Author's response to reviews

Title: Neuromyelitis optica in a middle-aged Ugandan female: case report

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Neuromyelitis optica in a middle-aged Ugandan female: case report
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Abstract

Background

Few cases of Neuromyelitis Optica have been reported in Africa. This is the first case report of Neuromyelitis Optica in Uganda. It highlights the need to have a high index of suspicion to promptly identify and treat appropriately these patients.

Case presentation

We present a 24 year old female of Bantu origin who presented initially with bilateral loss of vision and weakness of the lower limbs in 2010 that resolved completely after a few days. Eight months later, she presented with bilateral lower limb weakness and urinary incontinence that improved completely on steroids. This was followed four months later with an episode of quadriplegia that was treated with steroids and Azathioprine with some improvement but with residual sequel of using a walking aide.

Conclusion

The patient described here represents a phenotypic expression of a recurrent (multiphasic), steroid sensitive, inflammatory demyelinating disorder of the CNS occurring in a black Ugandan African woman. This case highlights the occurrence of Devic’s disease within our setting and the need to properly diagnose this condition even in a resource limited setting to prevent disability.

Key words,
Multiple sclerosis, Uganda, Neuromyelitis Optica
Background

Neuromyelitis optica (Devic’s syndrome) is defined as a devastating myelitis with the following; an acute unilateral or bilateral optic neuropathy, no clinical involvement beyond the spinal cord or optic nerves, and a monophasic or, rarely, a multiphasic illness [1-3]. The discovery of Neuromyelitis Optica (NMO) IgG, directed against aquaporin-4 (AQP4), has dramatically changed the clinical definition of NMO and is important in the diagnostic criteria of this disease [4, 5]. However, in resource-limited centers this may be a limitation in meeting the formal diagnostic criteria pathway due to laboratory diagnostic setbacks.

No cases have been documented in Uganda and this is the first case reported in Uganda or surrounding equatorial regions in Sub Saharan Africa. The low anticipation of such diseases in our setting coupled with diagnostic challenges often lead to mis-diagnosis and worse outcomes in patients that could have benefited from readily available treatment. We believe the insights offered here may be useful to many other resource limited settings.
Case Presentation

A 24-year-old African female of Bantu origin presented to us in 2010 with sudden bilateral loss of vision and progressive weakness in both her lower limbs for one day. She had been previously well with no known chronic medical conditions like hypertension or diabetes mellitus and had no preceding vaccinations or viral infections noted. She has lived all her life in Uganda. Her brain CT scan was normal and her blood work up was negative for polycythemia, thrombocytosis, and diabetes mellitus. Her systemic clinical examination including the neurological assessment at the time of initial medical presentation was normal. She was treated as a patient of transient ischemic attack with low dose aspirin (ASA) which she later decided to stop over the course of time.

Eight months later, she presented to us with inability to walk and urinary incontinence for 3 days. This was preceded by paresthesiae in the lower limbs followed by unsteady gait and subsequently, followed by inability to use both her lower limbs and urinary incontinence. She reported no history of recent vaccinations, ingestion of tinned meats or beef and no recent sore throat. Her vision this time round was normal with no complaints double vision or visual field defects. Her upper limbs were normal. She was nulliparous and reported normal menses. Reported no history of hypertension, diabetes and was not receiving regular medications.

Clinically, she had muscle power grade 2 on MRC scale bilaterally, with spasticity and brisk reflexes of the knees and ankles bilaterally; with bilateral up going plantars. She had a symmetrical sensory deficit below T10 to fine touch and pressure. Her vision was normal with no visual field defects or double images and no optic atrophy or optic neuritis was detected on
fundoscopy. She had a urinary retention and a urinary catheter was placed in situ. Her series of blood work requests returned negative for HIV1/2 testing and TPHA/VDRL for syphilis. Her blood peripheral film report revealed no malarial parasites or other hemoparasites. The full blood counts showed the white blood cell count (WBC) was $10.2 \times 10^3$/L, absolute neutrophils $7.1 \times 10^3$/L, lymphocytes $1.3 \times 10^3$, hemoglobin $11.6$g/dL and platelets $252 \times 10^3$. She had elevated acute phase reactants with an ESR of $25$mm/hr (Westergren method) and CRP $17$mg/L but Antinuclear Antibodies was negative. A lumber puncture performed showed the cerebrospinal fluid (CSF) was a clear and colorless, with a normal glucose. However, the CSF protein content was elevated at $60$mg/dL, while the white blood cell count in CSF was less than 5 cells /uL. Indian ink staining on CSF for Cryptococcus was negative and the Gram stain revealed no organisms. The Ziehl-Neelsen stain for tuberculosis revealed no acid fast bacilli. The VDRL on CSF was non reactive and cytology revealed no malignant cells. She had no clinical evidence of sarcoidosis, vasculitis, SLE or Sjogren’s syndrome. A brain and spinal MRI was requested for further evaluation,

