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A Case Report of Neuromyelitis Optica Spectrum Disorder (NMOSD) Treatment in Resource-Limited Setup: An Ethiopian Experience

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ABSTRACT

MOSD is a rare and disabling immune-mediated inflammatory Astrocytopathic disease characterized by demyelination and axonal destruction, typically involving the spinal cord and the optic nerve. Here we present a case report of a 53-year-old female patient who had a pertinent history of treatment for optic neuritis a few months back, currently diagnosed with Neuromyelitis Optica after she presented with a three-week history of weakness of lower extremity, headache, and neuropathic pain. She was pulsed with methylprednisolone and started on azathioprine, which significantly improved her clinical condition. When patients with optic neuritis and transverse myelitis occur, a high index of suspicion for NMOSD is essential. Establishing a diagnosis based on clinical and MRI findings is crucial for initiating therapy quickly, halting more harm, and avoiding a delay in diagnosis. Our experience treating our patient shows that Azathioprine is still a practical choice in resource-limited setups.

1 | Introduction

NMOSD is a rare and disabling immune-mediated disorder of the nervous system characterized by inflammation and demyelination with axonal damage, usually involving the spinal cord and the optic nerve [1]. The first description of NMOSD was reported by Eugene Devic, who described a new disease that was characterized by rapidly sequential acute myelitis and optic neuritis with severe disability, and his student Fernand Gault, who reviewed literature and gave a clinicopathologic analysis of the case [2]. The autoimmune-derived inflammatory process involving the spinal cord segments and optic nerves is associated with loss of axons, lymphocytic proliferation, usually around vessels, and necrosis of gray and white matter. B cell-derived NMOSD-specific autoantibodies that target aquaporin called AQP4 water channel protein, a protein that is abundantly seen in astrocytes found in the spinal cord and periventricular regions of the brain, resulting in activation of inflammatory cells resulting in the damage mentioned above to neuronal cells [3, 4].

The prevalence of NMO varies among different population groups and is affected by factors such as ethnicity, geography, and sex. The highest reported is in Afro Caribbean population [5]. Generally, higher incidence and prevalence are seen in African ethnicity compared to white ethnicity. To our knowledge there are no large-scale studies that describe the epidemiology of NMO in Ethiopia. A systematic review published in 2021 on Neuromyelitis Optica Spectrum Disorders in Africa included reports from 10 African countries. The total number of patients reported in this review was 410, with almost half from North Africa. The least

Abbreviation: NMOSD, Neuromyelitis Optica spectrum Disease.

Summary

- A high suspicion index is required to diagnose NMO, and Azathioprine can still be used as an effective treatment modality.

number of patients were from East Africa, including Ethiopia and Sudan, representing only 9% of the total patients. This review indicated that middle-aged women were most commonly affected, and one-third of patients had at least one relapse, although the outcomes for most patients were unknown [5]. This highlights the importance of large-scale studies to understand the local disease prevalence and clinical presentations.

The disease also appears to have a female predominance and is commonly seen in middle-aged individuals [6]. The typical clinical feature of NMOSD is the presence of a relapsing course of variable degrees of rapidly progressive optic neuritis and transverse myelitis, resulting in severe complications like blindness, motor and sensory impairment, and bladder dysfunction [3, 7].

The International consensus diagnostic criteria for Neuromyelitis Optica spectrum disorders, which mainly includes core clinical characteristics, MRI features, AQP4 IgG level, and exclusion of other alternative diagnoses, can be used to make the diagnosis of NMOSD in the presence or absence of AQP4- IgG status [8].

Here, we present a case report of a patient with a clinical diagnosis of NMOSD who had a significant treatment response to azathioprine therapy after steroid use.

