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Challenging Diagnosis and Management of MOG Antibody Disease (MOGAD) in a Seven-Year-Old Girl with Acute Disseminated Encephalomyelitis (ADEM): A Case Report and Literature Review

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Abstract

Background: Diseases associated with anti-MOG antibodies (MOGAD) are rare inflammatory conditions that have recently been recognised for their distinct clinical characteristics. These disorders predominantly affect children, with acute disseminated encephalomyelitis (ADEM) being the most prevalent manifestation. There is a lack of comprehensive data on this pathology in Africa. This study is the first documented case of MOGAD in West Africa. **Case Presentation:** A 7-year-old girl was admitted to the neurology unit with fluctuating motor impairment in all limbs lasting for 4 weeks. Neurological examination revealed spastic tetraparesis, along with extrapyramidal and cerebellar syndromes. 48 hours after admission, she presented with status epilepticus, with an EDSS score of 9.0. After neuroimaging and biological tests, the diagnosis of MOG antibody-associated disease (MOGAD) was confirmed. The patient's condition improved with corticosteroid treatment. However, anti-MOG antibodies remained positive after six months, leading to the decision to initiate immunosuppressive therapy to address the potential for relapse. **Conclusion:** MOGAD presents a considerable diagnostic challenge in tropical regions, largely due to the limited availability of magnetic resonance imaging and specific serological testing, leading to delays and inaccuracies in diagnosis.

Keywords: Acute disseminated encephalomyelitis (ADEM), Myelin oligodendrocyte glycoprotein antibody disease (MOGAD), case report, child, West Africa.

Introduction

Acute disseminated encephalomyelitis (ADEM) is a rare autoimmune demyelinating condition affecting the central nervous system (CNS), primarily observed in children. The disorder is characterised by a range of multifocal neurological symptoms that result from demyelinating lesions in the brain and spinal cord (1). Several cases of ADEM have been linked to the presence of anti-myelin oligodendrocyte glycoprotein (anti-MOG) antibodies, which are specifically found in the CNS. The spectrum of disorders associated with anti-MOG (MOGAD) includes various demyelinating conditions, such as monophasic forms like optic neuritis (ON), transverse myelitis (TM), and ADEM, as well as recurrent forms including multiphasic disseminated encephalomyelitis (MDEM), ADEM followed by one or more episodes of ON (ADEM-ON), and recurrent ON (2).

Recently, the disease spectrum has expanded to include phenotypes such as autoimmune encephalitis and presentations resembling leukodystrophy (2). Despite the global documentation of MOGAD cases, there remains a significant deficiency in epidemiological studies concerning this disorder in Africa, attributed to limited availability of neuroimaging and anti-MOG antibody testing resources (3,4). This case report documents the first case of MOGAD in Côte d'Ivoire.

Case Report

A 7-year-old right-handed schoolgirl with asymptomatic minor sickle cell disease (AC) had no notable prenatal or postnatal history. Her psychomotor development had been normal, and she had no prior neurological events. She was admitted to the neurology unit at Cocody University Hospital with a fluctuating motor deficit affecting all four limbs, which had progressively worsened over the preceding four weeks. This motor impairment had been accompanied by moderate headaches without aggravating factors, relieved by paracetamol, as well as neck pain, projectile vomiting, and intermittent fever. She was initially treated for severe malaria, followed by bacterial meningoencephalitis; however, the lack of clinical improvement led to her transfer to our neurology service.

Upon admission, neurological examination revealed signs of meningeal irritation; an extrapyramidal syndrome characterized by abnormal bilateral choreic movements; a kinetic cerebellar syndrome; and an asymmetric spastic pyramidal syndrome involving all four limbs, more pronounced on the left side. Her Expanded Disability Status Scale (EDSS) score was recorded as 9. Her level of consciousness was preserved, with a Glasgow Coma Scale (GCS) score of 15/15. Clinical evaluation also indicated signs of an infectious syndrome. Forty-eight hours post-admission, the patient experienced tonic seizures that began in the left hemibody, which subsequently generalized, rapidly progressing to a state of convulsive status epilepticus, resulting in a reactive coma assessed at 10/15 on the Glasgow scale.

Brain MRI performed upon admission (Figure 1) revealed multiple hyperintense lesions in both infratentorial and supratentorial regions on T2-weighted and FLAIR sequences, findings suggestive of acute disseminated encephalomyelitis (ADEM). Cervical spinal cord MRI, also conducted at admission, demonstrated imaging features consistent with transverse myelitis (Figure 2). Cerebrospinal fluid (CSF) analysis yielded

normal results. Immunological testing of the serum, performed via indirect immunofluorescence using transfected cells (Neuroimmun), was positive for anti-myelin oligodendrocyte glycoprotein (anti-MOG) antibodies and negative for anti-aquaporin-4 (anti-AQP4) antibodies.

