

Miller Fisher syndrome mimicking Wernicke encephalopathy during pregnancy

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Miller Fisher syndrome (MFS) is characterized by ataxia, areflexia, and ophthalmoparesis. Here we present a case of MFS mimicking Wernicke encephalopathy (WE) during pregnancy. A 31-year-old woman at 8 weeks of gestation presented with diplopia and ataxia after experiencing nausea and vomiting for several weeks. We initiated thiamine based on a suspicion of WE, which produced no clear effects. However, her symptoms began to improve following intravenous immunoglobulin treatment, and other findings finally lead to a diagnosis of MFS. Because ataxia and ophthalmoparesis can be misdiagnosed as WE during pregnancy, clinicians should consider MFS in the differential diagnosis.

Key words: Miller Fisher syndrome; Pregnancy; Wernicke encephalopathy

Miller Fisher syndrome (MFS) is a variant of Guillain-Barré syndrome (GBS) characterized by the acute onset of ophthalmoparesis, loss of deep tendon reflexes, and ataxia.¹ While some previous studies have suggested that the risk of GBS does not increase during pregnancy, others have indicated that the risk may increase during the third trimester and 2 weeks postpartum.^{2,3} The natural course of GBS during pregnancy is relatively mild, and mostly leads to good maternal and perinatal outcomes.³ However, there are few reports on MFS during pregnancy.⁴

Hyperemesis gravidarum characterized by severe nausea and vomiting may develop during early pregnancy. Such patients may exhibit ophthalmoparesis, ataxia, and a change in the mental status, resulting in a diagnosis of Wernicke encephalopathy (WE).⁵ While the differential diagnosis for acute ophthalmoplegia and ataxia should include WE, MFS, brainstem encephalitis, and brainstem stroke,¹ it is difficult to fully distinguish these conditions in the early stages of symptoms. Here we present a case of MFS mimicking WE during early pregnancy.

CASE

A 31-year-old woman at 8 weeks of gestation presented with dizziness, double vision, and gait disturbance. She reported that she had been experiencing nausea and vomiting for several weeks. A neurological examination revealed ophthalmoparesis in both eyes, mild dysarthria, ataxia, hyporeflexia, and paresthesia in both distal fingers. She had no history for diabetes mellitus, hypertension, recent immunization, or other special syndromes, but had experienced an upper respiratory infection approximately 1 week prior to her initial visit. Brain magnetic resonance imaging (MRI) was performed to exclude various diseases including WE, brainstem stroke, and structural lesions that may cause increased intracranial pressure, and produced no abnormal findings for these lesions.

The patient continued to experience nausea, vomiting, and reduced dietary intake for several weeks, and so she was tentatively diagnosed with WE associated with thiamine deficiency due to hyperemesis gravidarum during early pregnancy. Because very few patients with nonalcoholic WE present without typical brain MRI changes, we initiated treatment with thiamine infusions. This intervention appeared to produce a mild improvement in the lateral gaze limitation of both eyes, but most of the ophthalmoparesis symptoms did not show any improvement.

Due to her ataxia progressing, we began to consider other diseases. To exclude infectious or autoimmune causes such as rhombencephalitis, paraneoplastic syndrome, and inflammatory neuropathies—which can manifest initially as ophthalmoparesis and ataxia—we examined the cerebrospinal fluid, which revealed albuminocytologic dissociation: $0/\text{mm}^3$ red blood cells, $1/\text{mm}^3$ white blood cells, 56.3 mg/dL protein, and 63 mg/dL glucose. Nerve conduction studies (NCS) performed 4 days after symptom onset revealed that the H-reflex was absent from both lower limbs and F-waves were absent from the left common peroneal nerve. All of the other NCS findings were normal. Compound muscle action potentials were normal in both facial nerves. Examination of blink reflexes revealed prolonged ipsilateral R1 and R2 and contralateral R2 latencies upon left-side stimulation. Due to ophthalmoparesis and ataxia progressing over the following 3 days, the patient was diagnosed with MFS, and so she was treated with intravenous immunoglobulin (IVIg).

An enzyme-linked immunosorbent assay was performed to detect various antiganglioside antibodies, including immunoglobulin G (IgG) and IgM antibodies against the gangliosides GM1, GM2, GD1a, GD1b, GD3, GT1a, GT1b, GQ1b and GB1b, as described previously.⁶ Her serum was positive for IgG anti-GQ1b and anti-GT1a antibodies, but all of the other findings were negative.

We observed mild improvements in the lateral gaze in both eyes from the fourth day of IVIg treatment, after which the patient gradually recovered full ocular movement in both eyes. Mild improvements in ataxia were also observed. No adverse effects were reported during the 7 days after the IVIg treatment. She was discharged 2 days after the 5-day course of IVIg treatment, returning for follow-up on an outpatient basis 3 weeks later, at which time no ophthalmoplegia or ataxia was detected. However, since she did not return for follow-up after the initial outpatient visit, and we were unable to obtain precise information regarding maternal and fetal outcomes.

DISCUSSION

We have presented a patient in whom MFS had been misdiagnosed as WE during early pregnancy. Following IVIg treatment, the patient exhibited relatively good improvements in diplopia, ophthalmoparesis, and ataxia. While several studies have discussed neurological complications such as GBS during pregnancy, very few have focused on MFS.^{4,7} Regardless of the presence of pregnancy, GBS and MFS can be treated with IVIg and plasmapheresis.^{8,9}

Concerning the risk of fetal and maternal deaths, IVIg treatment can be recommended in neurological disease during pregnancy according to the EFNS guidelines.⁹ Due to the unfavorable and slowly progressive course of our patient's condition, we initiated treatment with IVIg, after which her symptoms improved rapidly.

