International Journal of Advances in Medicine
Sriharsha T et al. Int J Adv Med. 2023 Feb;10(2):167-170
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20230070

Case Report

An interesting case of seronegative neuro myelitis optica spectrum disorder

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Received: 21 December 2022
Revised: 11 January 2023
Accepted: 16 January 2023

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ABSTRACT

Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune disease that causes severe demyelination, especially in the optic nerve and spinal cord with typical clinical manifestations of acute optic neuritis and transverse myelitis. Seventy to ninety percent of the cases of NMOSD test positive for aquaporin 4 IgG Antibodies (AQP4 IgG Ab). Here we report a case of 22-year-old female who presented with history of diffuse headache since 1 week, history of double vision since1 week and excessive day time sleepiness since2 months. Patient had a past history of bilateral and simultaneous optic neuritis 9 months back. On further evaluation patient was diagnosed as seronegative NMOSD (AQP4 IgG Ab–negative).

Keywords: Seronegative neuromyelitis optica, Optic neuritis, Aquaporin-4 IgG antibodies

INTRODUCTION

Neuromyelitis optica (NMO) is a chronic inflammatory autoimmune disease of the central nervous system (CNS) characterized by acute optic neuritis (ON) and transverse myelitis (TM).[1]

International panel for NMO diagnosis (IPND) was established with the goal of developing improved diagnostic criteria. Core clinical characteristics to diagnose as NMOSD include: optic neuritis, acute myelitis, area postrema syndrome presenting with unexplained hiccups or nausea and vomiting, acute brainstem syndrome, symptomatic narcolepsy or acute diencephalic clinical syndrome, and symptomatic cerebral syndrome with NMOSD typical brain lesions.[2]

To diagnose as NMOSD with AQP4-IgG, it should include at least 1 core clinical characteristic and positive test for AQP4 IgG Ab and exclusion of alternate diagnosis. To diagnose as NMOSD without AQP4-IgG and unknown status of AQP4 IgG, and at least 2 core clinical characteristics should be present, out of which one should be either optic neuritis or acute myelitis with longitudinal extension of transverse myelitis (LETM) or area postrema syndrome, dissemination in space (2 or more different core clinical characteristics) and fulfilment of additional MRI requirements and negative for AQP4 IgG Ab.[2]

Additional MRI requirements include: acute optic neuritis showing normal brain MRI or optic nerve MRI with T2 hyper intense lesions or T1 enhancing lesions extending over optic nerve length or involving optic chiasma, acute myelitis with intra medullary lesion extending over >3 contiguous segments, area postrema syndrome with lesions in dorsal medulla or area postrema, and acute brainstem syndrome with peri ependymal brain lesions.

CASE REPORT

A 22-year-old female who presented in April 2022 with history of diffuse headache since 1 week, history of double

vision since 1 week, history of excessive sleepiness in the day time such as dozing off while watching television, while eating and while reading and interacting with people since 2 months. There was no history of head trauma, involuntary movements, hallucinations or drug intake. Patient had past history of blurring of vision and diminished vision 9 months back and on evaluation patient found to have bilateral optic neuritis and was treated with steroids for 3 weeks. On examination, General examination was normal. Vitals were stable. On neurological examination higher mental functions were normal, crossed diplopia was noted, though extra ocular movements were full. Bilateral fundus examination was normal. Other cranial nerve examination, Motor system examination and cerebellar examination were normal. Other systemic examination was normal.

Laboratory investigations showed normal complete blood count, liver function tests and kidney function tests. Patient was evaluated further for demyelinating disorders. Cerebrospinal fluid (CSF) analysis showed normal leucocytic count, normal protein (9.07 mg/dl) and glucose (75 mg/dl) and negative for oligoclonal bands (OCB). Test for serum aquaporin 4 IgG antibodies was found to be negative, test for myelin oligodendrocyte glycoprotein antibody (MOG Ab) was negative. MRI brain and spine was done and showed hyper intense T2 lesions or T2 weighted images in periaqueductal region meso-diencephalic junction and dorsal medulla (Figures 1-3). Visual evoked potential (VEP) revealed bilateral P100 showing prolonged latency and pattern reversal of VEP suggestive of bilateral optic neuritis. Epworth sleepiness scale was done and the score is 13 out of 24 which is suggestive of moderate excessive daytime sleepiness.

