JPSIM Journal of Pakistan Society of Internal Medicine

Case Report

A Rare Case of Area Postrema Variant (Intractable Vomiting and Hiccups) of Neuromyelitis Optica Spectrum Disorder (NMOSD) in a 25 Year Female Patient

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Abstract

Nausea and vomiting are commonest complaints in an emergency department in hospitals. Neuromyelitis optica spectrum disorders (NMOSDs) are CNS autoimmune disorders related to highly specific biomarkers for astrocytic water channel aquaporin-4. Area postrema syndrome (APS) is described as intractable nausea, vomiting, or hiccups that can be intermittent or may persist longer than 48 hours, and other pathologies should be excluded, as may be misdiagnosed with digestive system disorders.

Key Words: Neuromyelitis optica spectrum disorders, Chemo trigger zone, Intractable nausea.

How to cite this:

Hussain J, Banaras F, Tahir T, Fayyaz R, Ashfaq M, Usman M, Raza A. A Rare Case of Area Postrema Variant (Intractable Vomiting and Hiccups) of Neuromyelitis Optica Spectrum Disorder (NMOSD) in a 25 Year Female Patient. J Pak Soc Intern Med. 2023;4(2): 152-154

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DOI: https://doi.org/10.70302/jpsim.v4i2.2332

Introduction

In the accident and emergency department (A&E) of a hospital, the most abundant complaints of patients are epigastric discomfort, nausea, and vomiting with an admission rate of about 20%.[1] The most common differential diagnosis usually is gastroenteritis followed by migraine and cerebellar disorders. One of the rare neurological presentations of nausea and intractable vomiting is due to a lesion in the area postrema related to the fourth ventricle, a sensitive chemo trigger zone (CTZ), suggesting area postrema syndrome. Our experience with this patient evidenced that the area postrema variant of NMOSD is related to neurologist domain, and may missed by gastroenterologist and other physicians of medical field.

Neuromyelitis optica spectrum disorders (NMOSDs) are the CNS autoimmune maladies related to a highly specific biomarker for astrocytic water channel aquaporin-4,[2] usually found in the diencephalon, spinal cord, and a circumventricular organ lining the cavity of the fourth ventricle, highly vascularized, devoid of the blood-brain barrier(BBB), and act as vomiting/ hiccup center known as area postrema.[3] Area postrema syndrome (APS) is described as intractable nausea, vomiting, or hiccups (INVH) that can be intermittent or may persist longer than 48 hours, and other pathologies should be excluded, as may be misdiagnosed with digestive system disorders.4Unluckily, misdiagnosis of area postrema syndrome, a variant of NMOSD has catastrophic outcomes due to succeeding acute myelitis, optic neuritis, brainstem lesion and ultimately leads to neurological deficit. Sometimes APS can lead to respiratory failure and even cardiac arrest.[5]

Neuromyelitis optica spectrum disorder (NMOSD) has extensive diagnostic intricacy because of its multiple manifestations. This spectrum comprises optic neuritis, longitudinally extensive transverse myelitis (LTEM), area postrema syndrome (APS), acute cerebral syndrome, acute brainstem syndrome, and acute diencephalic syndrome.[6] Area postrema syndrome(APS) exhibits intractable nausea, vomiting, and sometimes hiccups found in 12% of NMOSD patients.[7] The APS diagnostic criteria in AQP-4 seropositivity comprises persistence of intractable nausea, vomiting, and hiccups for at least 48 hours, not relieved by antiemetic and excluding gastrointestinal disorders. In seronegative cases the MRI for the dorsal medullary lesion is mandatory. All medical specialists and gastroenterologists should be familiar with the area postrema variant of NMOSD for

proper management and referral.[8]

Case Report:

A 25-year young female patient, previously with no co-morbidities presented to the neurology outpatient department (OPD) with chief complaints of transient visual obscurations, decrease in vision, and difficulty in walking for the last four months. The event was sudden in onset, with vision loss for a few hours, and then recovers. However, she was complaining of blurring of vision, sometimes scotomas (dark blind spots in her visual field), followed by difficulty in walking and needed support to go washroom and minor daily activities. On general physical examination, there is a young female patient slightly confused, disoriented, good built, with GCS 10/15 not fully obeying the commands. The patient has mild pallor but no jaundice, clubbing, koilonychia, leukonychia, edema, thyromegaly, or lymphadenopathy was found. Neurological examination revealed altered mental status, normal muscle bulk, normal tone, power in upper limbs is 4/5, while lower limbs, in proximal and distal muscle, is 1/5, reflexes are normally elicited, right plantar is upgoing, left one is mute, broad-based gait with positive Romberg sign. The sensations of pain, temperature, vibration, and proprioception were impaired up to the umbilicus at T10 level as compared to the upper trunk where sensations are highly appreciated. The patient was admitted to the neurology unit and the diagnosis made was longitudinal extensive transverse myelitis (LETM), a variant of NMOSD based on hyperintense signals in the thoracic spinal cord involving three segments (figure1) and seropositivity of Aquaporin-4 antibodies. The full blood count and metabolic profile i.e. Serum sodium, serum potassium, serum calcium, and random blood sugar in a normal range. The treatment started during admission was an injection of methylprednisolone 1g IV for 5 days followed by 4 cycles of plasmapheresis. The patient was discharged on oral prednisolone 60mg/day with a tapper-off dose along with azathioprine for 6 months. The patient's power was improved to 3/5 in her lower limbs and she was quite well for 1 year. After 1 year she suddenly develops intractable nausea, vomiting, and hiccups that persist for 1 month. She did multiple visits to a gastroenterologist and medical specialist, different antiemetic and 5-HT3 antagonist (ondansetron) was used but the patient remains symptomatic. Finally, She visited a neurologist, MRI brain was done shows a hyperintense lesion in the area postrema just caudal to the fourth ventricle, diagnosis of area postrema syndrome was made (figure 2). She was started on steroids again and astonished by the sudden vanishing of intractable vomiting and hiccups. After that, she married and planned a pregnancy with 1 baby boy despite using azathioprine. The patient was an educated lady, a pharmacist by profession, and counseled for malignancy events, an adverse effect of azathioprine usage.

