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A Young Lady with Quadriparesis

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Abstract:

Neuromyelitis optica spectrum disorder (NMOSD) is a rare autoimmune disease, causing multifocal CNS inflammation affecting the optic nerves & spinal cord. In the 20th century, 'Devics disease' was considered as a variant of Multiple sclerosis(MS) that spared the brain. However, the discovery of IgG-class antibodies that bind to the water channel aquaporin-4 (AQP4-IgG) in serum from patients with Devic's disease, but not from those with typical MS, established NMO as a distinct entity with a chronic, relapsing course. Our patient, a 42-year-old woman has been suffering from vomiting for 2 months followed by inability to move all extremities for last 7 days. It was the very 1st episode of such type of illness. We are reporting this case to highlight the presentation of NMOSD, which is itself a rare disease, outcropped as 'Area postrema syndrome', an inaugural manifestation in this patient.

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Introduction:

Neuromyelitis optica (NMO) is a rare condition, characterized by myelitis and optic neuritis, which shares a number of clinical and radiological features with multiple sclerosis (MS). The groundbreaking discovery of a novel, pathogenic autoantibody (termed NMO-IgG or AQP4-Ab) in a subset of patients by Dr Lennon and colleagues in 2004, has led to a tremendous increase in interest in NMO. NMO-IgG/AQP4 antibody-positive NMO is now considered a disease entity in its own right rather than a subtype of MS.[1] The first clinical descriptions of NMOSD emerged over a century ago when Devic and Gault documented a series of patients with a monophasic course of bilateral (or rapidly sequential) optic neuritis and myelitis.[2]Six core clinical syndromes have been identified in NMOSD. They are classified by their location: optic nerve, spinal cord, area postrema of the dorsal medulla, other brain-stem regions, diencephalon, or cerebrum. These syndromes are manifested as acute attacks and relapses of neurologic dysfunction, with symptoms that typically evolve over a period of days.[3] Area postrema syndrome is the presenting feature of NMOSD in 10% of patients and occurs at some time during the disease in 15 to 40% of patients.[4,5] The median age at onset of the disorder is 40 years, but the disorder can affect people at any age, and up to 20% of cases are in children or in adults over the age of 65 years. Seropositive disease has a female preponderance that approaches 90%, whereas seronegative cases have an equal sex distribution.[6,7] Up to 3% of cases are familial.[8] Acute attacks of NMOSD, including the initial episode, usually occur in the absence of an identified inciting event, but approximately one third of cases are preceded by an infection, which is often viral, and in rare cases, an acute attack follows vaccination.[9] According to the international consensus criteria, the diagnosis of NMOSD is almost ensured if there is a characteristic first attack and AQP4-IgG antibodies are present.[3] Acute relapses are initially treated with intravenous glucocorticoids, but one study has shown short-term remission of symptoms in only 19% of patients treated with these drugs.[10]

Case summary:

A previously known healthy 42-year-old married, Muslim woman hailing from Chatkhil, Noakhali got admitted to

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Popular Medical College Hospital with inability to move all four limbs for 7 days & breathlessness for 2 days. She also developed urinary incontinence & inability to defaecate in the meanwhile. On query, there was a preceding history of intractable vomiting for 2 months for which she visited local physicians, gastroenterologists & was being treated with PPIs & anti-emetics. But it remained almost uncontrolled. Then 7 days before admission into our hospital, initially she developed gradually increasing weakness of lower limbs, got bed bound, and one day later the same occurred for the upper limbs. She was also having slight blurring of vision on and off. Her speech, orientation, consciousness level remained intact. She had no history joint pain, rash, headache, eye-ache, dry eyes or dry mouth, no lumps/bumps in the body, chest pain, palpitation, increased sweating, alopecia, oral ulcer or fever. She has lost 5 kg weight within the period of illness. On query, she gave history of vaccination against HBV, one month before developing weakness of the limbs. Two days before admission, she developed mild cough, breathlessness & difficulty in swallowing. Her physical examination revealed RR 26 breaths/min, SaO_2 94%, mildly anaemic, Fine crepitations over lower zones of both lungs due to aspiration pneumonia. On neurological examination, higher psychic function was intact. Tone was reduced in all extremities, power 1/5 & 0/5 in right & left lower limbs respectively & 3/5 & 2/5 in right & left upper limbs respectively. All jerks were absent except triceps, planter extensor on right side, absent on left. All modalities of sensation were reduced upto C4 level. Joint position & vibration sense were unaltered. Cranial nerve examination revealed no abnormality. Fundoscopic examination showed mildly blurred optic disc margin on temporal pole of right eye & superior pole of left eye.

On investigation, MRI whole spine revealed long segment extensive inflammatory lesion of whole length of spinal cord, MRI brain showed intra-axial enhancing lesion in lower medulla & inflammation of right optic nerve. Aquaporin-4 antibodies (AQP4-IgG) came positive, but negative Anti-MOG Ab. Besides, CBC showed neutrophilic leucocytosis with Hb 11.6 g/dl, Na 129 mmol/l, K 3.49 mmol/l. CXR showed radio-opaque shadow in the lower lobe of right lung. Upper GI endoscopy revealed single gastric polyp. ANA, S.TSH, FT3, FT4 all were normal.

She was treated with Methylprednisolone, antibiotics, supplementary oxygen, anti-emetic along with care for skin, eyes, bowel & bladder.