Considering the location of characteristic brain lesions and simultaneous bilateral optic neuritis on VEP, patient was treated as a case of seronegative NMOSD. Patient was given pulse therapy with methyl prednisolone 1 gm intravenously for 5 days. Patient was improved symptomatically after methyl prednisolone injection. Patient was discharged with oral steroids and tablet azathioprine orally 100 mg/day. Patient was kept on regular follow up and has remained asymptomatic till last review 1 month back (November 2022).

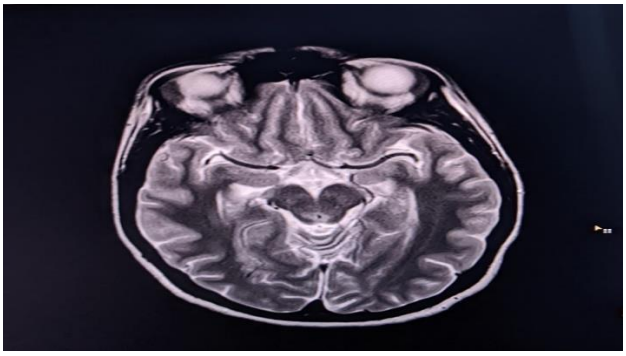

Figure 1: Hyper intense T2 lesions or T2 weighted images in periaqueductal region.

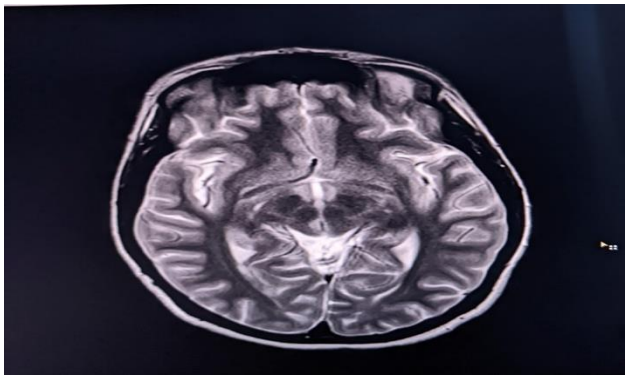

Figure 2: Hyper intense T2 lesions or T2 weighted images in meso-diencephalic junction.

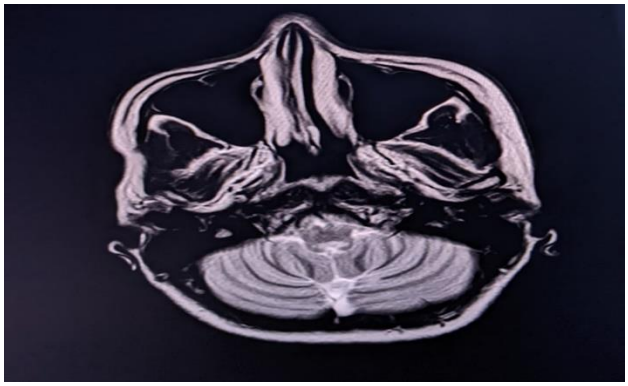

Figure 3: Hyper intense T2 lesions or T2 weighted images in dorsal medulla.

DISCUSSION

Giovanni Battista reported the first description suggestive of NMO in 1844, but it was only in 1894 that Eugene Devic and his student Fernand Gault first used the term neuromyelitis optica.[3] The prevalence of NMOSD ranges from 0.5–4/100,000, with highest incidence of up to 10/100,000 in blacks. AQP4-IgG Ab are present in up to 70–90% of NMOSD patients and is highly specific for the disease. In a recently conducted study 42% of seronegative NMOSD individuals tested positive for MOG Ab whereas, none of the seropositive NMOSD individuals showing MOG Ab.[4]

Haider et al reported a case of 27-year-old female who came with complaints of unexplained vomiting, dysphagia, dysphonia, and food regurgitation. MRI brain showed a small nonspecific area of signal abnormality in the right dorsal medulla. AQP4-IgG Ab was negative, hence confirmed the diagnosis of seronegative NMOSD with acute brainstem syndrome. This is an unusual presentation of seronegative NMOSD which is limited specifically to acute brainstem symptoms in the absence of optic neuritis and transverse myelitis symptoms.[5]

