Case study

A case report of Neuromyelitis Optica: an effective combination of Immunosuppressants, Corticosteroids and Plasmapheresis

Abstract

Agirl in her teens presented with decreased sensation in the right half of the face and right half of the tongue associated with dysphagia, vomiting, and aphasia for 2 weeks with sudden onset flaccid quadriparesis for 7 days with diminished vision in both eyes and double vision for 5 days, with no history of fever, convulsions, diarrhoea, headache, palpitations, shortness of breath, loss of consciousness or features suggestive of bladder and bowel involvement with no history of trauma or similar episodes in the past.

MRI Brain revealed features favouring a demyelinating condition. MRI Spine, autoimmune encephalitis panel, ANA profile, and VEP were normal. NMOSD Screen (IIFD-EUROIMMUN) MOG & AQP-4 analysis showed a positive titre of Anti-NMO antibodies. She was treated with intravenous Methylprednisolone, oral prednisolone, and mycophenolate mofetil with 5 rounds of plasmapheresis. In subsequent follow-up, there was an improvement in power and gait with an improvement in vision.

Comment [S1]: Impact research and suggestion

Comment [S2]: Add reference and research gap

Introduction

Neuromyelitis Optica spectrum disorder (NMOSD), formerly known as neuromyelitis Optica (NMO) or Devic's syndrome or Devic's disease refers to an autoimmune aggressive demyelinating disorder of central nervous system.

This report describes the management of a girl with a rare disease that can lead to permanent blindness, which can be avoided with prompt and aggressive treatment.

NMOSD is characterised by frequent attacks of acute optic neuritis and transverse myelitis, which can occur simultaneously or be separated by a variable length of time [1-5]. It is associated with serum aquaporin-4 immunoglobulin G (AQP4-IgG) antibodies [1-3]. NMOSD occurs more frequently in the form of polyphasic (90%) such as optic neuritis or myelitis, or both concurrently. Evidently, the monophasic form has only occurred in 10% of cases [1-2].

We report here a case of NMO occurring in a teenage girl who recovered dramatically with steroids, immunosuppressants, and plasmapheresis, and the dreaded complication of optic neuritis was avoided with early intervention.

Case Presentation

A girl on her teens, resident of West Bengal, India, hailing from a poor socioeconomic background reported to the outpatient clinic of IPGME&R-SSKM Hospital, Kolkata with decreased sensation on right half of the face and right half of tongue, associated with dysphagia, vomiting and aphasia for the past 2 weeks. The patient also complained of sudden onset weakness of both lower and upper limbs (lower>upper) for the past 7 days. The patient presented with diminished vision in both eyes and double vision for the last 5 days. There was no history of fever, convulsions, headache, palpitations, diarrhoea, shortness of breath, or loss of consciousness. The patient gave no history of trauma, nor were there any similar episodes in the past. Bowel and Bladder functions were normal.

Upon examination, the patient was disoriented with a Glasgow Coma Scale (GCS) of 10/15 (E4V1M5). The general examination was unremarkable. Neurological examination demonstrated a Lateral Rectus palsy in the right eye, nystagmus in the left eye while in adduction, global hyporeflexia, power 2/5 in lower limbs and 3/5 in upper limbs, and a non-reactive plantar reflex. An ophthalmological exam demonstrated that visual acuity was diminished. Fundoscopic examination showed normal optic discs and normal macula with no papilledema. Other systemic examinations were unremarkable. Based on clinical findings, a demyelinating pathology was considered provisionally, although ruling out other relevant aetiologies was mandatory.