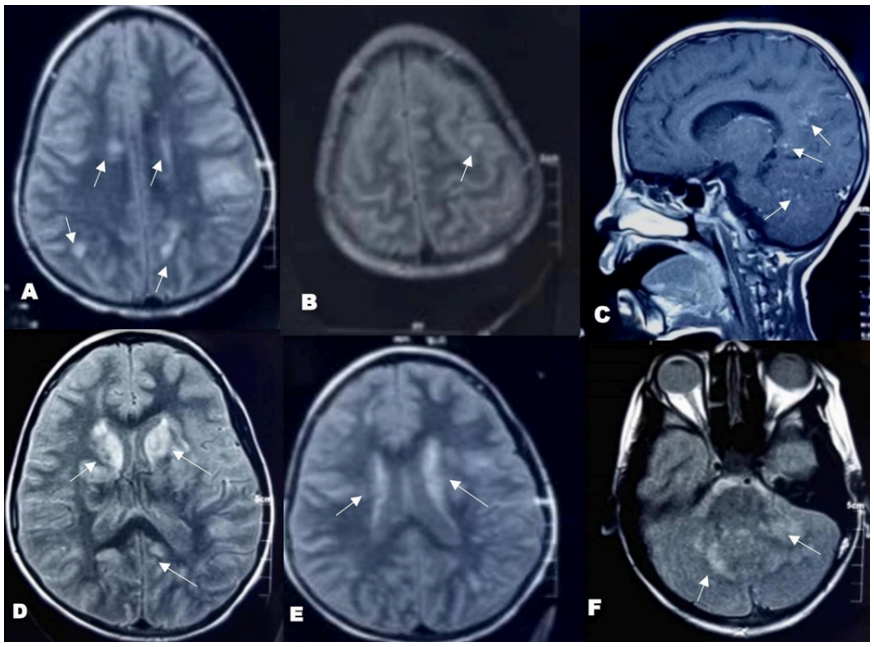

Figure 1: Axial sections of brain MRI at admission - fluid-attenuated inversion recovery (FLAIR) echo spin sequences (A, B, D, E, F) alongside, a sagittal section in T1-weighted echo spin following gadolinium injection (C). These images reveal Multiple areas of demyelination indicative of ADEM

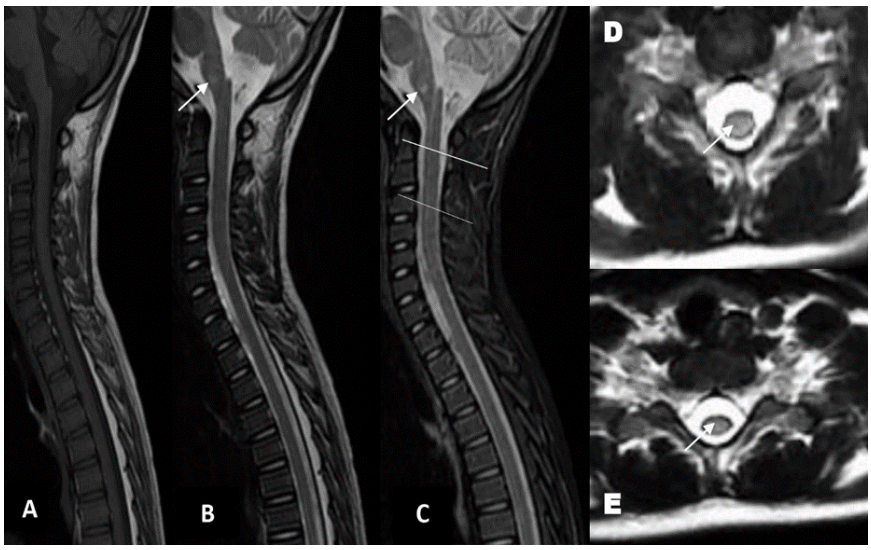

Figure 2: Cervico-thoracic spinal cord MRI performed upon admission: Sagittal sections T1-weighted spin echo sequence (A), T2-weighted sequence (B), T2-STIR sequence(C). Additionally, T2-weighted axial sections spin echo sequence (D and E), show a transverse myelitis with a bulbo-medullary junction significant lesion.

An established protocol for the management of status epilepticus was implemented, which included a loading dose of levetiracetam at 40 mg/kg, followed by a maintenance dose of 20 mg/kg administered in two daily doses. Concurrently, a corticosteroid treatment with methylprednisolone at 30 mg/kg was given for a duration of 5 days, subsequently reduced to 2 mg/kg for 2 months, with a gradual tapering over a period of 6 weeks.

