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Case report

Complicated pregnancy in a Neuromyelitis Optica patient at St Paul Hospital Millennium Medical College, Ethiopia: A case report

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Abstract

Neuromyelitis optica (NMO) is an autoimmune mediated demyelinating inflammatory disease that mainly affects the optic nerves and spinal cord. NMO usually occurs in women of reproductive age. NMO and pregnancy have complex relationships with several diagnostic and therapeutic implications. In this report, the first Ethiopian case of NMO in a 28years old woman who presented from rural part of the country mainly with progressive weakness of all extremities and history of complicated pregnancy was described highlighting the diagnostic and therapeutic challenges as well as residual morbidity of NMO in resource limited setups.

Keywords*:* NMO, *Complicated pregnancy, Ethiopia*

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Introduction

Neuromyelitis optica (NMO) is a severe and recurrent autoimmune mediated inflammatory disorder of the CNS. The demyelination of neurons mainly causes a simultaneously or sequentially extensive inflammation of the spinal cord (myelitis) and optic nerve (optic neuritis) [1].Antibodies of the IgG class against Aquaporin-4 (AQP4) are characteristically diagnostic of NMO, present in about 88% of patients with NMOSD and used to distinguish NMO from other demyelinating diseases of the CNS [2]. NMO is a rare disease with the prevalence range of 0.5–4/100,000 and may be slightly higher in certain racial groups[1]. According to the 2006 revised diagnostic criteria[3], the definitive diagnosis of NMO required the following three criteria: A. Optic neuritis, B. Acute myelitis, and C. At least two of three supportive criteria:- i. Contiguous spinal cord MRI lesion extending over ³3 vertebral segments, ii. Brain MRI not meeting the diagnostic criteria for multiple sclerosis, and iii. NMO-IgG seropositive status. NMO is more common in reproductive age women than men, with women comprising over two-third of all NMO patients [4]. Though studies of pregnancy outcomes among NMO patients were challenged by limited sample size as NMO itself is a rare disease entity, there are reports of increased rates of miscarriage and preeclampsia among reproductive age women [4].

Case presentation

A 28 years old female patient presented from rural part of Ethiopia with the complaint of progressive weakness of all extremities of three-month duration. Her body weakness initially started on the left -upper extremity, progressed to left lower extremity after 3-days, extended to right-lower extremity and right-upper extremities in 10-days and 15 days -interval, respectively. She had an associated history of decreased vision of right eye, urinary and fecal incontinences, tingling sensation and numbness of all extremities. She had painless loss of her left eye vision 3 years ago but did not seek any medical attention then. Otherwise, she had no family history of similar illness, history of diabetes or hypertension, and history of arterial or venous thrombosis. She had repeated bad obstetric history in the last three years which included recurrent abortion of three times. The first two miscarriages were claimed to be after 5-months of amenorrhea, and the third was after 6-months of amenorrhea. The first episode of miscarriage occurred about two months after she sustained painless visual loss of the left eye. She was living in rural area and had no antenatal care(ANC) during pregnancies which ended up with miscarriage.

She had ANC follow up for her last pregnancy which she delivered a healthy baby three weeks before the onset of the current illness. However, in this last pregnancy she was also diagnosed to have preeclampsia.

On physical examination, her vital signs were in the normal range. She had complete vision loss of left eye with fundoscopic findings of optic atrophy, and reduced visual acuity of the right eye.

During admission to our hospital, she had flaccid paralysis with quadriplegia, hyperreflexia (brisk with clonus) and bilateral up going plantar reflex. There was no pertinent finding on the rest of the systems. Laboratory investigations have revealed normal whole blood cell count, serum vitamin B-12 level, Anti-cardiolipin antibody, lupus anticoagulant, and anti-neutrophilic antibody(ANA) as shown in Table-1.

Table 1 Laboratory results of an NMO patient with complicated pregnancy diagnosed at St. Paul Hospital Millennium Medical College

CBC	WBC	7,200/mm3 (Neutrophils-54.2%)
	Hemoglobin	14.5gm/dl
	Platelet	190,000/mm3
Cerebrospinal Fluid(CSF) Analysis	White Cell count	15/mm3 (Lymphocytes-55%)
	Protein	20 mg/dl
	Glucose	57 mg/dl
	AFB	No AFB
	Indian Ink	No C. Neoformans
Anti-Aquaporin 4-Antibody	1:1600+++	Normal Reference range<1:10
Anticardiolipin antibody	IgG and IgM isotype	14 GPL
Serum Vitamin-B12	485 pg/mL	Normal
ANA	Negative	
HIV	Negative	
VDRL	Negative	

Her clear appearing CSF-analysis had cell count of 15/mm3, with neutrophil of 45%, and lymphocyte of 55%. The AQP4 antibody titer was done abroad (Germany) after obtaining financial support from charity organization and the result was found to be1:1600+++ titer (Normal Reference range<1:10). Her brain MRI showed bilateral atrophy of optic nerves with edematous signal changes of the right optic nerve. The MRI of spinal cord also showed extensive long segment hyperintensity on T2W and STIR imaging with syrinx (fig-1). Due to financial constraints post contrast MRI could not be done. Pattern reversal visual evoked potential (PRVEP) with monocular stimulation and midline recording was done suggesting bilateral anterior visual pathway dysfunction with mixed demyelination and secondary axonal degeneration predominantly involving the left eye (Table-2).