Upon admission, arterial blood gas analysis was done to rule out hypokalaemia, but electrolyte levels were within the normal range. To rule out any demyelinating pathology, a Nerve Conduction Study (NCS) was performed - which was normal. Following this, the patient was planned for an MRI of the Brain and Spinal Cord (Plain and Contrast) with a VEP Study. MRI of the Brain (***figure 1***) revealed a hyperintense large focus in the right middle cerebellar peduncle extending to adjoining cerebellar hemisphere, and brainstem in FLAIR and T2WI appearing isointense to hypointense in precontrast T1WI with no enhancement or restricted diffusion, with smaller, similar lesions in the medial thalami larger on the left side, head of the left caudate nucleus and putamen and subcortical white matter of left superior frontal gyrus – features favouring a demyelinating condition like multiple sclerosis or NMOSD. T2W images of axial and coronal sections **(figure 2)** of optic nerve and chiasma showed no radiological abnormalities. MRI of the Spine (***figure 3***) revealed no abnormalities. VEP Study was normal. To rule out any infective pathology and albumino-cytological dissociation, the cerebrospinal fluid study was done, in which the cell type and count, protein, sugar, chloride, and adenosine deaminase were within normal limits. It also revealed no abnormal cells, no bacterial/mycobacterial cells, and the culture showed no growth. Blood tests showed normal renal and liver function with mildly elevated CRP and normal levels of procalcitonin. Blood culture showed no growth. Neuroviral markers were sent to rule out Scrub Typhus, Japanese B Encephalitis, and Herpes simplex virus – which came out negative. So, to rule out any autoimmune pathology, an ANA profile and Autoimmune encephalitis panel consisting of NMDA, GABAB1/B1, AMPA1, AMPA2, and CASPR2 were sent - which turned out negative as well. CSF and blood paired oligoclonal band testing were sent to rule out multiple sclerosis which came out to be negative. At last, the NMOSD Screen (IIFD-EUROIMMUN) MOG & AQP-4 analysis was done, which showed a positive titre of Anti-NMO antibodies, finally reaching the diagnosis.

The patient was treated with intravenous Methylprednisolone 1 gram per day for 3 days followed by oral prednisolone 1mg/kg per day. But, with poor improvement, oral mycophenolate mofetil 500mg twice a day was added to the regimen along with 5 rounds of plasmapheresis on alternate days with fresh frozen plasma and parenteral albumin over a course of 10 days. The patient improved dramatically and was ambulatory within a week without support. She was discharged with proper physiotherapy and kept on oral mycophenolate mofetil 500mg twice a day and oral prednisolone 40mg once daily, which was tapered on an outpatient basis.

She was asked to follow up regularly in the clinic. In subsequent follow-up over 5 months, there is a marked improvement in power and gait with an improvement in vision. The patient is now completely healthy with a return to regular activities with no incidence of recurrence or deterioration.

Discussion

Comment [S3]: dd a discussion that illustrates that the case can be overcome with various treatments. It is necessary to study the scope of treatment based on patient characteristics

Neuromyelitis optica (NMO), belonging to the Neuromyelitis optica spectrum disorder (NMOSD), is an aggressive demyelinating disorder that primarily affects the optic nerves and spinal cord. With a predominance towards females with a ratio of 3-9: 1 female to male, NMO primarily affects adults between the ages of 30.5 and 55.2 years. [1,6,7] It was first reported by Sir Thomas Clifford Allbutt in 1870, followed by Eugene Devic and Fernand Gault in 1894. The latter studied 16 patients who lost their vision in one/both eyes within weeks of sudden onset of weakness of limbs. They introduced the French term "neuro-myélite optiquë aiugë" to show a new syndrome characterized by myelitis and acute optic neuritis. [8]

The disorder is chiefly characterised by episodes of optic neuritis and transverse myelitis, leading to visual impairment, loss of vision, pain, muscle weakness, and other neurological symptoms. In the spectrum of demyelinating diseases, NMOSD is distinct from the phenotypes of multiple sclerosis (MS) and other similar diseases. Researchers at The Mayo Clinic described the NMO antibody directed against aquaporin-4 (AQP4), which led to the development of NMOSD, quite different from multiple sclerosis, in the year 2004. Unlike MS, NMO is usually characterized by bilateral optic neuritis (rare in MS) or unilateral and the myelitis is transverse and longitudinally extensive (rare in MS) and has progressive symptoms (unlike MS). [9] NMO is associated with the presence AQP4 antibodies which target and damage the protective covering of nerve fibers, leading to inflammation and demyelination. The destruction of myelin leading to astrocyte death and cavitating necrosis in affected tissues occurs via IgG antibody directed against Aquaporin-4. [8,9]