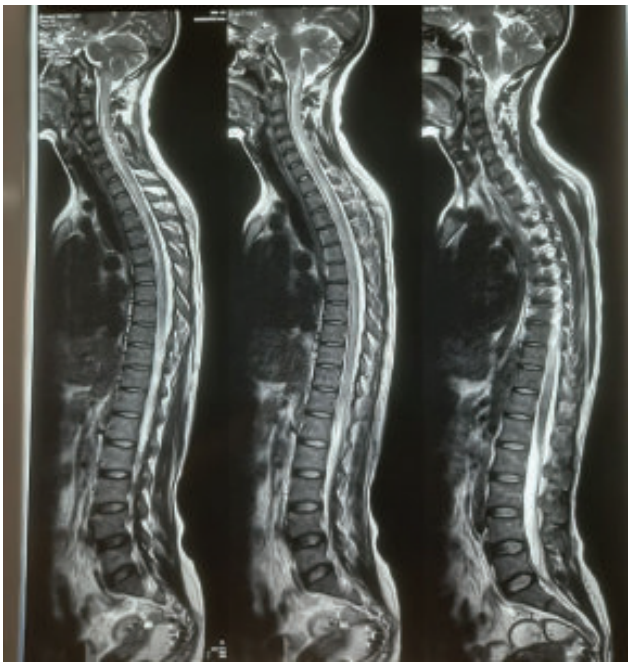

Figure 1: *MRI of spinal cord showing T2 high signal change noted in spinal cord extending from lower medulla to conus medullaris, in our patient.*

Discussion:

NMOSD is a relapsing, autoimmune, inflammatory disorder that typically affects the optic nerves & spinal cord. At least 2/3 of cases are associated with aquaporin-4 antibodies (AQP4-IgG) & complement mediated damage to the central nervous system.

NMOSD accounts for 1 to 2% of all cases of CNS inflammatory demyelinating disease in the United States and Europe, with multiple sclerosis being much more common, but NMOSD accounts for one third or more of cases of CNS inflammation in Asian and other non-White populations. A population-based study in the United States showed a higher prevalence for Blacks (13.0 cases per 100,000 persons) than for Whites (4.0 per 100,000).[11] A case report was done in Bangladesh in 1994 on NMOSD following chicken pox infection.[22]

The sentinel attack involves the optic nerve or spinal cord in more than 85% of affected adults. Patients with optic neuritis present with unilateral or bilateral visual loss or scotoma, dyschromatopsia, and ocular pain exacerbated by eye movement that is not distinguishable from optic neuritis in multiple sclerosis or from an idiopathic form.[2] Area postrema syndrome is the presenting feature of NMOSD in 10% of patients and occurs at some time during the disease in 15 to 40% of patients. Vomiting lasts a median of 2 weeks and, in up to two thirds of cases, presages an attack of optic

neuritis or myelitis. The syndrome can accompany myelitis when a destructive cervical lesion ascends into the brain stem, or it may be isolated and caused by nondestructive dorsal medullary lesions.[4,5]

Confirmation that an attack is due to NMOSD is greatly aided by the detection on MRI of characteristic lesions in the brain, optic nerve, optic chiasm, or spinal cord.[12] In the acute phase, T2-weighted MRI sequences may show new or enlarging inflammatory lesions, and T1-weighted sequences obtained with gadolinium may show enhancement of actively inflamed lesions. Abnormalities on orbital MRI have a predilection for the optic chiasm or the adjacent posterior optic nerve but may occupy the full length of the nerve. MRI of the spinal cord typically shows longitudinally extensive transverse myelitis, defined as a lesion that is at least three contiguous vertebral segments in length.[9,13] Although this pattern is characteristic of NMOSD, about 15% of sentinel myelitis attacks are associated with a shorter lesion that simulates multiple sclerosis.[14] Detection of a dorsal medullary lesion with the use of MRI is confirmatory of area postrema syndrome, but the lesion is small and visible for only a few days.[3]Seen on MRI scans, focal lesions in the brain stem, diencephalon, or cerebrum, even those that are asymptomatic, may also be indicative of NMOSD.[3]

About 80% of cases are seropositive,according to the international consensus criteria, the diagnosis of NMOSD is almost ensured if there is a characteristic first attack and AQP4-IgG antibodies are present.[3] The standard serum AQP4-IgG reference test is a live cell–based flow-cytometric assay with more than 80% sensitivity and more than 99% specificity.[15,16]

Attacks of NMOSD usually reach peak severity in several days, plateau, and then spontaneously subside, frequently leaving moderate-to-severe and permanent functional deficits.[10] Neurologic impairment is stable or may diminish during remission, but relapses lead to stepwise accrual of disability. The type, frequency, and severity of relapses are influenced by age, sex, and ethnic group.[17,18]

Five years after the onset of disease, nearly one quarter of untreated AQP4-IgG–seropositive patients require gait assistance, more than 40% are blind in at least one eye, and mortality approaches 10%.[17,19] Hospitalization rates and use of health resources are substantial.[20] In contrast to relapsing multiple sclerosis, in which late neurodegeneration and progressive functional deterioration may dominate the clinical picture, NMOSD rarely has a secondary progressive course.[21] Up to half of patients with NMOSD and AQP4-IgG have other detectable serum autoantibodies (e.g., thyroperoxidase, antinuclear, and Ro/SS-A antibodies), and one third have an autoimmune disease, most commonly thyroiditis, systemic lupus erythematosus, or Sjögren's syndrome.[9]

Four randomised controlled trials have tested the efficacy of three new therapies (eculizumab, satralizumab, and inebilizumab) for patients with neuromyelitis optica spectrum disorder that all showed a benefit in preventing future attacks.Efficacy, safety, tolerability, and practical considerations, including potential cost, differ for each drug and might affect the rate of use in real-world populations of patients with neuromyelitis optica spectrum disorder. [22]

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