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Original Research Article

A Rare Case of Neuromyelitis Optica Spectrum Disorder (NMOSD) Complicating Pregnancy

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Abstract

Neuromyelitis Optica spectrum disorder (NMOSD) is an antibody mediated neuroinflammatory disorder characterized by recurrent myelitis and optic neuritis. We present a case of pregnant lady presented with hyperemesis gravidarum at 16weeks of gestation. The patient had a rapid course of recurrent episodes of bladder and bowel retention and quadriparesis. MRI brain & spinal cord was suggestive of longitudinal extensive transverse myelitis and aquaporin 4 ab (AQP4-Abs) was positive. Patient was treated for Neuromyelitis Optica Spectrum Disorder (NMOSD).

Keywords: Pregnancy, Neuromyelitis Optica, Aquaporin 4, Hyperemesis Gravidarum.

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Introduction

Neuromyelitis Optica spectrum disorder (NMOSD) is a rapidly progressive autoimmune neuroinflammatory disorder characterized by recurrent myelitis and optic neuritis. We present a rare case of NMO complicating pregnancy.

Case Report

A 20year old primgravida, at 16 weeks of gestation presented to the hospital with chief complaints of multiple episodes of vomiting. Vomiting was bilious, projectile in nature, insidious without fever or other precipitating causes. Patient was treated as hyperemesis gravidarum and was discharged. A week later patient noticed difficulty in gripping the footwear, dragging of feet, and progressive weakness of right lower limb. On waking up next day morning, she noticed weakness of both the limbs, causing difficulty in walking, which was increasing gradually. There was noticeable bladder and bowel retention for which she was again hospitalized. Patient was catheterized for bladder retention and enema was given. While being evaluated for limb weakness, bladder and bowel symptoms, patient developed intractable hiccups. On neurological examination patient was conscious, coherent, and cooperative. The speech was normal and cranial nerves were normal (Table 1). The baseline investigations were sent along with viral screening, thyroid profile, CSF Analysis, IgM RA, AntiLA, ANA, ANCA, Anti Po Anti cardiolipin IgG, IgM and transthoracic 2 D echo (Table 2). Patient was evaluated with magnetic resonance imaging (MRI) of brain and spinal cord. MRI was suggestive of multifocal areas of demyelination in brain and spinal cord (Figure 1). The condition was diagnosed as multiple sclerosis (MS) complicating pregnancy and was treated with methylprednisolone 1gm, IV for 3days followed by oral prednisolone 40mg once a day, proton pump inhibitors (PPI) for gastroesophageal reflux disease (GERD) and racecadotril for autonomic gastropathy. While on prednisolone, patient developed weakness of right upper limb and inability to pass motion requiring enema. Patient was started on intravenous immunoglobulin (IVIG) 500mg/kg, with which there was improvement in the power of right upper limb. After 10 days patient again developed numbness and tonic spasms, shock like symptoms (Lhermitte's sign) in the upper limbs and developed weakness in the lower limbs. Repeat MRI brain & spinal cord was suggestive of demyelinating lesions in periventricular white matter and adjacent optic

chiasma and lateral cord sign in posterolateral Longitudinal extensive transverse myelitis. (Figure 2). Due to the relapse and recurring nature of the symptoms, patient was tested for aquaporin 4 ab (AQP4-Abs) which came positive. Diagnosis of Neuromyelitis Optica Spectrum Disorder (NMOSD) complicating pregnancy was established. The patient had a good remission and symptomatic improvement with azathioprine 50 mg once a day, prednisolone 40mg once a day and carbamazepine 100mg twice a day dose. All the medications were continued throughout the pregnancy. Multidisciplinary team was involved in monitoring the patient for leukopenia, thrombocytopaenia, features of preeclampsia and ultrasound gravid aspects of entire cervical cord suggestive of uterus was done for foetal growth and development. The obstetric course was complicated by the development of gestational diabetes mellitus (GDM), preeclampsia, IUGR and at 34 weeks of gestation patient had preterm labour with premature rupture of membranes (PROM). Patient had normal vaginal delivery and delivered a female child with a birth weight of 2.3Kgs. All the medications were continued in the postpartum period and lactation was allowed. Patient was started on postpartum thromboprophylaxis. The risk of recurrence of symptoms in the post-partum period explained to the patient. Both mother and child were discharged in stable condition.