Table 2 Pattern Reversal Visual Evoked Potential (PRVEP) demonstrating prolonged P100 latency on bilateral eyes and decreased P100 amplitude (mV) of bilateral eyes, more on the Left eye

Stimulation position	P100- **Latency(msec)**	**P100 Amplitude**(μV)
Left Eye	160	1.24
Left Eye	167.6	1.68
Right Eye	182.4	2.54
Right Eye	169.6	3.81

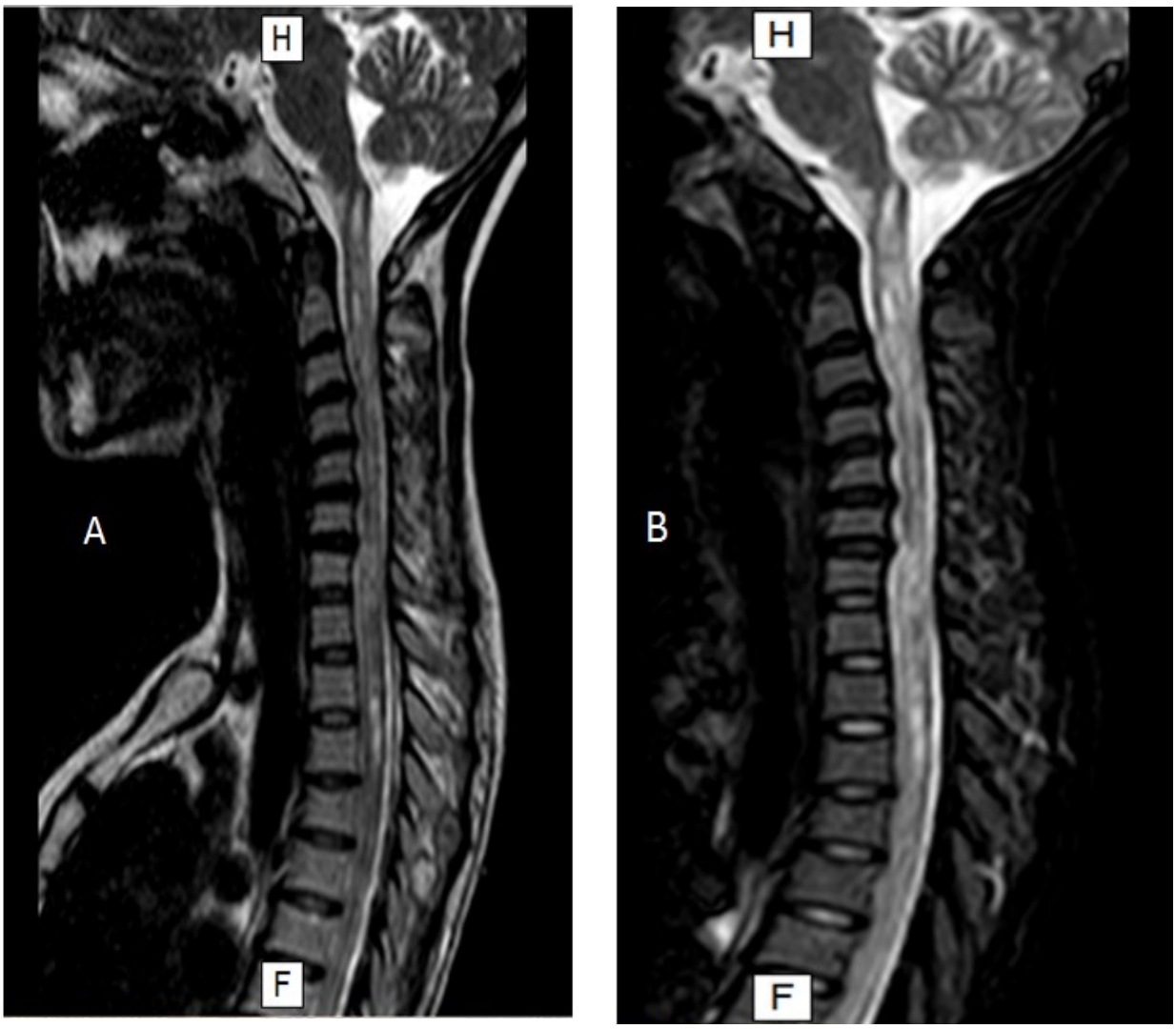

Figure 1. T2W (A) and STIR (B) imaging of the spinal cord from a 28years old Ethiopian women diagnosed to have NMO showing extensive long segment hyperintense lesions (foramen magnum - T6) with syrinx

She fulfilled all the required criteria for definitive diagnosis NMO and managed by multidisciplinary team. She was pulsed with high dose of intravenous Methylpredenisolone for 3-days and then oral prednisolone 1mg/kg daily with subsequent slow tapering. She was put on oral Azathioperin 100mg daily as a long term maintenance immunosupprsive therapy to reduce the risk of further relapse of the disease. In the course of 3-months follow up, she regained her vision of the right eye and also had marked improvement in muscle power of bilateral upper extremities from the initial muscle strength of 0/5 to 4/5 with deep tendon reflex of 2/4. Her condition on the lower extremities was the same(0/5, bilaterally) with hypereflexia and up going plantar reflex. There was also no change of urinary and fecal incontinences for which she was emotionally distressed and discontinued her follow up. It was not possible to restore the follow up despite multiple attempts over the phone.

