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Case Report

A case report on recurrent area postrema syndrome in AQP4-IgG-positive NMOSD

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Abstract

Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory condition of the central nervous system caused by severe immune-mediated demyelination and axonal destruction, mainly affecting optic nerves and the spinal cord. We describe a 26-year-old Nepalese woman with recent onset of headache, nausea, vomiting and hiccups indicative of Area Postrema Syndrome (APS). The antibody test for aquaporin-4 was strongly positive. Brain magnetic resonance imaging (MRI) showed a bilateral hyperintense signal in the area postrema (AP). The patient started on methylprednisolone, and then azathioprine was added. However, the patient was readmitted because of tingling in her right upper extremity and sudden onset of tremors. An MRI scan showed an enlarged lesion in AP. Rituximab was started on top of the previous treatment, and a second dose was given after 2 weeks. The patient had been monitored regularly and symptom-free for 5 months. Hence, we emphasize the immediate need for a diagnostic approach for NMOSD management.

INTRODUCTION

Neuromyelitis optica spectrum disorder (NMOSD) is axonal destruction of the central nervous system that primarily affects the optic nerves and spinal cord due to severe immune-mediated demyelination and is associated with positive serum aquaporin-4 immunoglobulin G antibodies (AQP4-IgG) [1]. One of the most common manifestations of NMOSDs is area postrema syndrome (APS) which manifests as nausea, uncontrollable vomiting and hiccups lasting several days [2]. A vomiting center is located near the floor of the fourth ventricle, which is pierced by tortuous capillaries [3]. Area postrema (AP) contains structures responsible for autonomic control and chemoreception and has loose endothelial connections contributing to APS [4]. These lesions are also associated with loss of AQP4 immunoreactivity and inflammation [3]. The neuroimaging findings support the initial presentation of nausea and vomiting for the condition neuromyelitis optica (NMO). Optic neuritis and transverse myelitis are two possible alternative diagnoses [4]. Diagnostic certainty and speedy treatment have made APS in patients with NMOSD less of a burden. However, in a developing country, where resources are scarce and patients often do not seek help until it is too late, the prognosis and outcome are less certain.

CASE REPORT

A 26-year-old Asian female complained of constant headaches, nausea, vomiting and hiccups with slurring of speech. She has had a headache for the past 1.5 months. Examination revealed tongue fasciculation, nystagmus while gazing to the left, increased deep tendon reflexes on the left side, ataxia and paresthesia on the base of the neck.

The hematology, biochemistry (including C-reactive proteins and Erythrocyte Sedimentation Rate) and coagulation profile were normal. She underwent brain and spine magnetic resonance imaging (MRI), which showed a focal hyperintense signal on various sequences (Fig. 1) affecting the AP region of the inferior dorsal medulla.

Furthermore, serum AQP4-IgG was strongly positive. Antibodies against the myelin oligodendrocyte glycoprotein (MOG) were, however, negative. Her symptomatic presentation, lab results and imaging findings strongly suggest APS with NMOSDs.

The patient was started on methylprednisolone injections, switched to an oral form, tapered over 2 weeks before discharge and then azathioprine was added. However, the patient was readmitted after 1 month with complaints of tingling in the right upper extremity for the previous 7 days and a sudden onset of tremors. She also had difficulty walking and dizziness. On examination, she had the right horizontal gaze, nystagmus and disturbed tandem gait. She also complained of heaviness, a burning sensation in the right extremity and an altered hemifacial sensation. Imaging with relevant, complete metabolic panels and complete blood count coagulation profiles was ordered. An MRI scan showed an enlarged lesion in the AP with a hyperintense signal encompassing the area extending the medulla (right side) and corticomedullary junction (Fig. 2).

Intravenous methylprednisolone and rituximab were administered to the patient and managed symptomatically. Her tingling and burning sensations were treated with amitriptyline. After 2 weeks, the second dose of rituximab was given and planned

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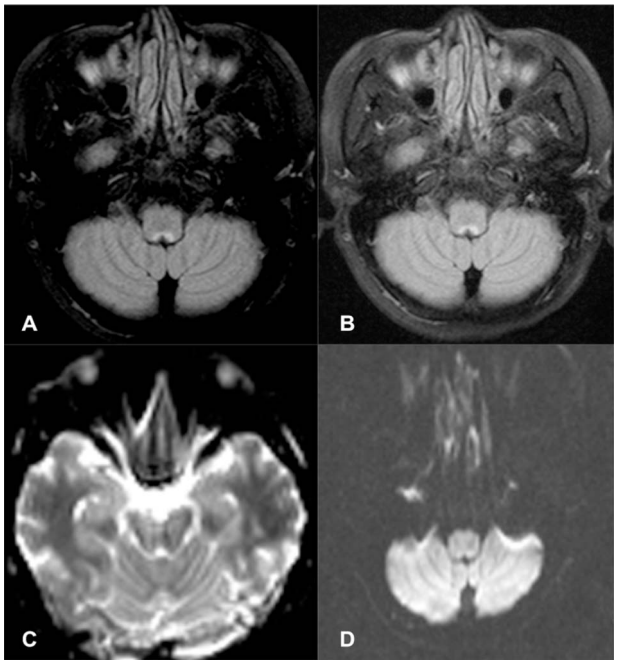

Figure 1. T2-weighted (A), T2-FLAIR (B), ADC (C) and DWI (D) MRI sequences in transverse sections indicating the involved area in the AP. ADC: apparent diffusion coefficient; dwi: diffusion-weighted imaging; FLAIR: fluid-attenuated inversion recovery; MRI: magnetic resonance imaging.

