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CASE REPORT

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Neuromyelitis optica spectrum disorder co-existing with antiphospholipid syndrome: A case report

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Key clinical message

Neuromyelitis optica spectrum disorder is an autoimmune disease, rarely presents with antiphospholipid syndrome. Diagnosis and management of NMOSD are challenging in the background of diverse presentations, especially in resource-limited settings.

Abstract

Neuromyelitis optica spectrum disorder (NMOSD) is a progressive demyelinating autoimmune condition resulting from the autoantibodies produced against aquaporin-4 (AQP-4) proteins which are widely distributed in astrocytes in the nervous system. In the setting of NMOSD, it is very crucial to consider other autoimmune diseases as differential diagnoses or co-occurrences due to the diversity of symptoms. NMOSD co-exists with other autoimmune diseases such as myasthenia gravis, thyroid disease, ankylosing spondylitis, pernicious anemia, thrombotic thrombocytopenic purpura, ulcerative colitis, and systemic lupus erythematosus. Few cases of antiphospholipid syndrome co-existing with NMOSD have been reported. In resource-limited settings, the published data are scarce, and therefore, autoimmune diseases are poorly studied. Therefore, late diagnosis and delayed treatment initiation pose long-term sequelae and hence poor prognosis. Here, we present a case of an African woman in her early 40s presenting with bilateral progressive loss of vision, transverse myelitis, extensive longitudinal hyperintense T2 cervical lesion, and AQP-4 autoantibody keeping with NMOSD. The co-existence of antiphospholipid syndrome, in this case, was supported by a history of recurrent pregnancy loss and positive antiphospholipid antibodies. This case underscores the importance of individualized-based medicine, especially in resource-limited settings.

KEYWORDS

neuromyelitis optica spectrum disorder, optic neuritis, recurrent pregnancy losses, secondary antiphospholipid syndrome

1 | INTRODUCTION

Neuromyelitis optica spectrum disorder is previously known as Devic's syndrome.[1–3] NMOSD is a progressive demyelinating autoimmune condition resulting from immunoglobulins subtype G1 produced against water channel protein aquaporin (AQP-4), which usually affects the cranial nerves, spinal cord, and central nervous system.[3–5] Pathophysiology of NMOSD remains elusive, but mainly is due to the production of autoantibodies directed against peripheral and central nervous systems.[6–8] These autoantibodies penetrate the blood–brain barrier causing attacks and destruction of astrocytes resulting in chronic inflammation and demyelination. Clinically, it is indistinguishable from multiple sclerosis and was thought to be a subtype of multiple sclerosis.[1,4] NMOSD is common during reproductive age, affecting more females than males.[6,7,9] The most common manifestations includes optic neuritis, longitudinally extensive transverse myelitis, area postrema syndrome, and acute brainstem syndrome with normal cognitive functions.[3,6,7,10] It's progression takes weeks to years as compared to other demyelinating diseases. NMOSD is an autoimmune disease and, therefore, sometimes presents with features in keeping with other autoimmune diseases like Lupus.[9,11,12] Despite being an autoimmune disease, rarely presents with antiphospholipid syndrome.

The 2015 revised international consensus criteria base the diagnosis of NMOSD on the presence of core clinical characteristics and serum AQP-4 autoantibodies.[11,13–15] Besides, other alternative diagnoses such as multiple sclerosis, Gullaine–barre syndrome, and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) should be excluded. The diversity of presentations and scarcity of published data on NMOSD especially from resource-limited settings poses diagnostic and management challenges. This highlights a need for clinicians to have heightened suspicion of NMOSD in diversity of symptoms especially in background of autoimmunity. Here, we present a case of young African woman in her early 40's presented with progressive visual loss, quadriparesis, double incontinences, and consecutive fetal loss. Ultimately, the pathological diagnosis of NMOSD with secondary antiphospholipid syndrome confirmed after serum AQP-4 and antiphospholipid antibodies (APLA) seropositivity.

2 | CASE HISTORY/ EXAMINATION

An African female in her early 40s presented with progressive visual loss for about 4 years. The visual loss started gradually on right eye then progressed to involve the left eye. It was accompanied with eye pain that worsened with eye movement and throbbing bitemporal headache. There was no history of fever, seizures, or altered mental status. She was diagnosed with idiopathic intracranial hypertension (IIH) despite normal initial MRI findings and normal cerebral spinal fluid opening pressure. There were no fundoscopic results that were documented. She was managed surgically with a ventriculoperitoneal shunt following poor response to acetazolamide.

