

Acute Transverse Myelitis in Pregnancy

—A Case Report and a Literature Review

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Abstract

Purpose: This case report highlights a rare instance of a 26-week pregnant woman presenting with limb numbness, diagnosed with acute transverse myelitis (ATM) following COVID-19 vaccination. Notably, she tested positive for neuromyelitis optica (NMO) but did not exhibit the typical symptoms of blurred vision. **Methods:** Data were collected from I Seha in governmental hospitals in Bahrain, providing a comprehensive overview of the patient's clinical journey. **Results:** The patient was treated with carbamazepine, steroids, and clexane, leading to the successful delivery of a healthy baby at 34 weeks. However, two years postpartum, she reported new episodes of blurred vision and numbness. Subsequent treatment with Rituximab resulted in significant improvement, with a diagnosis of Devic's disease established. **Conclusion:** Acute transverse myelitis is a rare condition, particularly during pregnancy, and in this case, symptoms of Devic's disease were masked by the absence of blurred vision. This condition predominantly affects females in their 20s during childbearing years and can lead to complications such as premature delivery. Effective management includes steroids and antiepileptic drugs, with clexane playing a crucial role in preventing embolisms. A delivery mode may vary based on obstetric factors, and MRI remains the gold standard for diagnosis. Close follow-up is essential for optimal patient outcomes.

Keywords

Acute Transverse Myelitis (ATM), COVID-19, Devic's Syndrome, Neuromyelitis Optica (NMO), Obstetric Management of ATM

1. Introduction

Acute transferred Myelitis (ATM) or Neuromyelitis Optica spectrum disorder (NMOSD) is one of the rare autoimmune diseases that occur in the central

nervous system (CNS), which mainly will target the spinal cord and the optic nerve, resulting in vision loss and paralysis. ATM affects women more than men with a ratio of 6 - 9:1. The risk of relapse increases during and immediately after the pregnancy [1]. The disease is mediated by antibodies that attack the water channel aquaporin 4 (AQP4) resulting in severe optic neuritis, myelitis and sometimes brainstem encephalitis [2].

Originally, the disease was known as Devic's disease, and it mostly followed a relapsing course. It was previously considered a variant of multiple sclerosis (MS). NMOSD is associated with IgG antibodies that affect AQP4 and myelin oligodendrocyte glycoprotein (MOG-ab), and this is the milestone that helps differentiate between the two diseases. Attacking the channels of AQP4 and MOG-ab will be followed by granulocyte and eosinophil infiltration, followed by demyelination and neural loss [3].

Many studies have highlighted the factors that could contribute to the disease's pathogenesis. Some are the female factors like the gonadal hormones, oestrogen and progesterone, which rise significantly during the pregnancy and decrease after the changes that occur in the immune system during the pregnancy affect the outcome of the NMOSD as oestrogen decreases the apoptosis of self-reactive B cells, and the high level of it can boost the peripheral B cells which in turn increase the disease activity as well as high oestrogen level during the pregnancy can deplete T-regulatory cells which can enhance the inflammation in NMO and increased regulatory natural cells as well [4] [5].

The main target antigen in NMOSD is AQP4 expressed in high amounts in the placenta. The antibodies can cross the placenta and be found in the blood of newborn infants without causing any symptoms therefore women with active NMOSD have a high risk of placental inflammation and miscarriage [6].

The literature has identified a poorer prognosis in NMOSD compared to multiple sclerosis (MS). A single relapse of NMOSD can result in permanent disability, therefore the key objective in disease management is early detection and relapse prevention by using long-term immunosuppressants. However, it has been reported that the overall prognosis of patients with ATM or NMOSD has significantly improved in the last two decades [4]. The treatment options during the pregnancy depended on disease status. Intravenous corticosteroid class C is the first choice during the acute relapse followed by plasmapheresis and intravenous immunoglobulin Class C. While the maintenance therapies were, Azathioprine class D, Rituximab class C, Mycophenolate mofetil class D, Methotrexate class X, Cyclophosphamide class D and Oral corticosteroid class C during the first trimester [7].

