and partial return of the expressive language. The patient,

Figure 2 Initial MRI scan showing decreased apparent diffusion coefficient signal in the left parietal lobe suggestive of ischaemic lesion.

Figure 3 Fluid-attenuated inversion recovery sequence of the cervical spine illustrating intramedullary signal change suggestive of demyelinating disease.

Figure 4 Follow up MRI scan, axial fluid-attenuated inversion recovery sequence, 24 hours after admission, showing numerous periventricular and subcortical white matter signal changes with progression of initial lesions.

Figure 5 Repeat imaging 6 months after initial presentation, axial fluid-attenuated inversion recovery sequence, is showing interval progression.

however, was still dysarthric with occasional paraphasic errors and word-finding difficulties.

OUTCOME AND FOLLOW-UP

During her first clinic visit, her exam revealed paraphasic errors, mild right facial droop, right foot drop and diminished light touch throughout the right side. She walked with a cane. Six months later, repeat MRI scan of the brain showed interval progression with a new enhancing pontine lesion (figures 5 and 6).

During her follow-up, her motor examination and 25-foot timed walk continued to improve. Eighteen months later, she is clinically stable on natalizumab.

DISCUSSION

TDL is a rare and highly heterogeneous subtype of MS. Here we report the first case of MS with tumefactive configuration, atypical clinical and neuroimaging features and aggressive course during pregnancy.

Despite rarity, TDLs often represent fulminant forms of MS. With an incidence of about 0.3 in 100 000 per year, the TDLs involve a large area of white matter and can cause multifocal symptoms. These lesions can often be associated with mass effect and oedema. As a result, diagnosis can be challenging as those lesions mimic strokes, tumours or abscesses.¹

In our patient, involvement of motor, somatosensory and language functions, in addition to the atypical appearance of the lesion on MRI images (ie, diffusion restriction in DWI sequences and decreased signal in correlating ADC sequences), was initially suggestive of ischaemia. It was only after detailed examination and re-evaluation of MRI scans that the diagnosis of MS was made. These radiological findings were atypical for demyelinating lesions, which typically demonstrate high signal intensity in both DWI and ADC sequences.⁷ Diffusion restriction with low ADC signal in demyelinating lesions has

Figure 6 Repeat imaging with and without gadolinium, 6 months after initial presentation, fluid-attenuated inversion recovery sequence, reveals a new enhancing pontine lesion.

rarely been reported. The majority of these cases were associated with TDLs or Balo's type demyelination but not during pregnancy.^{7,8}

Unlike most patients presenting with TDL as their first clinical event, our patient did meet the diagnostic criteria for dissemination in space in her first MRI scan of the brain. Gadolinium administration is contraindicated in pregnancy due to higher risk of adverse birth outcomes, such as stillbirth, neonatal death and a broad set of rheumatological, inflammatory or infiltrative skin conditions.⁹ In addition, there is growing evidence about dose-dependent neuronal gadolinium accumulation in the general population.¹⁰ The lack of gadolinium administration in this pregnant patient precluded the visualisation of gadolinium enhancing lesions that could have met the dissemination in time criteria. However, repeat MRI scan of the brain confirmed the dissemination in time and subsequently the diagnosis of clinically definite MS.

Our patient developed a rapid and disabling course with lack of initial response to the commonly used treatment modalities. She was a mild responder to intravenous steroids. Initially, she did not respond to plasma exchange. The poor response to both treatment modalities occurs infrequently in TMS.¹

As repeatedly shown in large studies, pregnancy decreases the relapse rate in patients with MS.² Contrary, our patient's first clinical attack occurred in the second trimester. This rare finding has been observed in a small cohort of patients by the Club Francophone de la Sclérose en plaques (CFSEP) and Radiologically Isolated Syndrome Consortium (RISC) group. In this cohort of patients with radiologically isolated syndrome, pregnancy was found to increase the disease activity and even precipitate the first clinical presentation of the disease.³ The existing data are unanimously suggestive of increased relapse rate in postpartum period and possible protective effect of higher number of pregnancies against MS.² Paradoxically, significant improvement in the patient's condition was noted

several hours after elective termination of her pregnancy. Although this improvement might indicate a different from expected hormonal influence in the pathogenesis of TMS, it is more likely to represent a delayed corroborating effect of steroids and plasma exchange on the clinical course of TMS.

Learning points

- ▶ Tumefactive multiple sclerosis is a rare subtype of multiple sclerosis (MS).
- ▶ Diagnosis can be challenging and may result in treatment delay.
- ▶ In highly active disease during pregnancy, the potential use of disease-modifying therapies should be discussed, and patient preferences should be recognised as an important facet of clinical decision-making.
- ▶ Although initial presentation and relapses of MS are uncommon during pregnancy, clinicians should be aware of this rare subtype of MS, potential initial presentation and unexpected course during pregnancy.

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