Discussion

Over the last decade, there has been a tense debate on whether NMO is a distinct entity or a form of MS [1]. Current advances in the clinical manifestations, neuro -imaging features, serologic finding and pathological hallmarks have established that NMO is a distinct demyelinating disease of CNS. Therefore**,** it is important to NMO from MS early, because NMO has a more severe morbidity than MS and standard MS-modifying therapies may not be effective on NMO [5, 6]. The natural history of untreated NMO is significantly worse than that of MS with acquisition of residual disability from initial relapses in the majority of patients. Hence, NMO requires early recognition of cases for early initiation of treatment for acute attacks [6].

The clinical presentation of our patient with myelitis and optic neuritis, extensive long segment spinal cord lesion demonstrated by the spinal MRI, the absence of characteristic lesions of MS in the brain MRI and abnormal serologic titer of anti-AQ4 immunoglobulin fulfilled all the criteria for definitive diagnosis of NMO. She had also frequent pregnancy complications since from the first presumed attack of NMO where she sustained painless visual loss of left eye with no other symptomatic myelitis. There are reports of optic neuritis with asyptomatic myelitis [7] and the rate of optic neuritis with asymptomatic myelitis as initial presentation of NMO reaches as high as 42% [8].

Recently, there are reports of untoward effects of NMO on the pregnancy outcomes [4, 9-10]. AQP4 is expressed on placental syncytiotrophoblasts and the expression is highest around mid-gestation and decreases subsequently [10]. Placental dysfunction, therefore, is associated with miscarriage, intrauterine growth restriction, preeclampsia, and stillbirth, providing a potential mechanism for an increased frequency of these complications in NMO[9-10]. NMO has increased the risk of miscarriage independent of risk of concomitant autoimmunity such as antiphospholipid syndrome(APS) [4, 9]. The risk of preeclampsia is at a rate much higher than in obstetric controls in pregnancies after NMO onset [4, 9]. Therefore, anti-AQP-4 antibody positive NMO better explains the underlying cause of frequent miscarriage and also preeclampsia which our patient experienced. The treatment of NMO constitutes therapies to reverse the acute symptoms of NMO and also to prevent the future relapses. Acute NMO of initial or recurrent episodes are usually treated with pulse of high-dose intravenous methylprednisolone (05gm-1gm daily for three to five consecutive days) as first-line therapy, followed by an oral prednisolone with gradual tapering until Steroid sparing maintenance immunosuppressants take effect [6, 9]. For patients with NMO having severe cervical myelitis, or for those refractory to steroids, rescue therapy with therapeutic plasmapheresis (seven exchanges of approximately 55 ml/kg each, administered every other day for 14 days) should be considered with the possible mechanism of removing autoantibodies, immune complexes and inflammatory mediators from the plasma [11].Despite our patient was pulsed with high of dose methylprednisolone followed by oral prednisone combined with oral Azathioprine, in the course of three-months follow up, she remained incontinent and paraplegic.

She regained her right vision and had marked improvement of upper extremities. Limited availability and financial constraints hindered further therapies including plasmapheresis. She was frustrated by the incontinences as well as the residual weakness of the lower extremities which has kept her bedbound and further impoverished the living of the entire family. She went to her rural dwelling after the three-months of close follow up. However, she discontinued her follow-up altogether and no means of re-communicating her again. Therefore, while addressing the overt neurologic condition of such patients, equal attention should also be paid to the psychosocial and emotional components of patients with residual extremity weakness and incontinences.

In conclusion, this case highlights that in resource limited areas since the diagnosis of NMO as well as its management is challenging and time consuming, high index of clinical suspicion is important to reduce the repercussion of delayed initiation of therapy. The atypical presentation of NMO with obstetric complications should also warrant high index of suspicion. In resource poor counties, patients with neurologic squeal have multiple undisclosed burdens and hence require adequate psychosocial attention in order to optimize the medical therapy.

Declarations

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Authors' contributions: Both authors were involved in the management of this patient. MDM written the manuscript, all authors read and approved the final manuscript

Abbreviations: AFB:Acid Fast Bacillus, ANA: Anti-Neutrophilic Antibody, AQP4: Aquaporin 4, CSF-Cerebrospinal Fluid, MRI: Magnetic Resonance Imaging, MS: Multiple Sclerosis, NMO-Neuromyelitis Optica, PRVEP: Pattern Reversal Visual Evoked Potential, STIR: Short-TI Inversion Recovery, VDRL: Venereal Disease Research Laboratory

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