2 | Case History

Initial Presentation: A53-year-old right-handed female patient who is a known hypothyroidism patient for the last 25years on levothyroxine 100microgram PO daily, a known type II DM patient for the previous 5years on glibenclamide 2.5mg PO daily and ertugliflozin 15mg PO daily, a known Megaloblastic anemia patient for the last 1year on cyanocobalamin 1mg IM monthly and Folic acid 5mg PO daily. Currently, she presented with 3weeks history of progressive lower extremity weakness, which initially started from her left leg and then progressed to involve her right leg within 5days of the onset of the illness. She also complained of band-like tightening sensation over her mid-torso, a burning pain and tingling sensation, and increased sensitivity to innocuous stimuli more pronounced in her left lower leg. She has no signs and symptoms of bladder dysfunction. Eighteen months back, she was diagnosed with optic neuritis after she experienced headaches and progressive painful visual loss of her right eye over 3months. Brain MRI was done at the time and showed right pre-chiasmatic optic nerve swelling and contrast enhancement, and ophthalmic evaluation revealed no vision on the right, for which she was admitted and was pulsed with methylprednisolone for 5days and discharged with prednisolone 60mg PO daily to be tapered off. She was then able to differentiate light and darkness post-treatment and had a follow-up at our neurology clinic. Otherwise, she has no history of loss of consciousness, trauma, difficulty of speech, dysphagia, behavioral change, or memory loss.

On Physical examination, all vital signs were within the normal range. Cardiovascular, respiratory, and abdominal physical examinations were all unremarkable. Neurologic Examination Summary: See Table 1.

3 | Methods

3.1 | Differential Diagnosis

Guillain-Barre syndrome, Idiopathic transverse myelitis and multiple sclerosis were the major differential diagnosis initially considered. After through clinical examination, typical imaging findings and AQP4 level determination, the diagnosis of NMO was done. Investigation Summary: See Table 2 *Spinal MRI*—see Figure 1A–C.

3.2 | Treatment

Our patient received treatment consisting of daily intravenous administration of Methylprednisolone at a dosage of 1g

TABLE 1 | Neurologic examination summary.

Glasgow Coma Scale: 15 (E 4 V 4 M 6)				
Mini-Mental Status examination: 25				
Cranial nerves	Pupils are mid-sized and reactive bilaterally			
	Visual acuity: Light perception on the right eye			
	All other cranial nerves are intact			
Motor examination	Symmetric muscle bulk, no induced or spontaneous fasciculation			
	Right upper	Right lower	Left Upper	Left Lower
Power	5/5	*1/5*	5/5	*1/5*
Tone	Normotonic	Hypotonic	Normotonic	Hypotonic
Reflexes	2/4	*1/4*	2/4	*1/4*

TABLE 2 | Investigation summary.

	29/12/21GC	15/4/22 GC	21/4/22 GC	3/5/22 GC
WBC	3000 cells/mm^3	5600 cells/mm^3	2400 cells/mm^3	6600 cells/mm^3
Neutrophil (%)	50%	86.6%	92.6%	78.6%
Hemoglobin(gm/dL)	15.8	11.6	11.7	13
Platelet cell/mm^3	122,000	141,000	170,000	141,000
Serum Electrolyte (K+/Na +/Cl-) mEq/L		2.69/139.3/110	4.58/145/116.6	3.37/139.2/108
Cr/Urea (mg/dl)		0.6/57		0.8/42
Liver enzymes U/L (AST/ALT/ALP)		29/15/61		43/16/91
Thyroid function	0.1 pg/dL	3.32 pg/dL		
Tests	0.21 ng/dL	1.34 ng/dL		
(FT3/FT4/TSH)	15 mU/mL	3.4 mU/L		
HgbA1C		6.5%		
Serum Vit B12 level	936 IU			

Autoimmune markers
- ANA qualitatively: Positive
- Anti-dsDNA Ab: Negative
- Anti-smith Ab: Negative
- C4 and C5 Complement level: Normal, Anti-Ro/La: Negative
- Anti Aquaporin-4- Positive (1:10)

Imaging
- NCS: sensory and motor peripheral axonal neuropathy; radiculopathy cannot be ruled out
- Chest X-ray—normal
- Echocardiography: Mild concentric LVH with ejection fraction of 60%
- Abdominal ultrasound: Unremarkable
- Brain MRI: Right pre-chiasmatic optic nerve swelling and contrast enhancement suggestive of optic neuritis
- Spinal MRI image: Figure 1A–C (Longitudinally extensive transverse myelitis extending from the C7 level and involving the entire thoracic cord up to the distal cord level).

for 5 days. This was followed by oral prednisolone, starting at 60 mg per day with gradual tapering and discontinuation. Additionally, Azathioprine was administered orally at a dose of 75 mg per day, which was gradually increased to 150 mg per day.