Table 1: Neurological Examination of the Patient

Motor System Examination		**Right**	**Left**
Inspection	Upper limbs	Hypothenar muscles wasted	Hypothenar muscles wasted
	Lower limbs	Nil abnormal	Nil abnormal
Muscle Tone	Upper limbs	Hypotonia	Hypotonia
	Lower limbs	Hypotonia	Hypotonia
Muscle power	Upper limbs	Proximal 4 -	Proximal 4 -
		Distal 4 -	Distal 4 -
	Lower limbs	Proximal 4 -	Proximal 4 -
		Distal 4 -	Distal 4 -
Limb coordination	Finger nose test	No action tremors	No action tremors
	Heel Shin test	No action tremors	No action tremors
Reflexes	Upper Limbs	Hyporeflexia of biceps, brachioradialis	Exaggerated in Biceps
	Lower Limbs	Exaggerated knee jerk & ankle jerk	Exaggerated knee jerk & ankle jerk
	Plantar	Extension	Withdrawal
Sensory Examination			
Pinprick	Upper Limbs	Normal	Normal
Vibration	Lower Limbs	Normal	Normal
Proprioception		Normal	Normal
Posture & Gait	Could not be done as the patient could not stand		

Table 2: Investigations Done

Investigation	**Report**
Complete blood picture	Hb 10.2gm%, WBC-8,700, Platelets – 2.2lakhs/mm^3
Random Blood Sugar	102mg%
Renal function tests	BU – 20mg%, Creatinine 0.7, Na+ 135, K+ 3.6, Cl- 99
Liver function tests	Bilirubin 0.6, SGOT 43, SGPT 38
Thyroid Profile	TSH – 2.88 IU/
Transthoracic echo	Normal ventricular and valvular function
HIV, HbSAg, HCV	Negative
CSF Analysis	40 cells with 100% lymphocytes , normal sugar & proteins ; ADA of 1.94
IgM RA, Anti LA, ANA,ANCA, Anti Po Anti cardiolipin IgG, IgM	Negative Positive
US Gravid uterus	Single live foetus of 16weeks gestation

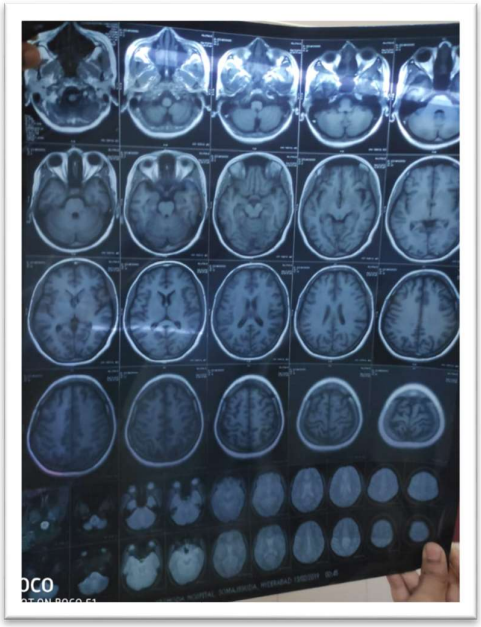

Figure 1: MRI brain & spinal cord S/O demyelinating lesions in periventricular white matter and adjacent optic chiasma