After seven days of treatment, the patient experienced a cessation of convulsive seizures and regained consciousness, achieving a Glasgow Coma Scale score of 15/15. However, a motor deficit was noted in all four limbs, with strength rated at 4/5 for both the right upper and lower limbs, and 3/5 for both the left upper and lower limbs, resulting in an Expanded Disability Status Scale (EDSS) score of 8.0.

After a month of hospitalization, the patient was discharged with an EDSS score of 5.0. She showed motor sequelae characterized by gait disturbances and moderate kinetic cerebellar syndrome; nevertheless, she could walk around 50 meters independently.

After six months, the patient showed an EDSS score of 1. Follow-up imaging of the brain and cervical region revealed a significant reduction in the previously identified lesions (refer to Fig 3 and Fig 4). The anti-MOG antibodies remained positive. Therefore, a treatment plan was implemented that included Azathioprine at a dosage of 2 mg/kg once daily, along with 1 mg/kg of Prednisolone for the first three months.

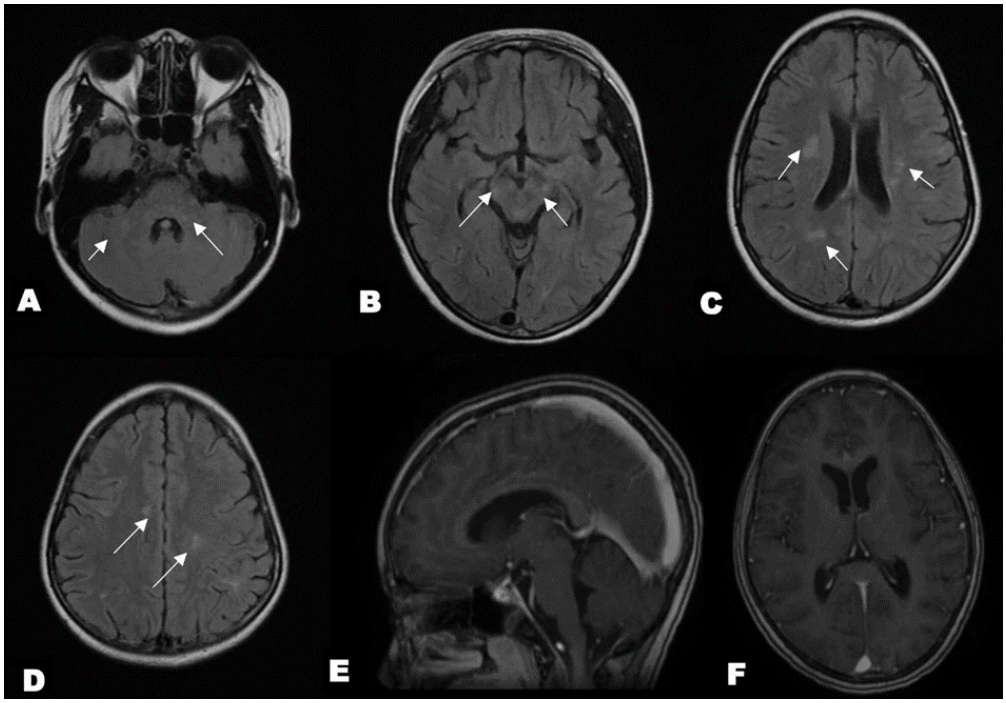

Figure 3: Brain MRI at 6-month follow-up: FLAIR sequences (G, H, I, J) and T1 3D images with gadolinium were obtained in both sagittal (K) and axial (L) sections. There was a considerable decline in the signal intensity from the cerebellar lesion, and enhancement was not observed.

