Case Study

A case of neuromyelitis optica spectrum disorder presenting as area postrema syndrome with coexisting juvenile systemic lupus erythematosus.

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Received on: 23-Nov-2023 Accepted for Publication: 20-Jan-2024

ABSTRACT

Background: Neuromyelitis optica spectrum disorder (NMOSD) are rare demyelinating disorders mainly involving transverse myelitis and optic neuritis together with highly specific anti-aquaporin-4 (AQP4)-IgG antibody and antimyelin oligodendrocyte glycoprotein (MOG)-IgG antibodies. Case reports of patients with systemic lupus erythematosus (SLE) and NMOSD have been reported. Though myelitis and optic neuritis are well described, they are rare manifestations of SLE and it is not known to what extent NMOSD contributes to these symptoms. The association of NMOSD with SLE is rarely reported in children.

Observation: We present a challenging case of a juvenile SLE patient who had area postrema syndrome (APS-intractable nausea, vomiting, and hiccups) as the presenting feature of NMOSD who went into remission following pulse steroids and Rituximab.

Conclusion: SLE patients with engagement of the spinal cord or optic nerve should be screened for (AQP4)-IgG and (MOG)-IgG antibodies. We also highlight the importance of timely diagnosis of these conditions in children, in order to guide therapeutic management, as treatment choices may vary and directly impact prognosis.

Key Words: Neuromyelitis optica spectrum disorder (NMOSD), area postrema syndrome (APS), systemic lupus erythematosus (SLE)

INTRODUCTION

Neuromyelitis optic spectrum disorder (NMOSD) is an immune-mediated CNS demyelinating disease that commonly presents as optic neuritis and transverse myelitis.[1] Roughly one-third patients present with brainstem syndrome including area postrema syndrome (APS) which is characterized by severe nausea, vomiting, and hiccups.[2] APS is usually associated with aquaporin-4 (AQP4)-IgG antibody rather than antimyelin oligodendrocyte glycoprotein (MOG)-IgG antibody.[1,2] Systemic lupus erythematosus (SLE) is a systemic disease that affects the CNS in 60% of its cases. There are several reports about the coexistence of NMOSD and autoimmune diseases mainly rheumatoid arthritis, sarcoidosis, myasthenia gravis, Sjogren's syndrome, Vasculitis and

SLE.[3,4] However, there is no consistent opinion whether NMOSD and SLE are independent diseases that can coexist with each other, or the serological findings are non-specific and AQP-4IgG or (MOG)-IgG can be seen in either condition.[4, 5]

Herein, we describe the clinical course of a juvenile SLE patient who developed APS as the presenting feature of NMOSD who later responded to pulse steroids and Rituximab.

Case Report/Description

A 17-year-old girl with SLE presented to us with severe headache and diplopia. She was diagnosed with SLE five years back on the basis of positive anti-nuclear, anti-double stranded deoxyribonucleic acid, anti-Smith, anti-ribonucleoprotein antibodies, hypocomplementemia, with alopecia, inflammatory arthritis, haemolytic anemia, leukopenia, Raynaud phenomenon and oral ulcers. She came to our clinic with fever, headache, diplopia, and myalgia of two weeks duration. MRI of the brain and orbits were both normal. CSF studies demonstrated low glucose (39 mg/dL), high protein (170 mg/dL), and pleocytosis (WBC 429 cells/uL) with neutrophilic predominance. CSF Adenosine Deaminase (ADA) levels were normal. She was treated with antibiotics for presumed bacterial meningitis and was discharged fourteen days later. CSF and blood cultures were negative. She was continued on hydroxychloroquine, azathioprine, and low-dose prednisolone. She was again readmitted two months later for intractable nausea, hiccups, vomiting, fever, and severe frontal headache. CSF studies again demonstrated low glucose (24 mg/dL), high protein (168 mg/dL), and pleocytosis (WBC 394 cells/uL) with neutrophilic predominance. She was treated with broad-spectrum antibiotics without significant clinical improvement. CSF cultures remained negative. Her conditions in terms of headache, nausea, and vomiting deteriorated, and she developed new onset diplopia. A repeat Brain and spinal MRI, demonstrated an isolated T2-weighted-Fluid-Attenuated Inversion Recovery (T2-FLAIR) enhancement in tegmentum of medulla and pontomedullary junction, which represents area postrema area; leading to our diagnosis of APS due to NMOSD (Figure 1). There were no optic nerve abnormalities on MRI