In a practical setting, the key clinic-radiological differences between Optic Neuritis (ON) due to other demyelinating diseases and NMOSD are necessary to be elucidated. Optic neuritis presents with sudden, unilateral loss of vision associated with pain, with pain worsened by eye movement. In contrast, NMOSD-related optic neuritis may have a more severe course and often involves simultaneous or sequential bilateral optic nerve involvement. While Optic Neuritis that is associated with multiple sclerosis (MS) recurs less frequently, NMOSD-related optic neuritis, which can have relapsing episodes.Optic neuritis in MS occurs mostly as an isolated episode with little to no systemic symptoms, whereas NMOSD, in lieu of involvement of spinal cord and brainstem is likely to be associated with nausea, vomiting, hiccups and respiratory muscle weakness. Radiological differences are key to understanding the diaspora of demyelinating disorders and help clinch the diagnosis. While OpticNeuritis associated with MS demonstrate higher likelihood of disseminated CNS involvement with multiple white matter lesions,NMOSD-related optic neuritisshows fewer or no typical MS-like lesions. The extent of optic nerve involvement is significant to distinguish between the disorders with NMOSD demonstrating more extensive and longitudinal involvement, with the inflammation extending at least half the length of the optic nerve on MRI. In contrast, optic nerve lesions in MS-related optic neuritis are less severe and shorter. Transverse myelitis involving multiple spinal cord segments is a hallmark of NMOSD unlike ON associated with MS.

The Diagnostic Criteria for Neuromyelitis Optica Spectrum Disorder has sub categories depending on the presence of AQP4-IgG.[5] For AQP4-IgG positive patients - 1. At least 1 core clinical characteristic

2. Positive test for AQP4-IgG using best available detection method (cell-based assay strongly recommended)
3. Exclusion of alternative diagnoses.
For patients NMOSD without AQP4-IgG or NMOSD with unknown AQP4-IgG status - 1. At least 2 core clinical characteristics occurring as a result of one or more clinical attacks and meeting all of the following requirements: a. At least 1 core clinical characteristic must be optic neuritis, acute myelitis with LETM, or area postrema syndrome b. Dissemination in space (2 or more different core clinical characteristics) c. Fulfillment of additional MRI requirements, as applicable2. Negative tests for AQP4-IgG using best available detection method, or testing unavailable3. Exclusion of alternative diagnoses.
The core clinical characteristics include – 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 lesions6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions.
The radiological findings that guide the diagnosis include 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 gadoliniumenhancing 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

SLE, Sjogren's Syndrome or Myasthenia gravis, and certain post-infectious states like EBV or CMV are often associated with NMO, however, no such association is seen in our case.
Although our case didn't show the normal CSF changes (increased white count with a neutrophilic predominance and raised IgG levels), the neuroimaging did reveal demyelinating changes in the right cerebellar peduncle, adjoining cerebellar hemisphere, and brainstem with smaller, similar lesions in the thalami, left corpus striatum, and subcortical white matter of left frontal lobe.
The treatment for NMO consists of Methylprednisolone (20-30 mg/kg/day up to 1 gm/day) for 3 to 5 days followed by tapering over 6 weeks. Other therapeutic modalities include plasmapheresis [10], Rituximab, Azathioprine, and Human IVIg. Steroids like Methylprednisolone has shown temporary improvement in the condition with concomitant use of cyclophosphamide to prevent recurrence, as was shown by Rilling et al (1999). No recurrence was reported for 18 months in patients treated with prednisolone and azathioprine for 2 months. [8,11]
Despite the available therapy, NMO or NMOSD has a guarded prognosis with evidence demonstrating 20% of patients to be functionally blind in one or both eyes and the development of permanent paraplegia/monoplegia in 31% of cases. [12]

Conclusion

Early recognition of NMO and NMOSD is very important alongside other demyelinating disorders because early detection can stave off the debilitating effects of the disease as much as possible.Optic neuritis could be avoided by prompt and aggressive treatment with corticosteroids, immunosuppressants, and plasmapheresis. As NMO is a rare disease, ruling out other common demyelinating pathologies is crucial.NMO can lead to major complications like optic neuritis, respiratory failure, paraplegia, or monoplegia, with a high mortality rate. Hence, awareness of the diagnosis among physicians is necessary and prompt treatment is crucial.