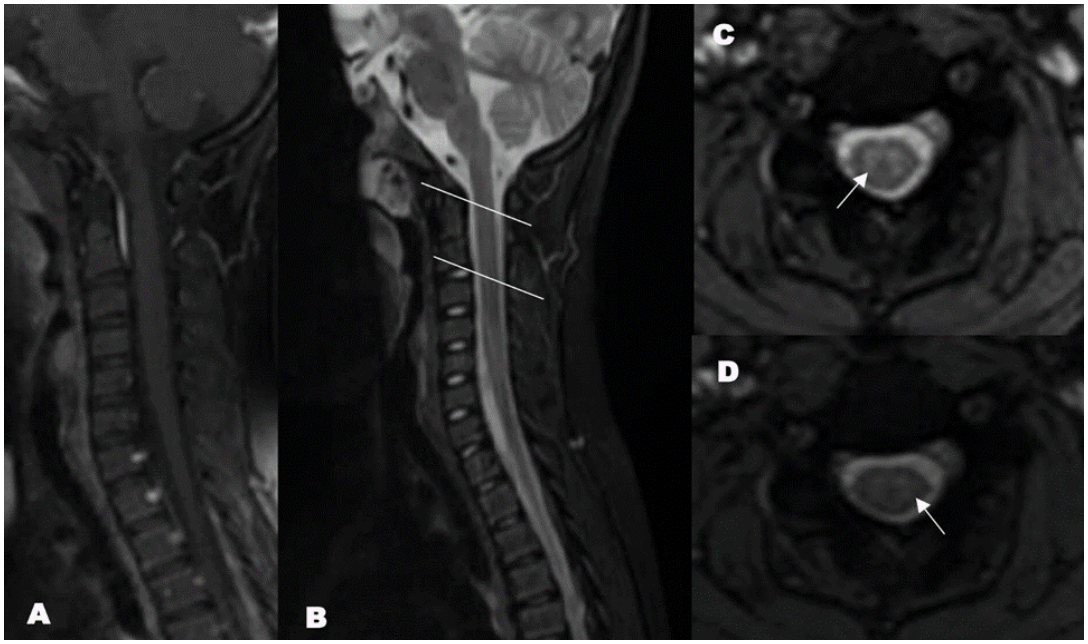

Figure 4 Cervical spinal cord MRI at 6-month follow-up : Sagittal section T1-weighted spin-echo sequence after gadolinium injection (A) and in T2-STIR sequence (B). Axial sections (C and D), T2-STIR sequence. There was a considerable decline in the signal intensity from the spinal cord lesion with no enhancement detected.

DISCUSSION

This case report presents the first documented instance of MOGAD in Côte d'Ivoire, involving a 7-year-old girl diagnosed with acute disseminated encephalomyelitis. Additionally, we explore the diagnostic and therapeutic challenges encountered in tropical settings, particularly in sub-Saharan Africa.

The prevalence of MOGAD is estimated to range from 1.3 to 2.5 per 100,000 individuals, while the incidence among children is reported to be 0.31 per 100,000 between 2015 and 2017(5). However, to date, no epidemiological studies have been conducted on the African population, which can be attributed to diagnostic challenges, particularly related to limited access to MRI and serological testing due to financial constraints.

The role of anti-MOG-IgG antibodies in ADEM is not well understood (6). Proposed mechanisms for the pathogenicity of anti-MOG antibodies include the opsonization of MOG, complement activation, antibody-dependent cellular cytotoxicity, and intracellular signaling. Environmental factors, particularly infections, may initiate these processes through cross-reactive immunity (7).

In 2023, diagnostic criteria for MOGAD were established following a structured consensus. These criteria are applicable to both adult and pediatric populations and necessitate the presence of three primary components: (A) the occurrence of one of six significant demyelinating clinical events, including optic neuritis, myelitis, acute disseminated encephalomyelitis, as well as focal or multifocal neurological deficits, brainstem or cerebellar deficits, and cortical encephalitis; (B) a positive test for anti-MOG IgG; and (C)

the exclusion of alternative diagnoses. A diagnosis is confirmed if a clearly positive test is obtained after verifying criteria (A) and (C). Conversely, a weakly positive result, a positive result without a specified titer, or a negative serum test with positivity in cerebrospinal fluid requires at least one additional clinical or radiological feature (**Table 3**) to establish the diagnosis of MOGAD(8).

In our patient, anti-MOG antibodies were found to be positive without a specific titer. The diagnosis of MOGAD was supported by clinical criteria, including acute disseminated encephalomyelitis characterized by tetraplegia and cerebellar syndrome. Imaging studies revealed hyperintensities in both the infratentorial and supratentorial white matter, the middle cerebellar peduncles, a central spinal cord lesion, and involvement of the basal ganglia. Previous studies have indicated that serum MOG-IgG antibodies are present in 30 to 65% of pediatric cases of ADEM and are frequently associated with meningeal syndrome and seizures (9), findings that were also observed in our case.