A year later following surgical management for IIH, she reported that her lower and upper extremities were becoming numb to touch. Shortly after, she noted difficulties with standing from a sitting position, climbing stairs, sitting without support, holding objects, writing, buttoning her shirt, and combing hair. Later on, she noticed difficulty with bladder and bowel control. Besides, there was no history of joint pain, weight loss, skin changes, or preceding acute illness with either respiratory or gastrointestinal symptoms. Her past medical history was notable for hypertension for 6 years, which was controlled by medications. However, her obstetric history was remarkable for recurrent pregnancy losses below 24 weeks of gestational age totaling an astonishing 11 unexplained abortions, juxtaposed against the joy of one living child making it a bad obstetric history. Despite the obstetric turmoil, her menstrual history remains unremarkable. There was no reported history of pre-eclampsia or eclampsia, venous or arterial thrombosis. None of her family members have had the same presentation.

On examination, she had normal higher center without signs of meningism. Cranial nerves were normal except for optic nerve. On comprehensive ocular examination, the ocular motility was normal in all directions of gaze, there was decreased visual acuity with light perception in both eyes and intraocular pressures were normal, 17 mmHg right eye and 18 mmHg left eye. Both pupils were dilated and not reactive to light. On fundoscopy examination, there was generalized optic disc pallor with peripapillary atrophy bilaterally. Macula appeared normal, retinal arteries were mildly attenuated, and the retina background was normal (Figure 1). Motor system examination revealed normal bulkiness on both extremities; muscles strength was 1/5 for both the lower extremities and 2/5 for both upper limbs. The deep tendon reflexes were brisk at the lower and upper extremities with bilateral extensor plantar response. Sensory examination revealed decreased pinprick sensation, fine touch, temperature, and vibration below cervical segment level 4 (C_4) and otherwise normal spine examination. Other systemic examinations' findings were normal.

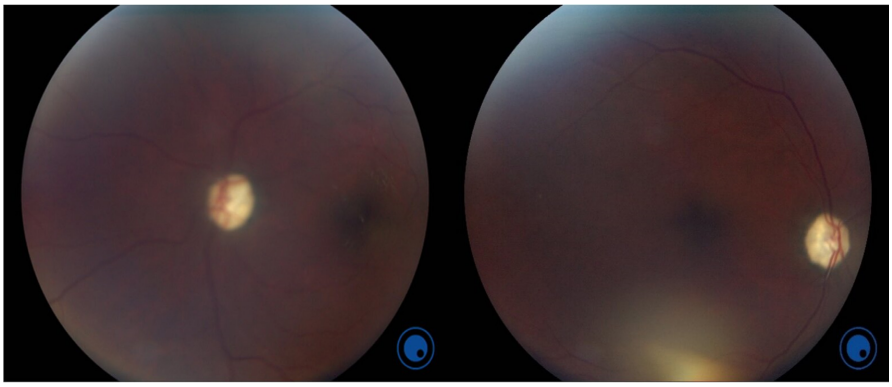

FIGURE 1 Optic neuritis fundus showing bilateral optic atrophy with normal retina background.

3 | DIFFERENTIAL DIAGNOSES, INVESTIGATIONS, AND TREATMENT

Following the patient's clinical presentations, the differential diagnoses included neuromyelitis optica (NMO), multiple sclerosis with clinically isolated syndrome (CIS), myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), idiopathic intracranial hypertension (IIH), systemic lupus erythematosus (SLE), Sjogren syndrome, and acute disseminated encephalomyelitis (ADEM). The index case met the criteria for NMOSD due to presence of progressive visual loss with fundoscopic findings keeping with bilateral optic neuritis, features suggestive of transverse myelitis (spastic quadriparesis, C_4 sensory level, fecal and urine incontinence, and upgoing plantar reflex), MRI findings demonstrating longitudinal extensive cervical spinal cord lesion with hyperintense signal in T2 and positive antibody against AQP-4 protein.[16] Co-occurrence of NMOSD with antiphospholipid syndrome in this case was supported by a history of recurrent pregnancy loss and positive antiphospholipid antibodies. Upon initial evaluation, IIH was considered as the cause of progressive visual loss and headache.[17] However, the likelihood was downgraded following unfavorable response to treatment (medical and surgical) and onset of new symptoms suggestive of transverse myelitis that were further supported by MRI findings. Likewise, multiple sclerosis was less likely considering bilateral visual loss in this case, extensive longitudinal plaque of demyelination in cervical spine extending more than three vertebral segments and positive AQP-4 autoantibody. The presence of bilateral optic atrophy and transverse myelitis was suggestive of MOGAD; however, the absence of cortical symptoms and negative myelin oligodendrocytes glycoprotein IgG antibody ruled out MOGAD[18] in the index case. Although ADEM presents with visual loss and transverse myelitis as the index case, it was ruled out because most patients with ADEM are male, it is quite common among the pediatric population than the latter, and the most common symptom of ADEM is encephalopathy that manifests as an alteration in level of consciousness. Moreover, patients with ADEM experience preceding infection or vaccination within 4 weeks before the onset of neurological symptoms.[19] Rheumatological conditions like systemic lupus erythematosus, neuro-Behcet disease (NBD), and Sjogren's syndrome were considered as potential causes of transverse myelitis, and optic neuritis although is uncommon. The absence of mucocutaneous manifestations, cortical symptoms like a seizure or cognitive impairment, and low titer of specific autoantibodies including ANA, dsDNA, anti-SSA, and anti-SSB reduced the likelihood of connective tissue diseases.[20–22] Although neurosyphilis uncommonly present with optic neuritis and transverse myelitis, it was considered an infectious cause of patient presentations; however, serology results came out negative.[16]

