Case Report

Atypical presentation of neuromyelitis optica spectrum disorder: A diagnostic conundrum

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ABSTRACT

Neuromyelitis optica spectrum disorder (NMOSD) is a relapsing, inflammatory demyelinating disorder of the central nervous system, most commonly presenting with optic neuritis and longitudinally extensive transverse myelitis. Diagnostic criteria rely on clinical features supported by aquaporin-4 (AQP4) antibody testing, but atypical presentations may occur, complicating recognition, especially in younger patients. We report the case of a 16-year-old female with congenital hypothyroidism and global developmental delay who presented with persistent vomiting, dysphagia, dysphonia, and vertigo. Clinical localization suggested brainstem involvement. Magnetic resonance imaging revealed lesions in the medulla extending into the cervicomedullary junction. Serum AQP4 antibody positivity confirmed NMOSD. The diagnosis was challenging due to the absence of optic neuritis and longitudinally extensive myelitis, and the patient's young age. She improved significantly with corticosteroids and azathioprine. This case highlights the importance of considering NMOSD in atypical brainstem presentations in adolescents. Awareness of such variants, along with prompt antibody testing, is crucial for early initiation of immunotherapy and favorable outcomes.

Key words: Area postrema syndrome, Congenital hypothyroidism, Demyelinating diseases, Devic's disease, Neuromyelitis optica

Neuromyelitis optica spectrum disorder (NMOSD) is an entity defined in the demyelinating spectrum of disorders ranging from multiple sclerosis to acute disseminated encephalomyelitis. This disorder is prevalent more in females than males and presents in adulthood, encompassing a variety of presentations ranging from area postrema syndrome (APS) to acute diencephalic syndromes [1,2]. Serum aquaporin-4 positivity aids in the diagnosis of NMOSD, but its absence does not rule out the disease.

Here, we present an atypical case of a 16-year-old female who presented to us with APS and acute brainstem demyelination with thyroid dysgenesis and cretinism. The patient posed a particular challenge in diagnosis in terms of the associated young age of presentation and the absence of optic neuritis.

CASE REPORT

A 16-year-old female, known case of cretinism and intellectual disability with global developmental delay due to congenital thyroid dysgenesis, on treatment T. thyroxine 100 mg, presented to us with complaints of persistent vomiting for a month, followed by difficulty in swallowing, difficulty in speaking, and complaints of vertigo for 20 days. Over the course of admission, the patient developed progressive weakness starting in the right upper limb in the form of difficulty in lifting her hand above the head, which progressed to the left upper limb in a span of 7 days, such that the patient had difficulty lifting her hands above the head. The dysphagia, dysphonia, and vertigo were acute in onset. Dysphagia was associated with nasal regurgitation of food and drooling of saliva from the mouth immediately after eating and was progressive over the next 7 days. These symptoms were not associated with difficulty in hearing, tinnitus, blurring of vision, bowel, or bladder symptoms.

The patient was conscious and aware of her surroundings and able to recognize her parents. However, subjective neurological assessment was difficult in view of cognitive dysfunction. Higher mental functions could not be assessed. Cranial nerve examination showed an

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absent gag reflex with left deviation of the uvula, and the rest of the cranial nerve examination was normal. There was regular up-beat nystagmus present in all gazes. (Video 1). Motor system examination did not reveal any visible wasting or hypertrophy. Spasticity was present in all four limbs. Shoulder abduction, bilaterally, showed a power of 3/5, and there was 4/5 power in all the rest of the muscle groups in the upper limb and normal power (5/5) in the lower limb. Hand grip was decreased in both hands. Superficial reflexes (corneal, conjunctival) were present with extensor plantar. Abdominal reflexes were absent. Reflexes were increased in the upper and lower limbs (biceps, triceps, supinator, knee, and ankle were +3). Sensory examination was difficult in view of her intellectual disability. Cerebellar signs were not elicitable except for nystagmus. Meningeal signs were absent. The back and spine were normal. Based on history, progression, and clinical findings, a demyelinating lesion localizing to the brainstem and cervical cord was suspected.

Routine investigations were done, shown as below (Table 1), suggestive of normocytic, normochromic anemia with slightly elevated erythrocyte sedimentation rate.

Magnetic resonance imaging (MRI) of the brain with contrast was done, which showed a focal, poorly defined signal intensity lesion in the circumventricular location of the posterior medulla on both sides, involving the area postrema extending into the cervical-medullary junction. Another similar morphology lesion was identified in the visualized upper cervical spinal cord at the C2 level, suggesting a possibility of NMOSD (Figure 1).

Her serum aquaporin-4 (AQP4) antibody, using an immunofluorescence assay, cell-based assay was sent, which was positive. Antinuclear antibody indirect immunofluorescence was +1 with a negative profile. Anti-myelin oligodendrocyte glycoprotein antibody was negative. Her thyroid profile was normal. A final diagnosis of APS with acute brainstem syndrome in NMOSD with congenital hypothyroidism was made.