This paper will present a diagnostic and therapeutic process of a 27 years old pregnant female who presented atypically with ATM. This paper will outline the clinical presentation, diagnostic evaluation, management strategies, and outcomes of the patient, emphasizing the importance of the multidisciplinary approach in the treatment of ATM and its association with NMO in the context of pregnancy.

2. Case Report

A 27-year-old Bahraini female, a primary gravida, presented to the emergency department at 26 weeks of gestation on October 15, 2021, with complaints of pain in her legs, hands, and back, accompanied by tremors.

She had experienced cervical muscle spasms on the right side for five days, followed by a cervical headache. She denied having a fever, experiencing trauma, or noticing any blurring of vision. These symptoms began within two months of receiving the COVID vaccine.

The patient also reported weakness and tremors in her upper limbs, as well as weakness and numbness in her lower limbs up to the knees, which led to difficulty in walking.

A neurologist examined her and found a slight unsteady gait, with a positive Romberg test and finger-pointing test, as well as a positive left-sided Hoffman sign.

Upper limb strength was scored at 5/5 across all myotomes, but there was decreased sensation in the left upper limb in the C5/C6/C7/C8/T1 regions. Lower limb examination showed 5/5 strength over L2/L3/L4 and S1, with decreased sensation at L3. The patient was also examined by orthopedics, and both specialties recommended an MRI.

Laboratory tests were conducted, all of which returned normal results, while the lumbar puncture revealed elevated white blood cell (WBC) count and protein levels, although cultures were sterile. Neuromyelitis optica (NMO) antibodies were detected in the cerebrospinal fluid (CSF).

MRI of the spine revealed acute segmental diffuse T2 and STIR hyperintensities (indicative of edema or inflammation) from the cervicomedullary junction up to the T 1 - 2 level, involving both halves of the spinal cord. The imaging showed diffuse cord edema, expansion, and patchy enhancement, consistent with features of acute transverse myelitis.

The patient was treated with intravenous methylprednisolone for five days, followed by oral prednisolone at a dose of 60 mg daily and carbamazepine at 100 mg for three days. The carbamazepine dose was increased to 200 mg daily but later reduced to 100 mg daily due to side effects, including a burning sensation and drowsiness.

Prophylactic enoxaparin was administered due to immobilization, and physiotherapy was provided to aid in the gradual improvement of weakness and sensation until the patient was able to walk. Pregnancy management involved reassuring the patient with ultrasound findings, which were normal for her gestational age. The patient was discharged and followed up regularly at both the antenatal and neurology clinics.

On December 6, 2022, the patient was admitted in labor at 34 weeks of gestation, complaining of hand numbness and colicky abdominal pain. Upon examination, she was found to be 4 cm dilated. The neurologist advised that she could proceed with a normal vaginal delivery. The patient underwent spontaneous vaginal delivery on December 7, 2022, giving birth to a single live male baby with a

birth weight of 1.670 kg and Apgar scores of 9 and 10.

Neurology recommended the continuation of prednisolone postnatally and scheduled follow-up MRI scans. A postnatal MRI follow-up showed resolution of the acute transverse myelitis (ATM), and the patient continued her medication.

In 2023, the patient reported blurring of vision, confirming a diagnosis of neuromyelitis optica (NMO) or Devic's disease. She was treated with Rituximab for six months and advised to follow up regularly. The patient is currently having dormant symptoms.

3. Discussion

Acute transverse myelitis (ATM) in pregnancy is a rare but serious neurological disorder that damages the spinal cord myelin, affecting the sensory, motor, and autonomic systems [8] [9].

The prevalence of ATM is approximately 4.6 cases per million per year [10]. The peak incidence occurs in adults in their 20s and again after the age of 40 [10], affecting males and females equally [10]. In another study ATM affects women more than men with a ratio of 6 - 9: 1. The risk of relapse increases during and immediately after the pregnancy [1], which in our case report, our patient is in her twenties and she's female. She was affected during her pregnancy and followed her delivery.

The causes of ATM can be related to autoimmune diseases [11] or acute infections, such as cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes simplex virus type 2, enterovirus, and varicella-zoster virus (VZV) [12]-[14].