3.3 | Conclusion and Result

The findings of our case report and other case reports originating from Ethiopia emphasize the importance of considering the diagnosis of NMOD for patients who meet the diagnostic criteria outlined by the 2015 International Panel for NMOSD. The diagnosis and management of NMOSD pose significant challenges within resource-limited settings. Azathioprine is an effective therapeutic option, thus serving as an alternative treatment choice for NMOSD patients residing in countries with limited access to immunotherapies such as inebilizumab, eculizumab, rituximab, and satralizumab, which are approved for NMOSD treatment. In our country, most these drugs are not readily available making optimal treatment more challenging. Hence, it is imperative to keep a high degree of clinical suspicion to avoid the detrimental effects of delayed diagnosis and treatment. Our patient 2 months after being discharged was able to walk with the support of a cane. By the fourth month of follow-up at our neurology clinic, the patient could walk without support. On her last followup, the patient was taking Azathioprine 150 mg per day and is in remission, except for a visual impairment in the right eye resulting from the initial attack. She was monitored for a total of 1 year after her initial diagnosis and did not visit our hospital with any complaints until the submission of this manuscript.

4 | Discussion

NMOSD is characterized by two primary clinical manifestations: optic neuritis and transverse myelitis. These manifestations can either co-occur or be separated by several years. Patients experiencing optic neuritis may present with a range of vision loss severity, often accompanied by eye pain that worsens during eye movement. On the other hand, individuals with transverse myelitis typically exhibit a symmetric weakness of the limbs (paraparesis or quadriparesis), bladder dysfunction, and sensory impairment below the level of the affected spinal cord [9]. Additional clinical features that can be observed in NMOSD include encephalopathy, fulminant cerebral demyelination, hypothalamic dysfunction, area postrema syndrome, and PRES [9, 10].

