Devic's disease in young male

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Abstract: Neuromyelitis optica (NMO) is a rare disease, common in white females and rarely reported in males [1]. It is usually associated with recurrent demyelinating spectrum that is autoimmune in nature[1].The diagnosis is usually confirmed by antibody biomarkers; however, they can be negative and lead to more dilemma in diagnosis. In addition, the prognosis and course of the disease varies in seronegative NMO from seropositive NMO[2]. Both populations get comparable care, with novel strategies being researched for patients with seronegative NMOs. A 18 Year old boy presented with gradual onset weakness in all four limbs with vision loss. His brain MRI also revealed changes suggesting optic neuritis. The patient met the criteria for diagnosis of NMO by having optic neuritis and myelitis by imaging studies with positive aquaporin-4 antibodies (AQP4-Ab).

ABBREVIATIONS:
AQP4-aquaporin-4
IgG-immunoglobulin G;
LETM-longitudinally extensive transverse myelitis lesions;
NMOSD-neuromyelitis optica spectrum disorders.

Keywords: Neuromyelitis optica spectrum disorders.

INTRODUCTION

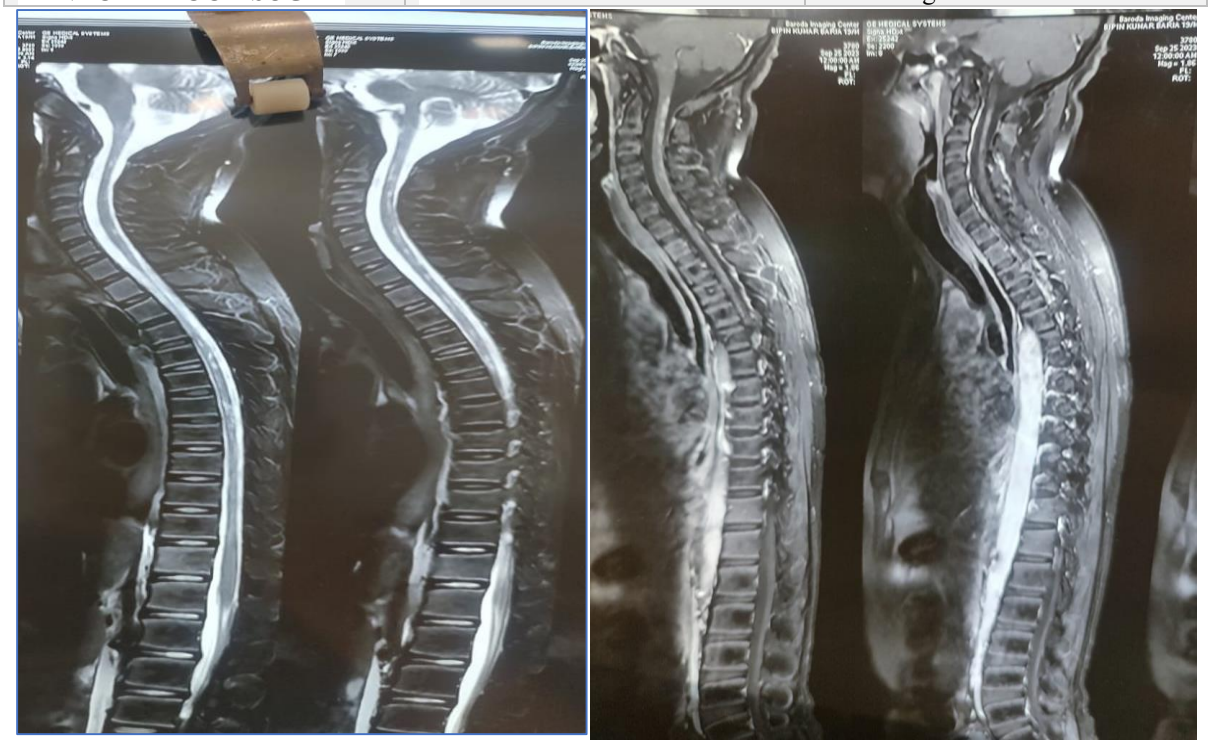
Neuromyelitis optica (NMO) is a rare, female predominance disease associated with recurrent autoimmune and demyelinating spectrum with cardinal manifestations. The diagnosis of NMO requires the following criteria: presence of optic neuritis, myelitis, involvement of spinal cord lesions in 3 or more segments by magnetic resonance imaging (MRI), initial MRI of the brain not meeting the criteria of multiple sclerosis, and seropositive aquaporin-4 antibodies (AQP4-Abs) [1]. Highly specific biomarker antibodies targeting the water channel protein AQP4 provided an insight into the immunopathology of NMO, which also served to predict relapse ratio [1,2]. Early differentiation between NMO and MS is particularly important because the course of NMO is more severe and the treatment strategies for attack prevention are different. Immunotherapy approved for MS treatment is ineffective and appears to aggravate NMO[3]. Immunosuppressive therapy is the treatment of choice for reducing NMO relapses.