Khadka et al reported a case of 35 year male with longitudinally extending transverse myelitis and Optic

Neuritis with confirmation of AQP4 IgG Ab negative status with presentation of bilateral below knee weakness and incontinence of bowel with MRI findings showing longitudinally extending transverse myelitis (LETM). He concluded that thorough investigation and high suspicion is the key in the detection of NMOSD with seronegative status as per the newly revised criteria. Prompt diagnosis and management is required to reduce the relapse of the disease.[6]

Gibbons et al conducted a study on NMOSD in 725 patients out of which only 7% were seronegative NMOSD. Their study concluded that the usual presentation is longitudinal myelitis with/without optic neuritis with absence of CSF-OCB and typical brain lesions help to distinguish this disease from multiple sclerosis.[7]

Dauby et al conducted a study retrospectively on AQP4 positive NMOSD patients and MOG associated disease (MOGAD) patients. This retrospective analysis confirms that AQP4 positive NMOSD and MOGAD do not only differ by etiology, but also by some clinical features and prognosis. As compared to MOGAD, AQP4 positive NMOSD is typically more frequent in females, occurs at an older age, involves the posterior optic nerve and relapses more frequently.[8]

Hyun et al done a study on CSF glial fibrillary acidic protein (GFAP) levels in double seronegative neuromyelitis optica spectrum disorder (DN-NMOSD). The majority of participants in the AQP4 positive NMOSD group showed significantly higher CSF GFAP levels, while no participant in the DN-NMOSD and MOGAD groups had increased GFAP levels.[9]

Etemadifar et al conducted a study on a total of 145 patients of neuromyelitis optica spectrum disorder. Out of these patients their study reported that there is only 3.4% of cases had presented with acute diencephalic syndrome.[10]

Carlander et al reported a case of 20-year-old female who presented with excessive daytime sleepiness and hypocretin deficiency.[11] Patient was tested positive for anti-aquaporin-4 antibody positive and diagnosed as NMOSD.

Poppe et.al reported two cases of NMOSD who presented with excessive daytime sleepiness with symmetrical hypothalamic lesions although anti-aquaporin-4 antibody titer was not measured in these cases.[12]

Besides the utilization of clinical features, MRI and serum antibody marker in the diagnosis of NMOSD, other modalities such as optic coherence tomography (OCT), visual evoked potential (VEP) and cerebrospinal fluid (CSF) analysis are also useful to confirm the diagnosis of NMOSD. OCT shows more markedly decreased retinal nerve fiber layer thickness and decreased macular volume in NMO/NMOSD than in multiple sclerosis.[13] For the clinical manifestation of ON, VEP has been mainly employed to show subclinical involvement of the optic nerve. The course on NMO can be monophasic or relapsing. It is associated with poor prognosis. Relapsing courses are associated with poorer prognosis.[14]

Our patient presented with excessive daytime sleepiness and double vision and headache and MRI brain showed lesions in periaqueductal region and meso-diencephalic junction and dorsal medulla. Patient was diagnosed as seronegative NMOSD and treated with steroids and patient remained asymptomatic during follow up.

CONCLUSION

This report discussed the case of a 22-year-old female who presented with excessive day time sleepiness which is rare in presentation. Patient also tested negative for AQP4-IgG Ab and MRI findings were positive hence confirming the diagnosis of seronegative NMOSD. Very few cases were reported with seronegative NMOSD. According to previous case studies only 3.4% of cases were reported as acute diencephalic syndrome. Hence patients who are negative for AQP4 IgG Ab and presented with symptomatic Narcolepsy should be evaluated further for the diagnosis of seronegative NMOSD and proper management should be given to prevent further relapse.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Sriharsha T, Sathish KM, Kumar AA, Raghav RJ, Vikrannth V, Raghavan V, Rajendran K. An interesting case of seronegative neuro myelitis optica spectrum disorder. Int J Adv Med 2023;10:167-70.