Further test revealed cerebral spinal fluid (CSF) opening pressure of 13 cm of H_2O and analysis showed moderate CSF pleocytosis of eight cells per millimeter with other biochemical values within normal limits; no atypical cells detected. Due to its unavailability, analysis of CSF for oligoclonal bands and AQP4 level were not performed. However, analysis of serum AQP-4 antibodies level showed seropositivity (titer, 1:320) (Table 1). MRI of the spine cord demonstrated longitudinally extensive spinal cord lesion involving the central cord with hyperintense signals in T2 and FAIR (Figure 2). While the MRI brain (FLAIR/T2 signals) demonstrated multiple abnormal rather-defined patches of hyperintense signals involving the subcortical and periventricular regions (Figure 3).

A 7-day course intravenous methylprednisolone 1 g once daily was provided before she was maintained on mycophenolate mofetil (MMF) 1 g twice daily, warfarin 10 mg daily and physical rehabilitation. Rituximab was not an option because is expensive and currently not incorporated in recent local guidelines for the treatment of NMOSD especially for insurance beneficiaries in Tanzania.

She has now recovered sensations in her lower limbs, with the exception of motor and visual symptoms.

TABLE 1 Laboratory test results.

S/no.	Test	Result	Reference value
1.	Serum AQP-4 IgG	1:320	
2.	Serum MOG-IgG	1:6	<1:10
3.	Anti-Cardiolipin IgG by ELISA	31 U/mL	<10
4.	Anti-Cardiolipin IgM by ELISA	35.6 U/mL	<10
5.	Lupus anticoagulant Antibody by ELISA	Positive	
6.	Rapid plasmin reagin (RPR)	Negative	
7.	C-reactive protein (CRP)	6.9	0.0–1.0 mg/dL
8.	Human immunodeficiency virus (HIV)	Non-reactive	
9.	Antinuclear antibodies (ANA)	1:57	<1:80
10.	Anti-Ds DNA abs and Anti-Smith abs	Negative	
11.	Anti SS-A and Anti SS-B antibody	3.2 U/mL	<7.0

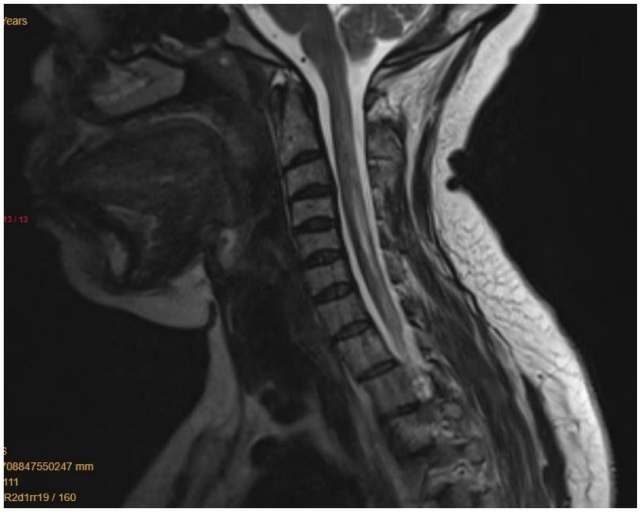

FIGURE 2 (Sagittal T2): The cervical cord demonstrates a longitudinally extensive spinal cord lesion, with hyper-intense signals in T2 and FLAIR images. The central cord is involved. No hemorrhage.