CASE REPORT

We present 18 year old male with no comorbidities presented to Dhiraj general hospital with complaints of weakness in all four limbs which was gradual onset and rapidly progressive and bilateral symmetrical since 4months. Later onset patient developed decrease in vision since 2 months in right eye and then in left eye since 15 days. No history of reddening of eyes and neck stiffness and headache. He also had hiccups on and off. He also had urinary incontinence and constipation. There is no significant family history or any past history. On fundus examination bilateral disc pallor was present. Visual evoked potential testing was done showing of No response in Right eye and in left eye prolonged response (pattern and flash) was recorded. MRI brain showing of multiple abnormal hyperintense signal seen on Flair/T2w images without restricted diffusion involving fronto-parietal lobe white matter, centrum semiovale and corona radiata. Diffuse small calibre of bilateral distal optic nerve and optic chiasm present was suggestive of Atrophy. Also Demyelinating lesions were present in spinal cord. There was no history of memory deficit, other cranial nerve palsies. CSF analysis was Showing of protein – 60mg/dl, glucose-106mg/dl(corresponding plasma glucose- 200), total cell count- 10/cumm in which lymphocytes were 100%.ANA is negative. Antibody against aquaporin-4 is positive and antibody against MOG is negative. On presentation pulse- 74min, Bp- 110/70mmhg, CNS- conscious, oriented to time,place and person. Tone was reduced in bilateral lower limb and was normal in both upper limb. Power was 3/5in upper limb and in lower limb Right knee flexor was 3/5, knee extensor was 5/5, hip flexor and extensor was 2/5 bilaterally. On Lt. side Knee flexor was 3\5 and knee extensor was 5\5. Reflexes were exaggerated in all four limbs. Pupils were reactive to light in both eye but perception of light was totally absent in right eye and in left eye finger counting at 3 feet was present and plantars were flexors bilaterally. Flaccid paraplegia with sensory loss below C2 was detected. Chest X ray was normal. A diagnosis of neuromyelitis optica spectrum disorder was made using the "International Panel for NMOSD Diagnosis (IPND) Diagnostic Criteria" (Table 1)(10). This patient treated with Inj. Methylprednisolone (1gm) for 3 days. In view of persisting paraparesis 5 cycle of Plsmapheresis was done and

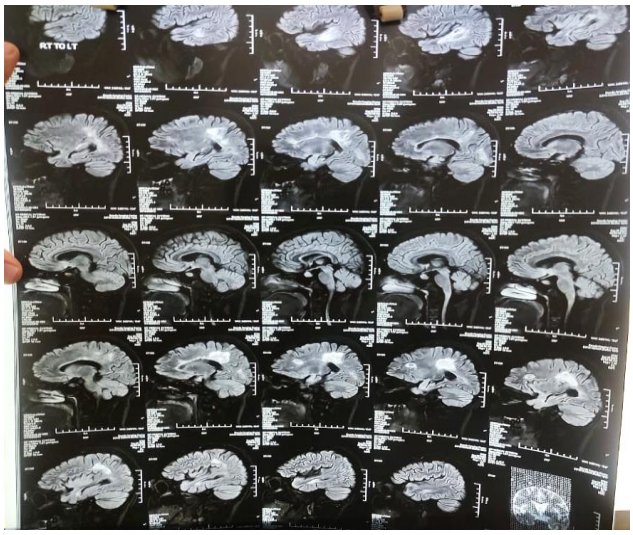
prednisolone 1mg/kg (40mg) PO daily for one month, and tapered over three-to-six months. The patient was scheduled to initiate azathioprine, 50 mg, PO twice daily.

Investigation	Patient's value	Reference value
Hemoglobin	13.1	13-17 gm/dl
WBC	16500	4000-11000 cells/mm3
PLATELET	2.47	1.5-4.5 lacs/mm3
SODIUM	138	135-145 mEq/L
POTTASIUM	4.1	3.5-5.5 mEq/L
S.CREATININE	0.8	0.6-1.3 mg/dl
RANDOM BLOOD SUGAR	122	70-140 mg/dl



A **B**

(MRI of the cervical **(A)** and thoracic **(B)** spinal cord. Sagittal T2-weighted imaging showed longitudinally extensive hyperintense lesion extending from C2 to T8.)



