Neurology Current Research

ISSN: 2687-6981

Case Report

# Neuromyelitis Optica Spectrum Disorder in a Male African Teenager - A Case Report

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## Abstract

Neuromyelitis Optica Spectrum Disorder (NMOSD) is an autoimmune inflammatory demyelinating disease of the Central Nervous System (CNS) which manifests with clinical features of optic neuritis, transverse myelitis, and other neurologic manifestations that may mimic multiple sclerosis. The diagnosis of NMOSD can be made using clinical, immunological and characteristic radiological features.

We report an 18-year-old male with complaints of weakness of all limbs, impaired vision, urinary and fecal incontinence over a period of one month. Physical examination revealed left optic atrophy and quadriparesis with sensory impairment extending to T2 sensory level. Expanded Disability Status Scale (EDSS) was 9. Magnetic Resonance Imaging (MRI) of the cervical spine showed longitudinal extensive transversal myelitis while the brain MRI was normal. The serum aquaporin-4 antibody was positive. The cerebrospinal fluid examination was normal with negative oligoclonal band. A diagnosis of NMOSD was made and the patient was treated with combination of corticosteroids and immunosuppressants. He was also commenced on physiotherapy and his EDSS improved to 5.5.

**Keywords: Neuromyelitis optica spectrum disorder; Mimic multiple sclerosis; Optic neuritis**

## Introduction

Neuromyelitis Optica Spectrum Disorder (NMOSD) is an autoimmune inflammatory demyelinating disease of the Central Nervous System (CNS) which manifests with clinical features of optic neuritis, transverse myelitis, and other neurologic manifestations that may mimic multiple sclerosis [1-3].

The discovery of aquaporin-4 antibodies (AQP4-IgG) in 2004 led to the recognition that patients can have more limited forms of the disease such as recurrent transverse myelitis without optic neuritis or symptoms beyond the optic nerve and spinal cord which may include area postrema syndrome, resulting in the current nosology of NMOSDs [2,4].

The diagnosis of NMOSD can be made using core clinical features, immunological features (AQP4-IgG) and characteristic radiological findings. Early differential diagnosis of NMOSD from Multiple Sclerosis (MS), Acute Disseminated Encephalomyelitis (ADEM) and other systemic autoimmune disorders is very important since NMOSD has a poor prognosis and often requires immunosuppressive treatment [5].

## Case Presentation

An 18-year-old male was admitted to the hospital with complaints of weakness of both upper and lower limbs a month prior to presentation. Weakness was gradual in onset and progressively got worse. It initially started on the right lower limb, and then later involved the left lower limb. Subsequently, both upper limbs got involved simultaneously.

There was no prior diarrhea, fever, headache or back pain. However, he noticed blurring of vision on the left eye about two weeks prior to onset of symptoms. There were no episodes of vomiting.

He noticed he had developed paresthesia of both lower limbs. He started having urinary and fecal incontinence about a week prior to presentation. These symptoms were also of gradual onset and progressively worsened since onset. There were no similar episodes in the past. There was no family history of similar illness.

There was no significant finding on general physical examination. On neurological examination he was conscious and alert. There were no signs of meningeal irritation. He had relative afferent pupillary defect of the left eye. Fundoscopy revealed optic atrophy of the left eye.

Muscle tone and deep tendon reflexes were reduced in all limbs. Muscle strength using Medical Research Council's (MRC) scale was grade 3 on the right upper limb, grade 1 on the left upper limb and grade 0 on both lower limbs. Plantar response was absent bilaterally. Light touch, pain, temperature, proprioception and sense of vibration were all impaired extending to T2 sensory level. The score of expanded disability status scale was 9.

Our working diagnosis at this time was NMOSD while differential diagnoses were acute idiopathic transverse myelitis, multiple sclerosis and systemic lupus erythematosus (Figure 1).

Sagittal T2 weighted imaging of the cervical spine revealed a longitudinal hyperintensity within the substance of the spinal cord which extends from C3 to C7 spinal cord levels.

Overall features of the spinal MRI done were in keeping with longitudinal extensive transverse myelitis involving spinal cord levels

**Citation:** Ozomma S, Philip-Ephraim E, Williams U, Oparah S, Idika K, Ohio E. Neuromyelitis Optica Spectrum Disorder in a Male African Teenager - A Case Report. Neurol Curr Res. 2021;2(1):1009.



**Publisher Name**: Medtext Publications LLC

**Manuscript compiled:** Jun 09th, 2021

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C3-C7. Brain MRI revealed no pathological finding.