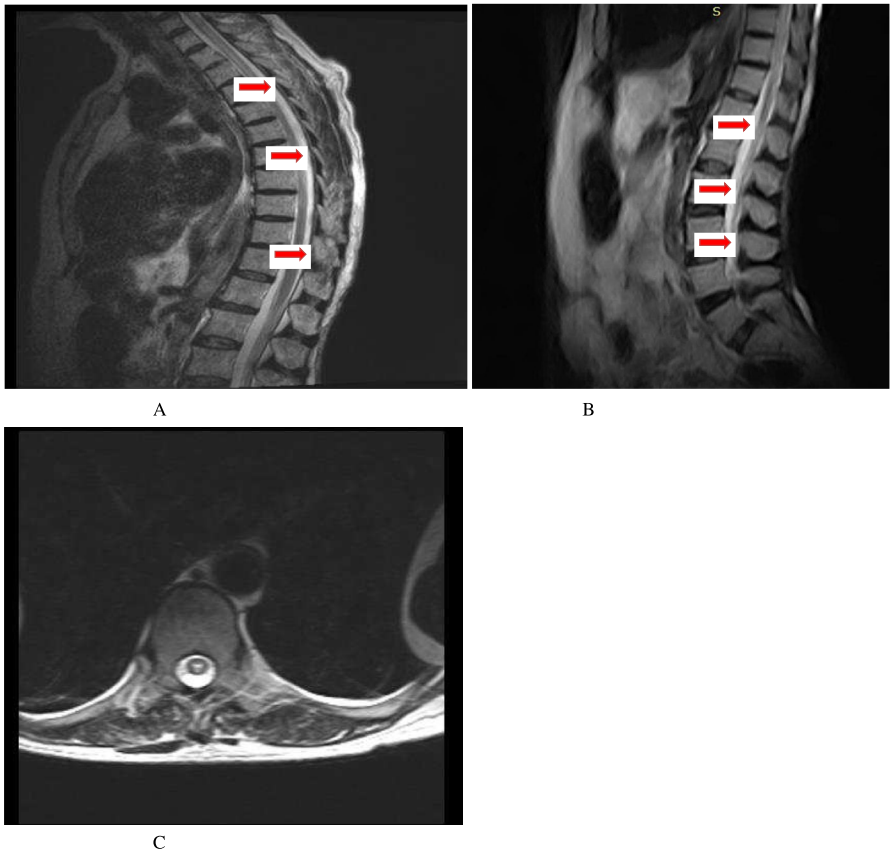

FIGURE 1 | Spinal cord MRI (A–C). There is increased T2 signal of the thoracic cord starting from C7 level and involving the whole thoracic cord up to the level of distal cord (Longitudinally extensive transverse myelitis, LETM red arrows) with possible development of syrinx.

Our patient meets the two core clinical criteria for the diagnosis of NMOSD, which include optic neuritis and longitudinally extensive transverse myelitis [11]. The positive anti-aquaporin-4 antibodies and the absence of other competing diagnoses further support her condition's alignment with the international consensus criteria. The previously conducted MRI, performed 18 months ago, indicated the presence of right pre-chiasmatic optic nerve swelling and contrast enhancement, which are suggestive of optic neuritis. Furthermore, the most recent Spinal MRI (Figure 1) revealed longitudinally extensive transverse myelitis extending from the C7 level and involving the entire thoracic cord up to the distal cord level. Our patient does not exhibit the clinical features typically associated with systemic lupus erythematous, and no indications suggest sarcoidosis. Laboratory tests have confirmed an adequate level of serum vitamin B12, effectively ruling out the most common alternative diagnosis for NMOSD. In the Ethiopian setup, the diagnosis of NMO can be quite challenging as AQP4 antibody test is not readily available. Physicians need to send samples outside of the country which also contributes to the delay in diagnosis.

Left untreated, NMOSD manifests as a recurring condition characterized by intermittent attacks, partial recoveries, and persistent disabling deficits. Patients with NMSOD acute attack are usually treated with high-dose parenteral steroids and Methylprednisolone to prevent further damage and restore neurologic function [12]. Patients with severe symptoms, especially with vision loss not responding to steroids, can also benefit from plasma exchange as an adjunctive therapy. Immunotherapy with Complement c5 inhibitors like eculizumab, Anti CD 19 antibodies like Inebilizumab, and Interleukin 6 receptor antagonists like Satralizumab are recommended in the prevention of future attacks in patients with AQP4 positivity as they all have shown effectiveness [13–15]. These groups of medications have a better quality of data and are hence preferred as opposed to other systemic immunotherapies like Azathioprine, methotrexate, and Mycophenolate Mofetil where the evidence is based on observational studies [16–18]. Yet, multiple observational studies and local data suggest that these agents can be efficaciously employed to treat NMOSD, leading to favorable clinical outcomes [9, 19, 20].

Based on our experience of treating this patient and local data from other documented cases, it is suggested that patients can be effectively treated with available therapies, leading to positive clinical and functional outcomes, unless newer immunosuppressive treatments targeting the underlying pathophysiology are available [9–11, 19–21].

Author Contributions

Bereket A. Molla: writing – original draft, writing – review and editing. **Sebhatleab T. Mulate:** conceptualization, writing – original draft, writing – review and editing. **Berhanu M. Abera:** conceptualization, investigation, validation. **Tseganesh M. Hailemariam:** investigation, resources. **Yared Z. Zewde:** supervision, validation.

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Ethics Statement

The authors have nothing to report.

Consent

The patient provided written informed consent for publication of the case report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

All data generated and/or analyzed are included in this published article.

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