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CASE REPORT

Perinatal Management of Neuromyelitis Optica Spectrum Disorder in Pregnancy: A Case Report

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Purpose: Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune inflammatory demyelinating disease of the central nervous system. Its onset and relapse are closely associated with pregnancy. The aim of this study was to evaluate the risks of NMOSD in the perinatal period.

Patients and Methods: A 35-year-old woman, gravida 4, para 1, at 21^{+4} weeks of gestation with NMOSD, was managed by a multidisciplinary team.

Results: The patient was diagnosed with NMOSD five years prior to the current pregnancy, following an abortion. She had been treated with pulse steroids and plasma exchange at the time of diagnosis. She had a previous normal full-term delivery. Eight months before the onset of NMOSD, she had an induced abortion. She then experienced a relapse of her condition, complicated by embryonic arrest. During the current pregnancy, she had uneventful antenatal visits and was maintained on corticosteroids and intravenous immunoglobulin (IVIG) with no neurologic sequelae. She gave birth to a healthy male infant and her condition remained stable at follow-up.

Conclusion: Women with NMOSD should consult with both neurologists and obstetricians to reduce the risk of pregnancy-related attacks.

Keywords: neuromyelitis optica spectrum disorder, pregnancy, abortion, immunosuppression therapy

Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune inflammatory demyelinating disease of the central nervous system that primarily affects the optic nerves and spinal cord.[1] Severe cases can result in blindness and paralysis. The prevalence of this rare disease is approximately 1–2 cases per 100 000.[2,3] It predominantly affects young adult females and non-Caucasian populations and is characterized by a high rate of recurrent attacks and disability. Pregnancy and abortion are significant risk factors for disease progression and relapse. Therefore, NMOSD during pregnancy is associated with an increased risk of miscarriage, gestational hypertension and preeclampsia. Miscarriage can be caused by damage to the placenta by circulating antibodies to aquaporin-4 (AQP4), which is expressed in the placenta by syncytiotrophoblasts. This damage leads to inflammatory changes and placental necrosis,[4] particularly in the second trimester of pregnancy. The management of reproductive problems in these patients is therefore an important clinical challenge. We report a case of NMOSD in pregnancy to raise awareness of the disease in the perinatal period and to discuss strategies for developing a reproductive plan for this special population.

Case Presentation

A 35-year-old woman, gravida 4, para 1, presented with a history of a healthy full-term spontaneous vaginal delivery in 2016 and an induced abortion in 2017. In June 2018, eight months after the abortion, she developed bilateral limb numbness and weakness, thoracic girdling sensations, accompanied by left temporal pain, itching at the base of the ear and dysuria. The use of acupuncture, tuina massage and eperisone did not result in any improvement. Magnetic resonance imaging (MRI) revealed

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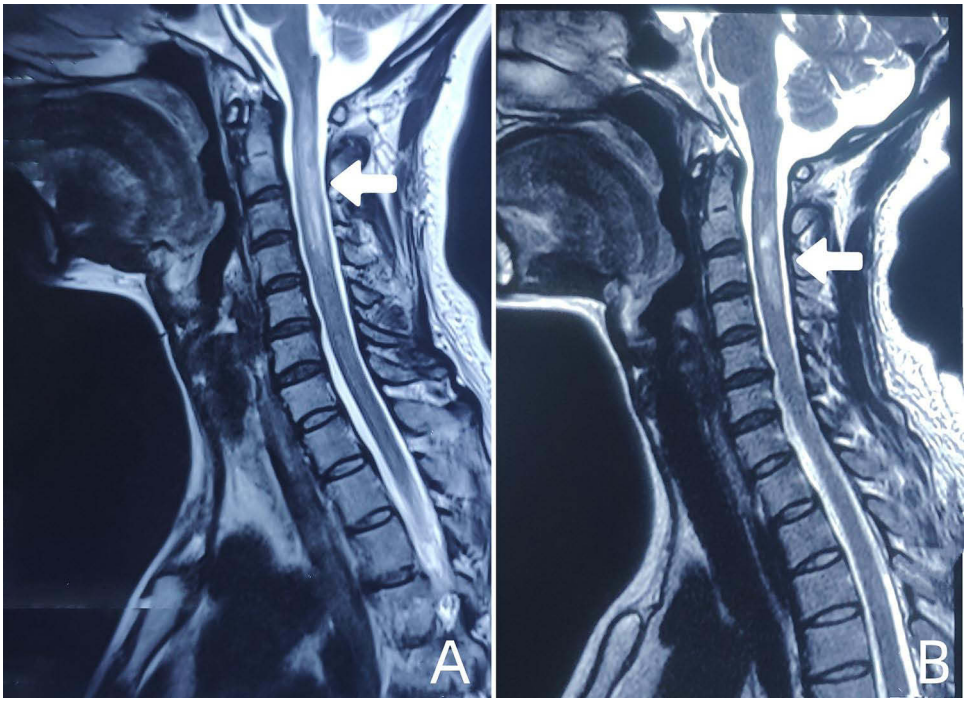