Table 1: ***Supporting clinical and radiological criteria (MRI) in cases of low positive titers or positive antibodies without a titer***

Core clinical attacks	Supporting features
Optic neuritis	➔ Bilateral simultaneous clinical involvement ➔ Longitudinal optic nerve involvement (>50% of the optic nerve length) ➔ Perineural optic sheath enhancement ➔ Optic disk oedema
Myelitis	➔ Longitudinal extensive myelitis ➔ Central cord lesion or H-sign ➔ Conus lesion
Brain, brainstem, or cerebral syndrome (including ADEM; cerebral monofocal or polyfocal deficits; brainstem or cerebellar deficits; cortical encephalitis)	➔ Multiple ill-defined T2-hyperintense lesions in the supratentorial and often infratentorial white matter ➔ Deep gray matter involvement ➔ Ill-defined T2 hyperintensity involving the pons, middle cerebellar peduncle, or medulla ➔ Cortical lesions with or without lesion and overlying meningeal enhancement

Validation of the 2023 International Diagnostic Criteria for MOGAD (adapted from Varley et al.(8)), ADEM = acute disseminated encephalomyelitis; MOGAD = myelin oligodendrocyte glycoprotein antibody–associated disease

The data concerning the management of MOGAD is both intricate and limited, particularly regarding large-scale research and the long-term monitoring of patients (9). There is a lack of well-defined recommendations based on large clinical trials for the treatment of MOGAD (9). The existing guidelines are largely shaped by those for NMOSD, with limited evidence available from retrospective observational research. Generally, patients with MOGAD exhibit a positive response to glucocorticoids

during episodes of acute demyelination, yet they are at risk of experiencing relapses if steroid doses are diminished or halted (2,9). A gradual tapering of steroids over a period of four to six weeks is frequently recommended following the initial event (9). In the event of a relapse, immunomodulatory therapies such as intravenous immunoglobulins (IVIg) or plasmapheresis may be considered. However, we opted against these treatments as the patient has exhibited improvement with corticosteroids. Clinicians typically employ immunosuppressive therapies, including azathioprine, mycophenolate mofetil, Rituximab (RTX), and intravenous immunoglobulins (IgIV), to reduce the risk of relapse in individuals with recurrent demyelinating conditions and positive MOG antibodies. Conversely, disease-modifying treatments such as interferon β and glatiramer acetate have not shown clinical efficacy in this patient population (9).

The commencement of immunosuppressive treatment for our patient was delayed due to findings that suggest uncertainty regarding the likelihood of relapse in individuals with MOGAD (9). This is especially pertinent for those who have shifted from a seropositive to a seronegative state, which may justify postponing long-term therapy (10). A consistently positive serology indicates an 88% probability of developing a multiphasic variant characterised by severe inflammation (9). A retrospective international analysis involving 121 paediatric MOGAD cases, conducted in 29 specialised centres across 13 nations, revealed that maintenance therapy was initiated during the first crisis in merely 16.5% of instances, while it was postponed until the second crisis in 83.5% of cases (11). In our case, the detection of anti-MOG antibodies beyond six months prompted the initiation of azathioprine at a dose of 2 mg/kg. Despite the maintenance treatment, more than 90% of patients experience a relapse within 13 months, with an average of 2.2 relapses in the first two years, underscoring the importance of vigilant monitoring [11]. Azathioprine has been chosen for its local availability and affordability. Retrospective studies indicate substantial reductions in relapse rates and stabilisation of EDSS scores in paediatric populations (2). Therefore, it is recommended as a first-line treatment option in the European guidelines for managing MOGAD (2).

Patients with persistent anti-MOG antibodies are at an elevated risk for polyphasic disorders, including multiphasic ADEM and post-ADEM epilepsy (9). The patient, who initially experienced a state of epilepsy, is currently undergoing antiepileptic treatment and has not had any further seizures. Her neurocognitive and functional prognosis is positive, although concerns remain regarding the potential for recurrence.

Predictive factors for poor prognosis in the context of MOGAD include the occurrence of transverse myelitis at initial presentation, which often results in residual disability (EDSS > 2). Additionally, an initial status of severe illness associated with ADEM or cortical encephalitis is likely to progress to refractory epilepsy and treatment resistance. Other significant indicators are the prolonged persistence of anti-MOG antibodies and a high relapse rate, exceeding seven episodes (12).

CONCLUSION

The diagnosis of MOG antibody-associated disorders presents significant challenges in tropical environments, primarily due to limited access to neuroimaging and serological testing. To minimise diagnostic delays and the occurrence of misdiagnoses, it is essential to perform routine testing for anti-MOG antibodies in pediatric patients presenting with demyelinating inflammatory syndromes. This approach not only guides treatment but also provides accurate prognostic information to patients and their families.

Although ADEM in MOGAD patients generally has a favorable prognosis, the potential for relapse and the occurrence of epilepsy remains significant complications. Therefore, it is imperative to implement rigorous clinical, radiological, and biological monitoring for these patients, and initiate maintenance therapy for those with persistent anti-MOG antibody titers.

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