The triad of MFS (ataxia, ophthalmoparesis, and areflexia) may be suspected to be caused by WE, which may occur in patients with nausea, vomiting, and reduced dietary intake, and so the administration of thiamine may be considered first.⁵ WE has been reported to occur occasionally in conjunction with hyperemesis gravidarum during pregnancy, excessive alcohol consumption, and long-term nutritional

deficiency.⁵ The neurological symptoms of WE are induced by hyperemesis gravidarum, and usually occur between the first and second weeks of pregnancy, after at least three weeks of persistent vomiting.⁵

The prognosis of patients with WE depends on when thiamine supplementation is initiated. Thiamine treatment was administered in our patient due to the initial suspicion of WE, but this did not produce any clear effects, and brain MRI revealed no lesions characteristic of WE. Furthermore, the abnormalities observed on NCS, late responses, and blink reflex impairments were suggestive of polyradiculopathy. A

previous review suggested a higher probability of MFS, since neuropsychological tests for MFS produce variable findings, and abnormal findings are usually scarce and minimal relative to those obtained in patients with GBS.⁸ Unfortunately, we were unable to distinguish between GBS and MFS due to the lack of follow-up NCS. Given these findings, conditions other than WE should be suspected, including MFS.

MFS has been reported only very rarely in pregnant women.⁴ While GBS tends to occur mainly during the third trimester and postpartum,³ the time of its onset remains to be elucidated for MFS during pregnancy. In the present

Table 1. Comparison of demographic and clinical characteristics between the present case and a previous case⁴

Characteristic	Present case	Ono et al. ⁴
Age (years)	31	26
Gestational age (weeks)	8	11
Antecedent infection	Upper respiratory infection	None
Duration of nausea, vomiting, or reduced dietary intake (weeks)	5	3
Wernicke-encephalopathy-related parameters		
Nystagmus and ophthalmoplegia	+	+
Change in mental status	-	-
Ataxia	+	+
Abnormal brain MRI findings	None	None
Response to thiamine	Poor	Poor
Initial subjective symptoms of Miller Fisher syndrome	Double vision, gait ataxia	Gait ataxia
Symptoms or signs during the disease course		
Dizziness	+	+
Diplopia	+	+
Facial palsy	-	-
Bulbar symptoms or signs	+	-
Limb weakness	-	-
Tingling in limbs	+	-
Areflexia	+	+
Gait ataxia	+	+
Respiratory muscle involvement	-	-
Neurophysiologic findings	Abnormal H-reflex, F-wave, and blink reflex	Unremarkable
Albuminocytologic dissociation	+	-
Antiganglioside antibodies	IgG anti-GQ1b and anti-GT1a	Anti-GQ1b, anti-GD1b, and anti-GT1a
Treatment	IVIg	None
Time to recovery	3 weeks	7 months
Maternal and fetal outcomes	Unknown	Unremarkable

MRI, magnetic resonance imaging; IgG, immunoglobulin G; IVIg, intravenous immunoglobulin.

case we initially suspected WE due to the occurrence of hyperemesis gravidarum during early pregnancy. However, if an obstetrician or neurologist attempts to differentiate MFS with a higher priority in patients with ophthalmoparesis and ataxia during pregnancy, the frequency of MFS may be higher than reported previously.

Table 1 compares the demographic and clinical characteristics between our patient and the patient described by Ono et al.⁴ Although common characteristics were observed, some differences were also evident. The present patient had a previous infection, albuminocytologic dissociation, and abnormal electrophysiologic findings, leading us to suspect MFS following treatment for WE. Since none of these features were present in the patient reported by Ono et al.⁴, that diagnosis was more difficult. Moreover, the previous patient did not receive IVIg treatment and required approximately 7 months to recover. Although differences in anti-ganglioside antibodies were identified after the acute phase, serologic phenotypes have yet to be elucidated. Nonetheless, the results of antibody tests can be used to diagnose the disease more definitively.

The dearth of reported cases makes it difficult to distinguish the clinical features of MFS during pregnancy. However, as observed in the present case, previous infection, albuminocytologic dissociation, electrophysiologic findings, and anti-ganglioside antibody results may aid in the diagnosis of MFS in pregnant patients. Furthermore, when thiamine treatment has no effect in patients with suspected WE due to ophthalmoparesis and ataxia during early pregnancy, diseases such as MFS should be considered in the differential diagnosis.

The present study had some noteworthy limitations. Since we were unable to follow up the clinical course of the patient, we could not report maternal and fetal outcomes. In addition, given the clinical characteristics of MFS and the relatively good course, IVIg treatment alone might not have fully explained the relatively rapid improvement observed in our patient.

In conclusion, this case report highlights the need to consider MFS in pregnant patients with ophthalmoparesis and ataxia when treatment for early WE does not induce a rapid improvement. Although previous studies have indicated that IVIg treatment is safe during pregnancy, further investigation is required to confirm this. Nonetheless, our findings

ultimately suggest that IVIg can be used in patients with MFS during pregnancy.

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Conflicts of Interest

The authors have no financial conflicts of interest.

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