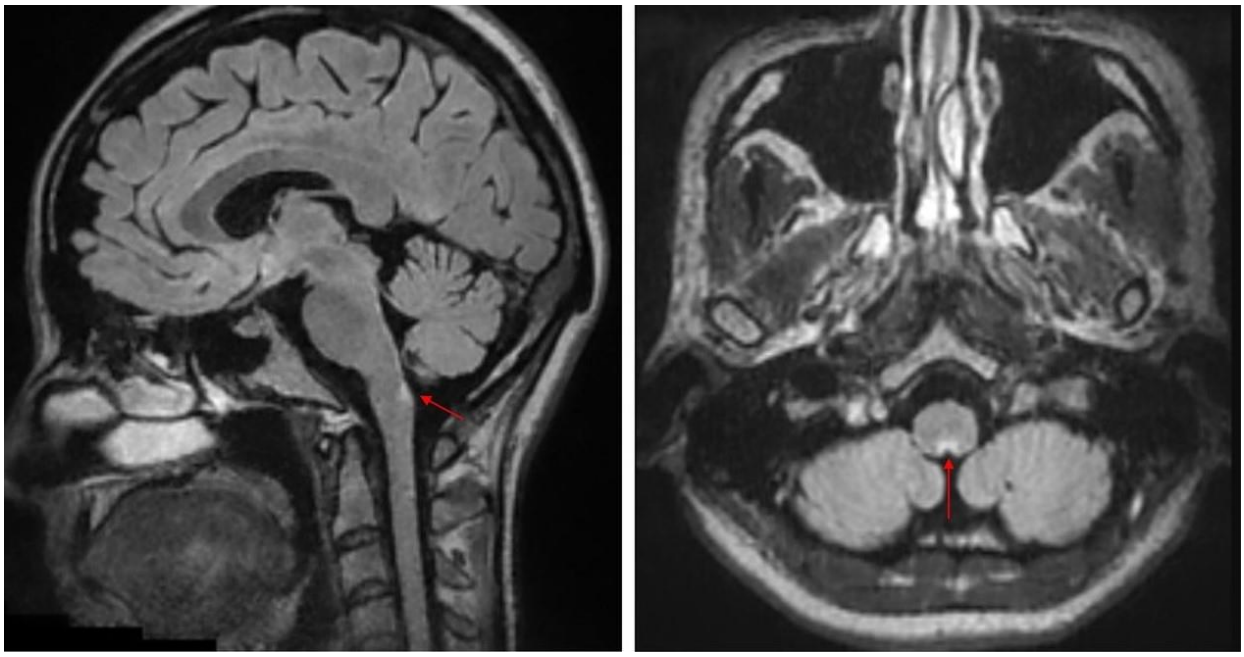
orbit and ophthalmology examination was normal. AQP4-IgG and MOG-IgG were both positive. The patient was diagnosed with seropositive NMOSD with coexistent SLE. She received pulse dose methylprednisolone (30mg/kg/day) for 3 days along with Rituximab 1000 mg IV on day 0 and day 14 was administered for long-term treatment of SLE and prevention of future NMOSD relapses. Hydroxychloroquine was continued, and azathioprine was stopped. She was discharged on a prolonged glucocorticoid taper. One year down the line, both SLE and NMOSD remained well-controlled without any relapse.

Discussion: Here, we present a rare case of juvenile SLE and NMOSD that highlights the importance of timely diagnosis of these coexistent conditions in order to guide targeted therapeutic management. In NMOSD, complement deposition and demyelination may involve multiple spinal cord segments, the brain, and the optic nerves. Though rare, patients with SLE can develop brain and brainstem inflammation and myelitis (NPSLE).[6] A recent study investigated the frequency of autoantibodies classically associated with neuropsychiatric SLE (NPSLE) in patients with NMOSD.[7] Eighty-eight percent of patients with coexisting NMOSD had AQP4-IgG in the serum, whereas AQP4- IgG was only present in the serum of three percent of patients with NPSLE alone. In addition, no AQP4-IgG's were found in SLE patients without neuropsychiatric symptoms.[7] MOG-IgG antibodies were only detected in patients with NMOSD who were negative for AQP4-IgG. The authors concluded that patients with demyelinating NPSLE should be tested for AQP4-IgG and MOG-IgG in order to help identify comorbid SLE and NMOSD.[7] AQP4-IgG can be considered diagnostic for NMOSD, while none of the other antibodies were diagnostic of demyelinating NPSLE. Our child was seropositive for both the antibodies. Double-positive NMOSD is found to have a high relapse rate and residual disability. High-dose intravenous steroids are first-line therapy for acute flare of both NMOSD and SLE. However, the choice of steroid-sparing agent should be tailored to the active underlying disease. SLE is treated with hydroxychloroquine in addition to other immunosuppressive agents depending on the involved target organ. In NMOSD, recent data suggest that rituximab, eculizumab, satralizumab, and

inebilizumab are most effective in preventing relapse.[8] It is important to determine which disease is clinically active in order to appropriately tailor therapy. Though both disorders share similar neurologic manifestations, antibody testing for AQP4-IgG and MOG-IgG may help identify coexisting NMOSD.

Figure 1:

A) B)



MRI T2 FLAIR sequence demonstrating bilateral lesions in the area postrema (highlighted by arrows) in the (A) sagittal and (B) transverse planes.

Hyperintensity in this area at the level of the medulla oblongata with associated severe nausea and vomiting is consistent with a diagnosis of area postrema syndrome- a characteristic presentation of neuromyelitis optica disorder (NMOSD).

Key Message: This case illustrates that juvenile SLE and NMOSD may co-exist. It is critical to determine which disease is clinically active in order to appropriately tailor therapy. Though both disorders share similar neurologic manifestations, antibody testing for AQP4-IgG and MOG-IgG may help identify coexisting NMOSD. It is imperative to identify coexisting SLE and NMOSD as

treatment differs, and inappropriate treatment can lead to irreversible and severe neurologic outcomes in children.

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