C

(MRI brain showing of multiple abnormal hyperintense signal seen on FLAIR/T2w images without restricted diffusion involving fronto-parietal lobe white matter, centrum semiovale and corona radiata)

Table 1[10]

The 2015 International Panel for NMOSD Diagnostic Criteria for Adult Patients

Diagnostic criteria for NMOSD with AQP4-IgG

1. At least one core clinical characteristic

2. Positive test for AQP4-IgG using best available detection method (cell-based assay strongly recommended)

3. Exclusion of alternative diagnoses

Diagnostic criteria for NMOSD without AQP4-IgG or NMOSD with unknown AQP4-IgG status

1. At least two core clinical characteristics occurring as a result of one or more clinical attacks and meeting all of the following requirements:

(a) At least one core clinical characteristic must be optic neuritis, acute myelitis with LETM, or area postrema syndrome

(b) Dissemination in space (two or more different core clinical characteristics)

(c) Fulfillment of additional MRI requirements, as applicable

2. Negative tests for AQP4-IgG using best available detection method, or testing unavailable

3. Exclusion of alternative diagnoses

Core clinical characteristics

1. Optic neuritis

2. Acute myelitis

3. Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting

4. Acute brainstem syndrome

5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions

6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions

Additional MRI requirements for NMOSD without AQP4-IgG and NMOSD with unknown

AQP4-IgG status

1. Acute optic neuritis: requires brain MRI showing (a) normal findings or only nonspecific white matter lesions OR (b) optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium enhancing lesion extending over >1/2 optic nerve length or involving optic chiasm

2. Acute myelitis: requires associated intramedullary MRI lesion extending over >3 contiguous segments (LETM) OR >3 contiguous segments of focal spinal cord atrophy in patients with history compatible with acute myelitis

3. Area postrema syndrome: requires associated dorsal medulla/area postrema lesions

4. Acute brainstem syndrome: requires associated periependymal brainstem lesions

Discussion

Neuromyelitis optica spectrum disorder is an autoimmune disease of the central nervous system with a predilection for the optic nerves, spinal cord, and brain stem regions. IgG antibody to aquaporin-4, a water channel protein in the astrocyte foot processes of central nervous system structures, defines the epicenter of autoimmunity. Serum AQP4-IgG is detected in 80% of patients with NMOSD. Half of AQP4-IgG negative NMOSD are categorized under myelin oligodendrocyte glycoprotein (MOG)-antibody positive oligodendrocytopathic NMOSD. It is still unclear how double-negative NMOSD works. NMOSD is driven by complement and antibody-mediated cellular toxicities, which are immunopathologic factors.[1, 2] Peaks in NMOSD epidemiological frequencies have been observed in middle-aged adults and individuals of non-White descent.[6]

Clinical syndromes in NMOSD include bilateral optic neuritis, longitudinally extensive transverse myelitis, area postrema syndrome, acute brain stem syndrome, diencephalic syndrome, and symptomatic cerebral syndrome. Area

postrema syndrome presents with intractable hiccups, nausea, and vomiting. Narcolepsy, insomnia, and inappropriate diuresis are features of diencephalic syndrome. Acute brain stem syndrome presents with cranial nerve palsy, long tract signs, and ataxia. Acute confusional state, delirium, and seizures are features of symptomatic cerebral syndrome.[1–4] This patient fulfilled the diagnostic criteria for "NMOSD with unknown AQP4-IgG" as evidenced by the presence of two core clinical characteristics such as optic neuritis and acute myelitis. It has shown dissemination in space with two sites. Differential diagnoses of the case include multiple sclerosis, systemic lupus erythematosus (SLE), neurosarcoidosis, and subacute combined neurodegeneration (SCND). Patchy, peripheral, short spinal segment lesions are a common finding in multiple sclerosis.[3,4] The lack of other clinical features of SLE and negative serological test for ANA exclude opticospinal lupus. Normal chest X-ray finding does not favour sarcoidosis. Absence of risk factors for vitamin B12 deficiency like malabsorption of any cause makes SCND less likely. Acute attacks of NMOSD are usually treated with intravenous methylprednisolone.

MANAGEMENT

Corticosteroids are the main choice in the acute phase. Intravenous methylprednisolone is administered with a dose of 1-1.5 grams in 3-5 days [14, 15, 5, 11, 13]. Intravenous dexamethasone at a dose of 5 mg can be also a choice of corticosteroids [14]. Therapeutic plasma exchange (TPE) can be considered if the patient's condition does not improve or neurological symptoms worsen. Therapeutic plasma exchange dosage is carried out by giving 5-7 cycles in a period of 2 weeks with a dose of 1-1.5 plasma per time TPE [14, 15, 13, 12, 16].Maintenance therapy with immunosuppressive drugs such as oral prednisone, azathioprine , mycophenolate mofetil and rituximab has shown benefit in reducing subsequent relapses. Inebilizumab, eculizumab, and satralizumab are approved immunotherapies to treat NMOSD and prevent relapses, and reduce burden of accrual neurological deficits. Sivelestat, ublituximab, ravulizumab, and aquaporumab are newer biologics under clinical evaluation.[7]

CONCLUSION

The case emphasizes the existence of neuromyelitis optica spectrum disorder in clinical settings of the developing world. High index of suspicion of this rare disease is required to avoid delayed diagnosis and treatment.

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