A study indicated that the main causes of ATM during pregnancy were traumatic (73%), inflammatory (13%), vascular (7%), and infectious (7%) [15]. Unlike our case report, it was related to covid 19 vaccine.

However, another study showed the disease is mediated by antibodies that attack the water channel aquaporin 4 (AQP4) resulting in severe optic neuritis, myelitis and sometimes brainstem encephalitis [2], which supports our case as she had optic neuritis after her delivery.

Originally, the disease was known as Devic's disease and mostly followed a relapsing course. It was previously considered a variant of multiple sclerosis (MS). Our patient didn't have MS.

NMOSD is associated with IgG antibodies that affect AQP4 and myelin oligodendrocyte glycoprotein (MOG-ab), and this is the milestone that helps differentiate between the two diseases.

Attacking the channels of AQP4 and MOG-ab will be followed by granulocyte and eosinophil infiltration, followed by demyelination and neural loss [3]. In our case the disease affected her limbs in motor and sensory patterns.

Many studies have highlighted the factors that could contribute to the disease's pathogenesis. Some are the female factors like the gonadal hormones, oestrogen and progesterone which rise significantly during the pregnancy and decrease after the changes that occur in the immune system during the pregnancy. It affects the

outcome of the NMOSD as oestrogen decreases the apoptosis of self-reactive B cells, and the high level of it can boost the peripheral B cells which in turn increases the disease activity as well as high oestrogen level during the pregnancy can deplete T-regulatory cells which can enhance the inflammation in NMO and increased regulatory natural cells as well [5], which supports our case.

Many recent studies have shown that acute transverse myelitis (ATM) can occur after infection with the coronavirus disease (COVID-19) or following COVID-19 vaccination [16]-[20]. Our patient received the vaccine. One study indicated that the Oxford-AstraZeneca vaccine was the most. Our patient had Pfizer.

Studies showed it's commonly associated with myelitis, with 12 cases out of 31, followed by Pfizer (8 out of 31), Moderna (7 out of 31), Sinopharm (3 out of 31), and Janssen (1 out of 31).

The incidence in females was higher than in males, with a ratio of 17 females to 14 males [21].

Symptoms of ATM depend on the location of the affected spinal cord lesions and may include numbness, weakness, loss of sensation, impaired motor skills, dysfunctional sphincter activity, and hypertension [22], which our patient had the most symptoms.

Neurological examination, lumbar puncture, MRI, and blood tests are considered the ideal methods for diagnosing ATM [23]. MRI usually shows **cord swelling** if transverse myelitis is present [23].

In our case the MRI showed diffuse T2 and STIR hyperintensity from cervico-medullary junction up to D1-2 level involving both halves of the cord. The diffuse cord edema, expansion and patchy enhancement are features that suggest acute transverse myelitis (**Figure 1**).



Figure 1. Diffuse T2 and STIR hyperintensity from cervico-medullary junction up to D1-2 level involving both halves of the cord. The diffuse cord edema, expansion and patchy enhancement are features that suggest acute transverse myelitis.

Patients with lesions above T10 - T11 may not feel labor pain, [24] which can complicate childbirth; however, our patient experienced colicky abdominal pain.

The risk of severe complications increases if the lesion involves the cervical segment, potentially leading to respiratory failure [25]. Fortunately, our patient did not experience this complication.

The literature has reported many explanations for pregnant women with ATM, as this group of pregnant women has a higher rate of complication. The AQP4 IgG antibodies that are produced by the hypothalamus during the acute phase of ATM can cross the placenta and act by binding on the AQP4 that produced on the placental syncytiotrophoblasts, although the expression during the first to the third trimester is decreasing, the consequences can be highly threatening, as it increases the neutrophils infiltration, affecting the placenta by causing inflammation and increasing the rate of fetal death. In contrast, in the current case report. The patient developed the ATM during the last week of the second trimester which decreased the percentage of autoantibody crosses throughout her placenta [4].

The prognosis of acute transverse myelitis (ATM) depends on the degree of improvement observed within 3 to 6 months. Patients typically require rehabilitation and intensive physical therapy [26], which our patients continue to receive.