4 | DISCUSSION

NMOSD is previously known as Devic's syndrome and is a progressive inflammatory demyelinating autoimmune condition that is characterized by the presence of autoantibodies, particularly IgG_1, against the water channel protein AQP-4.[1–3] Initially, NMOSD was classified as a subtype of multiple sclerosis due to its clinical presentations.[3,5,7,13] The central nervous system is mostly affected and usually presents with features suggestive of chronic inflammation leading to demyelination of neurons due to invasion and destruction of astrocytes by anti-NMO antibodies.[2,3,11] The course of NMOSD is progressive over weeks to years as compared to other demyelinating diseases and can be monophasic or relapsing–remitting patterns.[4,7] In 2015, the international revised consensus diagnostic criteria were recommended for the diagnosis of NMOSD.[3,6,23] These include any of the core clinical characteristics; optic neuritis, longitudinally extensive transverse myelitis of ≥3 spine segments, area postrema syndrome, symptomatic narcolepsy, or acute brainstem syndrome without cognitive impairment and positive serum AQP-4 autoantibodies.[6,7,11] Besides, few patients with NMOSD may be seronegative accounting for 10 to 20% but still present with other core clinical characteristics.[2,24,25]

About 20%–30% of NMOSD cases have a variety of symptoms that resemble those of other autoimmune disorders.[12,23] Other autoimmune diseases that have been reported to coexist with NMOSD include myasthenia gravis, thyroid disease, ankylosing spondylitis, pernicious anemia, ulcerative colitis, systemic lupus erythematosus, and thrombotic thrombocytopenic purpura.[26–28] The development of autoantibodies as a result of complement pathways, activation of interleukins, particularly IL-6, and molecular mimicry of autoreactive B cells represent the hallmarks of the co-occurrence of disease.[2,27,28] NMOSD occurs as a result of these autoantibodies invading and destroying the nervous system's astrocytes.[23,29] In this instance, an African female in her early 40s qualified criteria for NMOSD due to a history of progressive loss of vision, transverse myelitis, and positive autoantibody against AQP-4. The co-existence with the antiphospholipid syndrome, in this case, was supported by a history of recurrent pregnancy loss and antiphospholipid antibody seropositivity.[27] The index case correlated with a few published cases regarding their pathogenic domains, clinical presentations, diagnostic criteria, and management approaches.[12,30–32] Despite the rarity of the disease and scarcity of published data in our settings, it was very challenging to diagnose and manage NMOSD, especially when co-existing with other autoimmune conditions. This case highlighted the importance of broadening

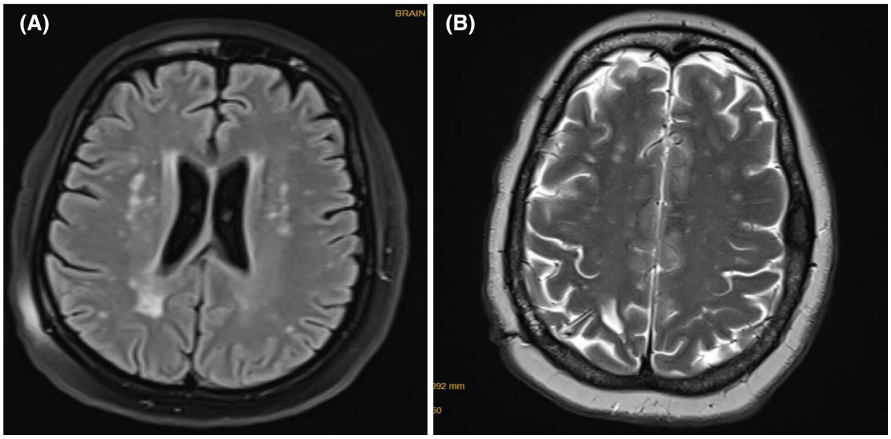

FIGURE 3 (A, B) (FLAIR/T2 signals): Multiple abnormal rather-defined patches/foci of hyperintense signals in T2 and FLAIR images are seen involving the subcortical and periventricular regions.

differentials among clinicians in any case with a component of autoimmunity.

5 | CONCLUSION

This case highlights the diagnostic complexity of neuromyelitis optica spectrum disorder (NMOSD), emphasizing the importance of individualized-based medicine in uncovering elusive diagnoses and guiding effective management strategies especially in resource-limited settings.

AUTHOR CONTRIBUTIONS

Gidion Edwin: Conceptualization; writing – original draft; writing – review and editing. **Francis Msagati:** Conceptualization; writing – original draft; writing – review and editing. **Francisca Komanya:** Supervision; writing – review and editing. **Baraka Alphonce:** Supervision; writing – review and editing. **John Meda:** Supervision; writing – review and editing. **Azan Nyundo:** Supervision; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare there is no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this case report are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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