Figure 2: Lateral cord sign in posterolateral aspects of entire cervical cord

Discussion

Neuromyelitis Optica spectrum disorder (NMOSD) is an antibody-mediated disease of the central nervous system predominantly affecting the women in the reproductive age group. The term neuromyelitis Optica was coined by Eugene Devic and was known as Devic's disease. The identification of aquaporin-4 water channel and detection of AQP4-Abs in 2004, distinguished NMOSD from multiple sclerosis. The incidence of NMOSD ranges from 0.05–0.40 per 100,000 with female preponderance (3:1–9:1). [1] The clinical features of NMOSD reflects the inflammation of optic nerve, spinal cord, and the brainstem. Twelve percent (12%) of the patients present with intractable nausea, vomiting and/or hiccoughs which is a manifestation of area postrema syndrome (APS) secondary to periaqueductal inflammation and lesions. [2, 3] In our present cases the presenting complaint was intractable vomiting and was treated as hyperemesis gravidarum. The hallmark symptoms are acute attacks of bilateral or rapidly sequential optic neuritis, transverse myelitis (often causing

limb paresis or paralysis, sensory loss), APS, acute brain stem syndrome, acute diencephalic syndrome, and acute cerebral syndrome. The patient can have longitudinally extensive transverse myelitis (LETM), spinal cord syndrome, especially with paroxysmal tonic spasms, loss of bladder or bowel control or intractable bladder retention. NMOSD can have typical relapsing course with acute attacks occurring over days and with variable degrees of recovery. Our patient had all the symptoms of NMOSD except for optic neuritis.

The major differential diagnosis for NMOSD is MS and longitudinal extensive transverse myelitis. The discovery of autoantibody biomarkers like aquaporin-4 IgG promoted the improved understanding of disease pathogenesis of NMOSD and MS. Anti-aquaporin-4 antibody is specific for NMOSD. Takahashi et al tested 148 sera and analysed the relation of anti-AQP4 antibody titres of patients with NMO, and similar high-risk miscellaneous diseases. They found that anti-AQP4 antibody assay was 91% sensitive (95% CI 79-100) for NMO and 85% (65-100) for high-risk syndrome, and 100% specific (91-100) for NMO and high-risk syndrome. [4] The other differential diagnosis includes acute disseminated encephalomyelitis, intrathecal tumours, systemic lupus erythematosus, vascular abnormalities, vitamin B12 deficiency and viral infections like HIV. MRI of the brain and the spinal cord could rule out the intracranial causes in the present case and the laboratory tests could rule out the possibility of lupus, vitamin deficiencies and viral infections. The presence of all core symptoms except optic neuritis, aquaporin 4 IgG positive and exclusion of the other conditions could clinch the diagnosis of NMOSD complicating pregnancy in the present case.

The immunomodulatory condition of pregnancy can modify the onset or relapse of attacks in NMOSD patients. AQP4 expressed in the human placenta helps to mediate maternal-fetal fluid exchange. Deng et al in their study expressed the view that increased levels of AQP4 on the placenta may trigger autoimmune reactions, stimulating production of AQP4-ab in the serum. 6 Women conceived after the onset of NMOSD and those conceived at times of high disease activity, may be at increased risk of pregnancy loss. Increased risk of miscarriage, premature deliveries and preeclampsia has been reported in the study by Noor et al. 7 Shimizu et al reported increase in the annualized relapse rate (ARR) in the postpartum period. 8

The treatment of NMOSD depends on the mode of presentation and the clinical course, as relapses are more severe and can be permanent in NMOSD than in MS. The disease-modifying medications like glucocorticoids, azathioprine, rituximab, and eculizumab are considered safe in pregnancy. 9 Our patient was on AZA, and prednisolone. Prednisolone though tolerated well, can cause premature delivery. Our patient needed chronic steroid therapy which might have contributed to premature delivery, diabetes, and asymptomatic bacteriuria. The mode of delivery can be either vaginal or operative. 10 Though studies show the safety of epidural and spinal anaesthesia our patient did not opt for labour epidural. Lactation during azathioprine treatment seems to be relatively safe. Awareness about the condition and early identification of the cases can help to identify the predictors of adverse outcomes of NMOSD in pregnancy.

Conclusion

NMOSD can present first time in pregnancy and relapses can be more frequent and permanent. Awareness about the condition, early recognition, and a multidisciplinary approach with involvement of neurologist, neuro -ophthalmologist, high-risk obstetrics team, and neonatologist is essential for the successful management of NMOSD complicating pregnancy.

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