One of the key challenges in managing ATM in pregnancy is the need to balance the treatment of the neurological condition with the safety of the developing fetus. In this case, the patient was treated with corticosteroids and carbamazepine to manage the acute symptoms of ATM. Adjustments in medication dosages were made based on the patient's response and tolerance to the treatment, emphasising the importance of close monitoring and individualised care in pregnant patients with neurological disorders.

Studies have shown that steroids are an effective treatment for ATM, while antiepileptic medications, such as pregabalin and carbamazepine [27], can help manage neuropathic pain. Recent trials have also explored the implantation of stem cells as a potential therapy for ATM [28].

The use of antibiotics is sometimes necessary in cases of confirmed infection, along with anticoagulants. One case involved a 20-year-old pregnant woman from Senegal who had acute transverse myelitis (ATM). She was treated with IV corticosteroids and ciprofloxacin [24].

The decision to initiate prophylactic anticoagulation with enoxaparin due to the patient's immobilisation is a crucial aspect of the management of pregnant patients with ATM. Pregnancy itself is a hypercoagulable state, and neurological conditions such as ATM can further increase the risk of thrombotic complications. Prophylactic anticoagulation helps mitigate this risk and is an important consideration in the overall care plan for pregnant patients with neurological disorders. A case study done in France, a pregnant woman developed deep venous thrombosis (DVT) alongside ATM. Such cases should have received enoxaparin as prophylaxis, similar to what our patient received and the one from Senegal. Both

of these patients underwent caesarean sections, unlike our patient [15] [25].

The successful delivery of a healthy baby at 34 weeks gestation in this case is a positive outcome, underscoring the importance of coordinated care between obstetrics and neurology teams. The decision to continue prednisolone postnatally and schedule follow-up MRI scans is essential to monitor the resolution of ATM and ensure ongoing management of the patient's neurological condition.

Long-term follow-up is crucial in patients with ATM, particularly in the postpartum period, as there may be a risk of disease recurrence or complications. Continued monitoring, symptom assessment, and appropriate interventions are necessary to optimise the long-term outcomes for both the mother and the newborn.

Two years following experiencing ATM, the patient complained of blurred vision, which can indicate neuromyelitis optica (NMO). The combination of ATM and NMO is referred to as Devic's disease [25]. However, unlike patients with Devic's disease, she did not experience any relapses during her pregnancy or postpartum period. Additionally, she did not have blurred vision during her pregnancy. Devic's disease can also lead to preeclampsia and premature delivery [29] [30].

A study conducted in Canada involving 13 pregnancies showed that Devic's disease resulted in 8 term births, 3 preterm deliveries, and 2 miscarriages [29]. Patients presented with symptoms such as imbalance and blurred vision, which were treated with azathioprine, amitriptyline, IVIG, and plasma exchange [30] none of which were administered to our patient, who ultimately recovered. Gabapentin was the treatment of choice for patients suffering from NMO [30].

4. Conclusions

ATM is a rare neurological condition characterised by inflammation of the spinal cord, leading to motor, sensory, and autonomic dysfunction. It can occur as a result of various aetiologies, including autoimmune disorders, infections, and post-vaccination reactions. It is more affecting childbearing age and among females more than males.

Devic's disease is when symptoms involve the optic nerves, and the spinal cord (ATM) and CSF showed positive NMO antibodies. Both can cause maternal and fetal morbidities. Addressing the unique challenges and considerations of neurological disorders in pregnant patients, healthcare providers can strive to achieve the best possible outcomes for both the mother and the newborn.

The gold standard investigation is MRI. This highlights the importance of a multidisciplinary approach, individualised care, and close monitoring in the management of ATM in pregnancy.

Continued postnatal care, including the maintenance of prednisolone therapy and follow-up MRI scans, is essential to monitor disease resolution and prevent potential complications in the postpartum period. Long-term follow-up and ongoing assessment are crucial to address the risk of disease recurrence and ensure the well-being of both the mother and the newborn.

Ethical Approval

Ethical approval from the Research Committee for Government Hospitals was obtained. Research approval serial number: 92-220824.

Consent

Written and informed consent was obtained from the patient, (kindly note that the author Zainab is the patient).

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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