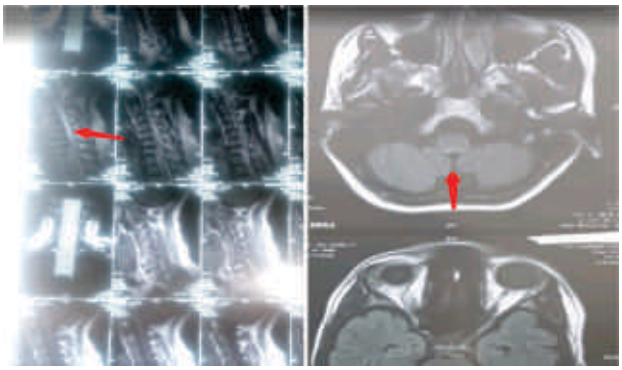

Figure1 *(LETM)* **Figure 2** *(Area postrema lesion)*

Discussion

We present a case of a young lady with 1 month of intractable nausea, vomiting, and hiccups who had multiple visits to gastroenterologists and medical specialists. The correlation between NMO (Neuromyelitis optica) and area postrema syndrome are not well recognized and hardly coexist, easily missed by the non-neurologist. The emergency physician should be aware of this syndrome as nausea and vomiting are common ED complaints and repeatedly have gastrointestinal causes. The area postrema syndrome could be the primary signal of NMO in the absence of other neurological manifestations.

In the past, the clinoradiological features and response to immunomodulators favor a diagnosis of an autoimmune inflammatory process of the central nervous system affecting the spinal cord and brain stem. The basics for the symptoms of intractable nausea, vomiting, and hiccups following the quadriparesis, were added by neuroimaging suggesting the contribution of area postrema, and lastly proven by serological antibody testing. The APS is demarcated as acute or sub-acute, single or multiple, occasional or uninterrupted nausea, vomiting, or hiccups, persisting for at least 48 h, without any other underlying cause. Our patient suffered vomiting and hiccups, sudden at onset, and continued for 4 weeks instead of regular treatment taken by gastroenterologist.[6] A study conducted by Khedr, E.M et al, showed that out of 90 diagnosed NMOSDs patients, twenty(22.2%) patients had unresolved intractable vomiting and hiccups persisted for 3 weeks, seventeen(18.8%) were AQP-4 positive, seven(35%) were considered a clinically isolated syndrome(CIS) of APS, Latter on diagnosed as NMOSD was made after relapse. Thirteen (65%) cases were diagnosed after the neurological deficits, the commonest feature in all patients was acute myelitis, and neuroimaging shows thirteen patients have a lesion in the medulla oblongata near the fourth ventricle. Moreover, 80% of cases show LETM, while 35% have an extension of cord involvement up to area postrema.[9]

Similar results of APS were obtained in the Egyptian case series by Salama at el,[10] had dissimilarity with another Egyptian NMOSD study conducted by Kishk at el in which there is only one case presented with APS reported. In short, the incidence of APS varies among different states ranging from 3% -43% of NMOSD patients.[11]

A case series study conducted by Zhou et al of NMOSD patients with APS variant shows that young females are most commonly affected.[12] Kitley and his colleagues show a relation of AQP4 antibody seropositivity, with area postrema accessible target site in younger population.[13] A international multicentric study conducted by Shosha et al showed that 58-68% APS events lead to transverse myelitis or optic neuritis. Hence, quick diagnosis and commencement of immunosuppressants would inhibit the progress of further overwhelming neurologic deficits.[14] Multiple studies have shown that spinal cord lesions spreading to the area postrema are specific for NMOSD. However, Dubey et al study suggested that it is more specific for AQP4-antibody-positive NMOSD when INVH exists with the extension of a spinal cord lesion to the Area postrema, aiding in the diagnosis of NMOSD-APS along with neuroimaging.[15] The treatment options for acute management of NMOSD are high-dose steroids i.e 1g IV methylprednisolone daily, followed by oral prednisone taper-off. Plasmapheresis is the ideal treatment alternative in refractory cases. The approved immunomodulatory agents are eculizumab (complement factor C5 inhibitor), inebilizumab (CD-19 inhibitor), and satralizumab (IL-6 receptor inhibitor). Rituximab has also revealed a useful effect, with a relapse prevention rate of up to 67%.[16] Other frequently used immunosuppressive drugs are azathioprine, mycophenolate mofetil, and tocilizumab with counseling the patients for associated malignancies.

Conclusion

APS as a core logical variant of NMOSD is not a rare presentation as was formerly assumed and can occur in both AQP4 and MOG-seropositive patients. The clinical features of INVH after the elimination of alternative diagnoses are the most significant pinpointing tool.

Conflict of Interest: *None*

Funding Source: *None*

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