Figure 1 Initial and relapse MRI enhancement images of the patient. (**A**) Initial episode: long segmental abnormal signal in the cervical cord (arrow), striated long T1 signal seen from the medulla oblongata to the C7 vertebral level. (**B**) Relapse: abnormal signal (arrow) of the spinal cord is seen at the level of C2-4.

swelling of the medulla oblongata and long segments of the cervical spinal cord at the level of C7, with hyperintense signal (Figure 1A). Serological test for anti-AQP4-IgG (aquaporin-4 immunoglobulin G) was positive at a titer of 1:10. She was diagnosed with NMOSD. Plasma exchange and steroid pulse therapy were performed three times. After tapering the steroids, medications were discontinued in March 2019. Relapse occurred in February 2020, with the anti-AQP4 titer 1:100. MRI was re-evaluated and showed patchy hyperintensity signal of the lesion (Figure 1B). Intravenous immunoglobulin (IVIG) at a dose of 0.4 g/kg was given for five consecutive days, followed by oral prednisone acetate tablets 30 mg daily. From July 2020, IVIG at a dose of 20 g was administered monthly. In October 2020, the AQP4 antibody titer was reduced to 1:320. In March 2021, she experienced a miscarriage, and the AQP4 antibody titer was 1:100. She was immediately treated with IVIG 0.4 g/kg for three days, and steroid treatment was resumed at the previous dose. Rituximab was started at a dose of 500 mg every six months from April 2021 to October 2022. After the last infusion, she conceived naturally. During this time, prednisone was maintained at 5 mg daily. Her last menstrual period was on December 13th 2022. Prednisone was increased to 10 mg per day, and IVIG was added at 20 g per month starting from week 8 of gestation. The last IVIG injection was given at 29 weeks' gestation. Prenatal screening tests were low risk. A multidisciplinary consultation was coordinated in the second trimester.

Antenatal visits during pregnancy were uneventful. She was admitted to the hospital on September 12, 2023, for labor induction with a dinoprostone vaginal insert. She delivered a male infant vaginally at 39^{+1} weeks of gestation, with a neonatal Apgar score of 10–10 points at one and five minutes. The Bakri balloon was used to manage postpartum hemorrhage, and there were no other obstetric complications. Prednisone was increased to 20 mg/d during labor and was tapered to 15 mg/d after delivery. IVIG was administered at a dose of 0.4 g/kg for five consecutive days, and low-molecular-weight heparin was used for thromboprophylaxis. She initiated breastfeeding and planned to resume immunosuppressive therapy after weaning. Both the mother and the infant were healthy during follow-up.

Discussion

NMOSD is an autoimmune neurological disease with a high prevalence among women of childbearing age.[5] Unlike multiple sclerosis,[6] pregnancy exacerbates NMOSD. During the three months postpartum, the disease re-enters an active

phase and is particularly prone to relapse compared to during pregnancy.[7] In addition, NMOSD during pregnancy has been associated with adverse pregnancy outcomes.[8] Because a single inflammatory attack can lead to irreversible disability, the treatment regimen must be tailored to the individual patient's needs.