Over the course of admission, the patient developed aspiration pneumonitis and was intubated. She was given antibiotics and methyl prednisolone 500 mg 12 hourly and subsequently put on oral steroids and started later after a course of 2 weeks with azathioprine. Other supportive measures were provided along with her thyroid medication. She subsequently improved and was discharged.

The patient has improved power in both upper limbs to 5/5. Persistent neurological deficit in the form of upbeat nystagmus was present. All other complaints have been resolved completely. Currently, the patient is on T. azathioprine 50 mg od and T. thyroxine 100 mcg od with other supportive medication.

Table 1: Routine investigations with CSF analysis of the patient.

Investigations	Values	Reference range and units
Hemoglobin	10 g/dL	11–15 g/dL
Total counts	8400 cells/cmm	4000–10000 cells/cmm
Differential counts (Neutrophil/ Lymphocyte/ Eosinophil/ Monocytes)	58/36/3/3	Neutrophils: 40–80% Lymphocytes: 20–40% Eosinophils: 1–6% Monocytes: 2–10%
Erythrocyte sedimentation rate	32	0–19 mm
Serum urea	30.10 mg/dL	14–40 mg/dL
Serum creatinine	0.76 mg/dL	0.6–1.2 mg/dL
Serum sodium	135 mEq/L	135–145 mEq/L
Serum potassium	3.4 mEq/L	3.5–5.1 mEq/L
CSF examination		
Glucose	76 mg/dL	50–80 mg/dL
Protein	144 mg/dL	15–60 mg/dL
Total count	0 cells/μL	0–5 cells
Differential count	Not possible	
On wet mount	NAD	
CSF OCB	Negative	

CSF: Cerebrospinal fluid, OCB: Oligoclonal bands

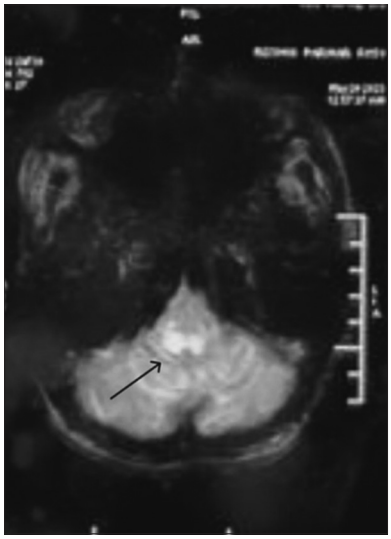

Figure 1: Magnetic resonance imaging findings of the brain

DISCUSSION

NMOSD is an antibody-mediated inflammatory astrocytopathy distinct from multiple sclerosis. The 2015 International Consensus Criteria expanded its definition to include core features beyond optic neuritis and longitudinally extensive transverse myelitis (LETM), such as APS and acute brainstem/diencephalic syndromes [1,3,4]. APS, characterized by intractable nausea, vomiting, or hiccups, results from lesions in the dorsal medulla, where AQP4 channels are highly expressed [5,6]. It may present as an isolated syndrome, often misattributed to gastrointestinal disorders, leading to diagnostic delay [7,8]. Pediatric-onset NMOSD with APS is particularly challenging, since optic neuritis and myelitis may be absent initially [9].

MRI typically demonstrates T2/fluid-attenuated inversion recovery hyperintensities in the dorsal

Video 1: Regular upbeating nystagmus in all gazes suggestive of brainstem involvement.

medulla or cervicomedullary junction, which, when associated with APS, are highly suggestive of NMOSD [6,7]. Cerebrospinal fluid (CSF) findings may include pleocytosis and elevated protein, but unlike multiple sclerosis, CSF-restricted oligoclonal bands are uncommon [10]. MOG-antibody disease (MOGAD) can mimic NMOSD, but isolated APS is rare in MOGAD, and radiological features often differ [11]. Thus, serological confirmation with AQP4-IgG remains central for diagnosis.

Immunotherapy is essential to prevent relapses, as each attack contributes to disability. High-dose corticosteroids are first-line for acute management; plasma exchange is reserved for refractory cases [12]. For long-term relapse prevention, targeted biologics have transformed NMOSD outcomes. The complement inhibitor eculizumab (PREVENT trial) and its long-acting analog ravulizumab significantly reduced relapses in AQP4-positive NMOSD [4,13]. The anti-CD19 monoclonal antibody Inebilizumab (N-MOmentum trial) also showed durable efficacy [15]. Similarly, satralizumab, an interleukin-6 receptor blocker, demonstrated significant reduction in relapses as both monotherapy and add-on [14,15]. In settings with limited access to biologics, conventional immunosuppressants such as azathioprine and mycophenolate mofetil remain widely used, though with less robust evidence.

CONCLUSION

Our patient presented with isolated APS and brainstem syndrome without optic neuritis or LETM, yet was seropositive for AQP4-IgG, fulfilling criteria for NMOSD. The coexistence of congenital hypothyroidism added complexity, as neurological assessment was limited by cognitive impairment. This case underlines the importance of considering NMOSD in adolescents with unexplained persistent vomiting and brainstem symptoms, and highlights how early recognition and immunotherapy can yield favorable outcomes.

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AUTHORS' CONTRIBUTORS

All authors have contributed equally.

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