Cerebrospinal Fluid Analysis (CSF) demonstrated normal cell count, normal glucose/protein, and negative oligoclonal bands.

Results of antibodies to aquaporin-4 revealed positive titre: Aquaporin 4 antibodies IgG 1:100 (Reference range 1:<10). Autoimmune antinuclear antibodies including Antinuclear Antibody (ANA) and Antidouble Stranded DNA (Anti-dsDNA) antibody analysis were normal.

Viral markers for Human Immunodeficiency Virus (HIV), Hepatitis C Virus (HCV) and Hepatitis B Virus (HBV) were negative. Venereal Disease Research Laboratory (VDRL) test was non-reactive. Urine Lipoarabinomannan (LAM) test was also negative.

Eventually, a diagnosis of NMOSD was made using the updated diagnostic criteria for NMOSD which was published by the International Panel for NMO Diagnosis in 2015.

Patient was initially placed on intravenous methylprednisolone 500 mg daily for 5 days. He was then continued on oral prednisolone 30 mg daily and was subsequently placed on oral azathioprine 50 mg twice daily to prevent relapse.

He was commenced on physiotherapy as well. His muscle strength made remarkable improvement to MRC grade 4 in all the limbs and the expanded disability status scale improved to a score of 5.5. This was also accompanied by resolution of urinary and fecal incontinence. He was then discharged home to be seen as an outpatient on follow up visits.

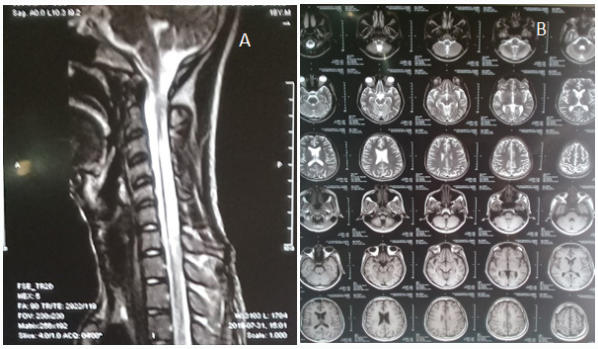


**Figure 1**: Spinal (A) and cranial (B) Magnetic Resonance Imaging (MRI) while on admission.

## Discussion

NMOSD is a rare autoimmune inflammatory disease that causes severe demyelination, especially in the optic nerve and spinal cord with typical clinical manifestations of acute optic neuritis and transverse myelitis [3].

The term Devic disease arose from a report by Devic and his student Gault who described the autopsy findings of a patient who died from recurrent episodes of concurrent transverse myelitis and optic neuritis [6]. It was later coined Neuromyelitis Optica (NMO) on account of the most common clinical manifestations associated with it, namely optic neuritis and transverse myelitis [3]. The discovery of AQP4-IgG led to the recognition that patients can have more limited forms of the disease (eg, recurrent transverse myelitis without optic neuritis) or symptoms beyond the optic nerve and spinal cord (eg, area postrema syndrome), resulting in the current terminology of NMOSD [2,4].

In general, the prevalence of NMOSD seems to be higher among populations of African descent when compared to other populations which is in contrast to the prevalence of multiple sclerosis [7,8]. However, NMOSD remains a rare disease, even in Africa [8,9]. This could be as a result of diagnostic difficulties encountered in most of the developing countries in Africa [10]. A study by Osuntokun, which reviewed hospital admissions at the University College Hospital Ibadan, Nigeria between 1957 and 1967, reported 95 cases of NMO with an estimated prevalence of 43 per 100,000 hospital cases [9]. The female to male ratio of AQP4-IgG positive NMOSD is 9:1 and the median age of onset is in the fourth decade [1]. Interestingly, this patient was male in his second decade of life.

The cardinal clinical features of NMOSD include longitudinally extensive transverse myelitis involving three or more vertebral segments; often followed by tonic spasms and occasionally accompanied by pain or pruritus, optic neuritis often severe (may be bilateral) and episodes of intractable nausea, vomiting or hiccups from area postrema involvement. This patient had longitudinal extensive transverse myelitis and unilateral optic atrophy. Other clinical features of NMOSD include narcolepsy, Syndrome of Inappropriate Secretion of Antidiuretic Hormone (SIADH), other hypothalamic presentations (eg, anorexia), acute myopathy with hyperCKemia, brainstem syndromes (eg, ophthalmoplegia, hearing loss, opsoclonus/myoclonus), myeloradiculitis, encephalopathy (Posterior reversible encephalopathy syndrome-like; Acute disseminated encephalomyelitis-like), cognitive dysfunction and hydrocephalus [11].