The MRI of the cervico-thoracic spine revealed large multiple ill-defined hyperintensity lesions involving the cervical and thoracic spine cord up to T4 - T8 vertebral level on T2 weighted images. These were appearing hypointense on T1 weighted images probably representing myelitis or demyelination. No cord compressive lesions were found on the spinal MRI and the brain MRI was normal. A diagnosis of neuromyelitis optica was made based on the diagnostic criteria excluding the antibody assays [6].
She was started on pulse methyprednisolone 1g for 5 days with complete resolution of her symptoms. She was discharged from hospital on tapering oral steroids but unfortunately, the patient stopped the low dose oral steroids after two months of treatment. Due to lack of prior experience of the disease, she was not started on long term steroid sparing immune-suppressants like azathioprine or mycophenolate mofetil which are readily available within the country though costly.

In February 2011 that is four months later, she returned to our care with sudden loss of sensation and numbness in the upper limbs and weakness in the lower limbs. Her power grading using the Medical Research Council (MRC) was four minus in the upper limbs and two in the lower limbs respectively. We were unable to repeat the MRI scan due to the limited resources to evaluate the presence of new lesions and the extent. The patient then received pulse therapy of Methyprednisolone 1g once a day for 5 days with improvement in the lower limbs, power increased to 4 minus after about two week’s admission. She was able to walk with support and was started on daily tapered Prednisolone and Azathiprine starting at 2mg/kg/day, divided into two daily doses. She was not tested for the thiopurine S-methyltransferase (TPMT) mutation. Individuals having this mutation can develop significant bone marrow toxicity with Azathioprine; however, she gets routine monthly blood check especially the white cell counts. She was recommended to physiotherapy for muscle strengthening exercises and bladder training. She has remained fairly stable, able to walk with aid of a walking stick and is still under our follow up. She is currently maintained on Azathioprine 100mg daily and has been gradually tapered off her oral steroids. We are continuing to monitor her WBC counts for leucopenia and liver function associated with Azathioprine toxicity every month. She has remained stable and has not suffered any more relapses since then.
We are unable to perform the aquaporin 4 antibodies in our setting.

Discussion

This case shows the complexities of diagnosing Neuromyelitis optica in resource limited setting especially in geographic areas initially thought not to have a burden of this disease. It is reported to be rare in our setting though cases have been documented elsewhere [7-9]. And hence there is a need to adequately prepare for similar treatment challenges. Therefore, a high index of suspicion is required to make this diagnosis early and illustrate the need for early and prompt diagnosis made to delay unfavorable outcomes [1, 3]. Meeting the 2006 revised diagnostic criteria of NMO [6] in our settings may still be difficult especially with the serological assays. Clinicians need to rely on the other criterion and clinical judgments and initiate treatments so as to delay the consequences of the disease. In our case highlights the fact that lack of the laboratory diagnostic criteria such as detection of oligoclonal bands and of AQP4 antibodies does not preclude the diagnosis and correct treatment approach in cases like the one described. Conclusions

Our case report is further strong evidence that Neuromyelitis optica occurs in Uganda and Africa as a whole and requires a high index of suspicion and improvement health care provision to NMO patients in our setting. Proper training of medical personnel and students to promptly make a diagnosis and refer such cases for specialized care in required. Our patient had three episodes over a span of two years and suffered delays in instituting treatment due to lack of awareness as well as planning long term care for the patient. The availability of easier and faster assays would help in decision making of patient care. The limitations of determining oligoclonal bands and
NMO-IgG antibodies in resource limited setting should not delay the process of making a diagnosis of NMO in tropical Africa.

Consent issues.

Written informed consent was obtained from the patient for publication of this case report and accompanying images. Confidentiality and privacy have been maintained, no identifiers have been used. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Abbreviations
NMO – Neuromyelitis optica
HIV – human immunodeficiency virus
IgG – Gamma globulins
MS – Multiple Sclerosis
CT – Computerized tomography

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
All authors stated above made substantive intellectual contributions to a published case report. MK treated the patient and wrote the article; AM treated the patient, helped to draft the manuscript; SM participated in the treatment of patient and helped to draft the manuscript and helped in making the diagnosis of the patient; MK helped to draft the manuscript.

All authors read and approved the final manuscript.

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