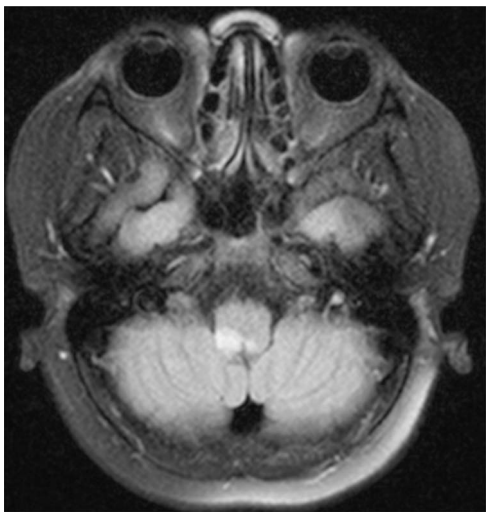

Figure 2. MRI T2-FLAIR sequence demonstrating hyperintense signal involving AP extending to the right side of the medulla and corticomedullary junction has significantly increased. FLAIR: fluid-attenuated inversion recovery.

for the next dose every 6 months. The patient was followed up regularly and had been symptom-free for 5 months.

DISCUSSION

In this report, we discuss a 26-year-old female from Southeast Asia (Nepal) and emphasize the importance of raising awareness of NMOSD as a diagnostic option to avoid a potentially severe prognosis.

According to various studies, NMOSD has a prevalence of 0.37–10 per thousand adults. Differences based on ethnicity, geography and gender are recognized. Females have a documented incidence of NMOSD up to 7.6 times higher than males [5].

APS is described as at least a 48-h of intractable nausea, vomiting or hiccups [1, 3]. Structures in the AP are responsible for autonomic control and chemoreception; when stimulated appropriately, these structures cause nausea and vomiting (a 16-fold increase in NMO) [4]. Wingerchuk *et al*. published the latest criteria for NMOSD, combining a variety of clinical symptoms and radiological findings with AQP-4 antibody status that increased the diagnostic sensitivity by 76%. Under appropriate clinical conditions, detection of AQP4 IgG antibodies is required to confirm the diagnosis, excluding other differential diagnoses [1].

On T2-weighted MRI, longitudinally significant lesions in the spinal cord, particularly those involving the grey matter of the central spinal cord and extending to three or more vertebral levels, are strongly diagnostic of NMOSD [6].

Multiple sclerosis and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) are the most common differential diagnoses. MOGAD can be easily distinguished from NMOSD as both have reliable serum indicators [7]. NMOSD differs from other demyelinating diseases by significant differences in disease progression, outcome and pathogenesis of the underlying disease and response to disease-modifying multiple sclerosis therapy. Other differentials include systemic lupus erythematosus (SLE), neurosarcoidosis and subacute combined neurodegeneration[8].

Seronegative NMOSD is managed in the same way as seropositive. Acute attacks with glucocorticoids and/or plasma exchange and preventing attacks with immunotherapies have improved NMOSD outcomes, but there is no definitive data [9]. If intravenous steroid treatment is poorly responsive or fails, therapeutic plasma exchange is considered. Immunosuppressive medications, i.e. oral prednisone, azathioprine, rituximab and mycophenolate mofetil, have been found to reduce flare-ups when used as maintenance therapy. The best-studied drugs are azathioprine and rituximab, followed by mycophenolate mofetil, with some data suggesting that rituximab is the most effective [10].

For seropositive patients with NMOSD, we recommend eculizumab, inebilizumab, satralizumab or rituximab. However, the best drug regimen and treatment length are unknown. Frequency of relapses, the severity of the first attack, older age at disease onset and an association with other autoimmune disorders are poor prognostic factors [9, 10].

The diagnostic challenges in healthcare settings with limited resources can result in delayed diagnosis and treatment. This case report emphasizes the importance of raising awareness of NMOSD as a diagnostic option to avoid a potentially devastating prognosis.

CONCLUSIONS

The disease spectrum of NMO presents as the APS without other neurological symptoms. Many cases of NMO manifest atypically and relapse frequently. The MRI lesions in the AP, the emetogenic centers and positive antibodies are highly diagnostic of NMOSD. Immediate diagnosis and treatment with intravenous steroids followed by rituximab for maintenance therapy can significantly improve the condition without neurological morbidity and mortality.

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CONFLICT OF INTEREST STATEMENT

There are no conflicts of interest.

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ETHICAL APPROVAL

The UDM National Institute of Neurological and Allied Sciences' IRC granted ethical approval.

CONSENT

Written informed consent has been received from the patient.

GUARANTOR

Ramesh Shrestha is the guarantor of this study.

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