NMOSD is associated with an increased risk of several obstetric complications. Spontaneous abortion is the most common,[9] and seropositive for AQP4-IgG is an independent risk factor. Moreover, pregnancies that end in miscarriage following an episode of NMOSD exhibit higher disease activity before and during pregnancy compared to pregnancies that result in a live birth, and therefore in need of treatment more often.[9] Although AQP4-IgG can cross the placenta and be detected in fetal umbilical cord blood, the majority of newborns are seronegative by three months of age[10] and do not develop NMOSD-related symptoms. Nour et al[9] found that NMOSD increased the risk of hypertension and preeclampsia, but the association was primarily due to concomitant autoimmune disorders (eg, systemic lupus erythematosus, antiphospholipid syndrome, and Sjögren's syndrome). Although this association has not been fully supported by clinical trials and histopathology evidence, all women with NMOSD are considered as high-risk pregnancies and require close monitoring to prevent hypertensive disorders of pregnancy.

The mode of delivery and the method of anesthesia used during labor are inconclusive. Currently, NMOSD is not an indication for cesarean section; therefore, the choice between vaginal delivery and cesarean section for NMOSD depends on obstetric factors. In this case, the patient was multigravida so that induction of labor was recommended in the absence of other obstetric comorbidities. Considering that this patient had an inflammatory response detected in the cerebrospinal fluid at initial presentation, the anesthesiologist preferred intravenous administration based on clinical and personal experience.

Immunosuppressants are an important component of sequential therapy, and their use significantly reduces the risk of pregnancy-related relapse.[8] Glucocorticoids, azathioprine, and rituximab are treatment alternatives prior to pregnancy. Current guidelines and expert opinions recommend continuing treatment during pregnancy. However, patients and their families need to be informed that all of these medications are relatively safe for use during pregnancy. Data on fetal teratogenicity of these drugs are mainly derived from other diseases, such as kidney transplantation and rheumatoid arthritis. Adverse effects include: long-term use of glucocorticoids may increase the risk of gestational hypertension and gestational diabetes mellitus; therapeutic doses of azathioprine may increase the risk of intrauterine growth restriction, prematurity,[11] and atrial septal defects.[12] Rituximab may increase the risk of miscarriage and neonatal lymphopenia, but the reduction in B cells is reversible after 6 months of life. Therefore, to minimize the risk during pregnancy, it is generally recommended to cease contraception after the last infusion of rituximab. If pregnancy has not occurred after 6 months, the drug can be administered again.[7] This recommendation differs from the US Food and Drug Administration (FDA) approval, which suggests that pregnancy should be considered 12 months after discontinuation of the drug. It is essential to communicate such details to the pregnant woman and her family in a well-informed manner. Although the French Multiple Sclerosis Society[13] does not recommend IVIG therapy for relapses during pregnancy, its off-label use in pregnant and breastfeeding patients is considered safe and widely accepted.

The short follow-up period was a limitation of our study. A focus of recent research is predicting the risk of relapse during the postpartum period. If there are frequent relapses prior to conception, immediate immunotherapy after delivery is recommended.

Conclusion

Pregnant women with NMOSD are at high risk of miscarriage and preeclampsia. Multidisciplinary consultation, including neurologists and obstetricians, is recommended at the beginning of preconception or early pregnancy to share expertise and resources with patients and their families.

Data Sharing Statement

The authors declare that all data supporting the findings of this study are available within the article.

Ethics Approval

The Ethics Committee of Obstetrics and Gynecology Hospital of Fudan University approved the study (No. 2023-91) on August 7th 2023. Institutional approval was required to publish case details.

Consent to Publish

The patient gave consent for the publication of photograph(s) and case history and other details within the text to be published in journals used for scientific purposes.

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Disclosure

All authors declare that there is no conflict of interest in this study.

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