AQP4-IgG is a serum biomarker found in approximately 80% of patients with NMOSD while a proportion of the remaining 20% may be accounted for by another serum antibody biomarker, Myelin oligodendrocyte glycoprotein (MOG-IgG) [12].

This patient tested positive to AQP4-IgG antibody which strengthened the diagnosis of NMOSD. We also screen for possible coexisting autoimmunity and parainfections. In this patient, autoimmune antibodies including ANA and anti-dsDNA analysis were normal. Viral markers for HIV, HCV and HBV were negative. VDRL test was non-reactive and urine LAM test was also negative. The negative oligoclonal bands on CSF in addition to the clinical findings made the possible diagnosis of multiple sclerosis to be very slim.

Systemic autoimmune disorders such as systemic lupus erythematosus, Sjögren syndrome, and antiphospholipid antibody syndrome or their autoantibody biomarkers frequently coexist with NMOSD, and could be a marker of poorer prognosis [13]. A patient with any of these autoimmune diseases with at least one cardinal feature of NMOSD should prompt AQP4-IgG testing [13].

The MRI of the spinal cord in NMOSD show typical features of Longitudinal Extensive Transversal Myelitis (LETM), a lesion that extends over three or more segments of the adjacent spinal cord and are central on axial view, with ring or variable enhancement [14]. Brain MRI features may vary from normal or nonspecific features to lesions in the area postrema, perithird/fourth ventricle, splenium, diffuse corpus callosum, pencilthin ependymal or cloud enhancement [15]. MRI of the optic nerve may reveal bilateral enhancement of more than 50% of optic nerve with more of posterior optic pathway involvement [16]. In this patient, an MRI scan of the spinal cord

showed features of myelitis involving C3-C7 while a brain MRI examination was normal. Longitudinally extensive spinal cord lesions are not specific for NMOSD. They have been demonstrated in patients with other autoimmune or inflammatory diseases, including SLE, Sjögren's syndrome, neuro-Behçet disease, parainfectious disorders and multiple sclerosis [17]. It was therefore necessary to assay for viral and autoimmune markers which were negative for this patient. NMOSD can be life threatening if the lesion extends to the cervical spinal cord and brain stem because it has the potential of causing respiratory failure.

The updated diagnostic criteria for NMOSD by the International Panel for NMO Diagnosis stratifies the diagnosis of NMOSD by those with AQP4-IgG and those without AQP4-IgG (including those for whom testing is unavailable). The criteria use core clinical characteristics focusing on the three cardinal manifestations of optic neuritis, myelitis, and an area postrema syndrome, in addition to less common manifestations of other brainstem attacks, diencephalic episodes, and cerebral episodes. The presence of one of the core clinical characteristics in addition to AQP4-IgG seropositivity and exclusion of other aetiologies allows the diagnosis of NMOSD with AQP4-IgG to be made. The criteria for patients who are AQP4-IgG seronegative requires additional characteristic radiologic features to be present to help avoid misdiagnosis. According to the criteria this patient had NMOSD with AQP4-IgG based on his AQP4-IgG seropositivity with the presence of two cardinal features, optic neuritis and longitudinal extensive transverse myelitis which was confirmed radiologically [2].

NMOSD attacks are mainly treated with corticosteroids, plasma exchange and intravenous immunoglobulin while maintenance therapy for relapse prevention include azathioprine, methotrexate, mycophenolate mofetil, rituximab, cyclophosphamide and tocilizumab [18-20]. Plasma exchange was not required for this patient as he responded well to corticosteroid therapy and was subsequently placed on maintenance therapy. Choice of maintenance therapy may depend on local availability, cost, patient preference, and duration of concomitant oral steroids needed while the immunosuppressant takes effect [1]. Azathioprine was used for this patient on the basis of availability and affordability. While on azathioprine the patient tolerated the medication without serious side effects and care givers were able to sustain procurement of the medications despite being in a resource poor setting where health insurance was not universal.

Long term rehabilitation such as physiotherapy is necessary. This played a huge role in the recovery of our patient's motor deficits.

## Conclusion

This case of NMOSD in a male African teenager highlights the need to create more awareness on the presence of this disorder in our society. The presence of any of the cardinal features of NMOSD in a patient should raise a high index of suspicion which should prompt adequate screening for the disease. Finally, there is a need to implement policies to strengthen and encourage more research on demyelinating disorders such as NMOSD in Sub-Saharan Africa.

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