References

Comment [S4]: add the latest references from reputable journals for at least the last 5 years

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Figures

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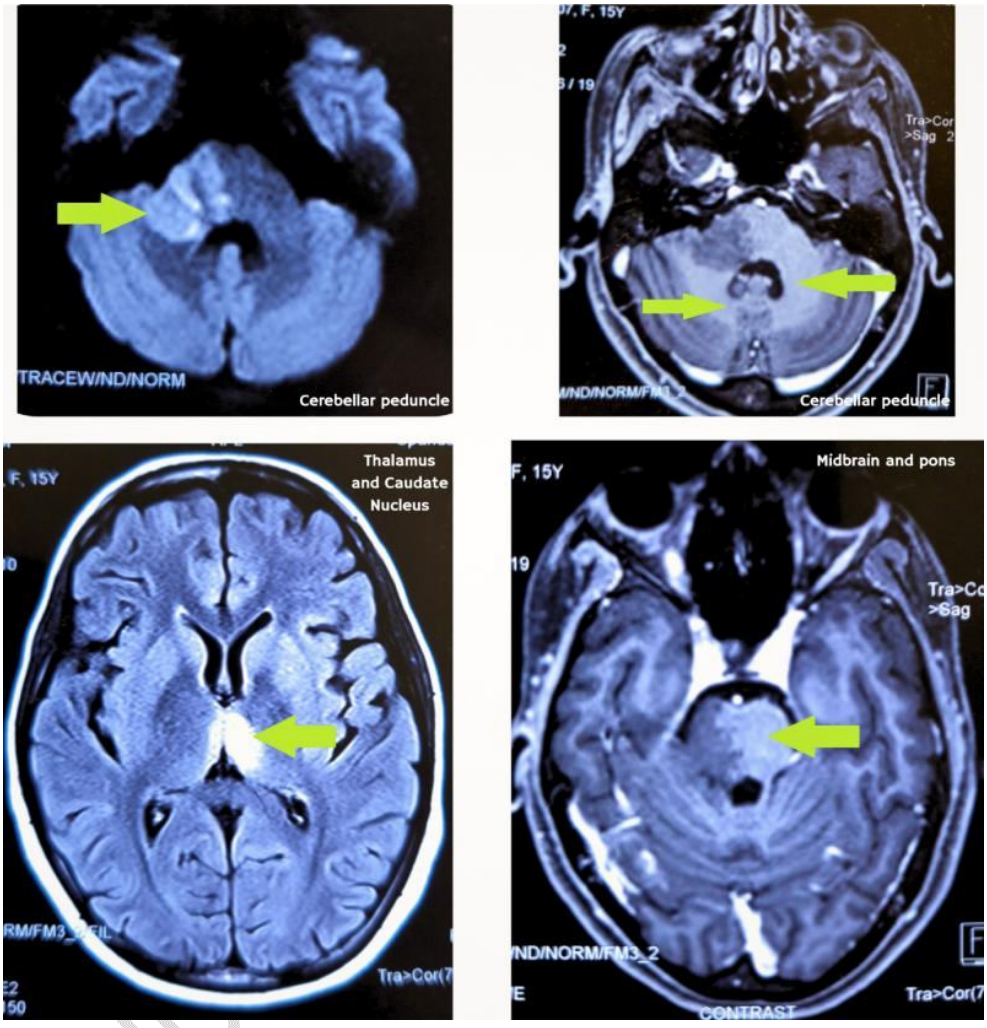

Figure 1: MRI Brain showing lesions in thalamus, caudate nucleus, cerebellar peduncle and brain stem(arrow).

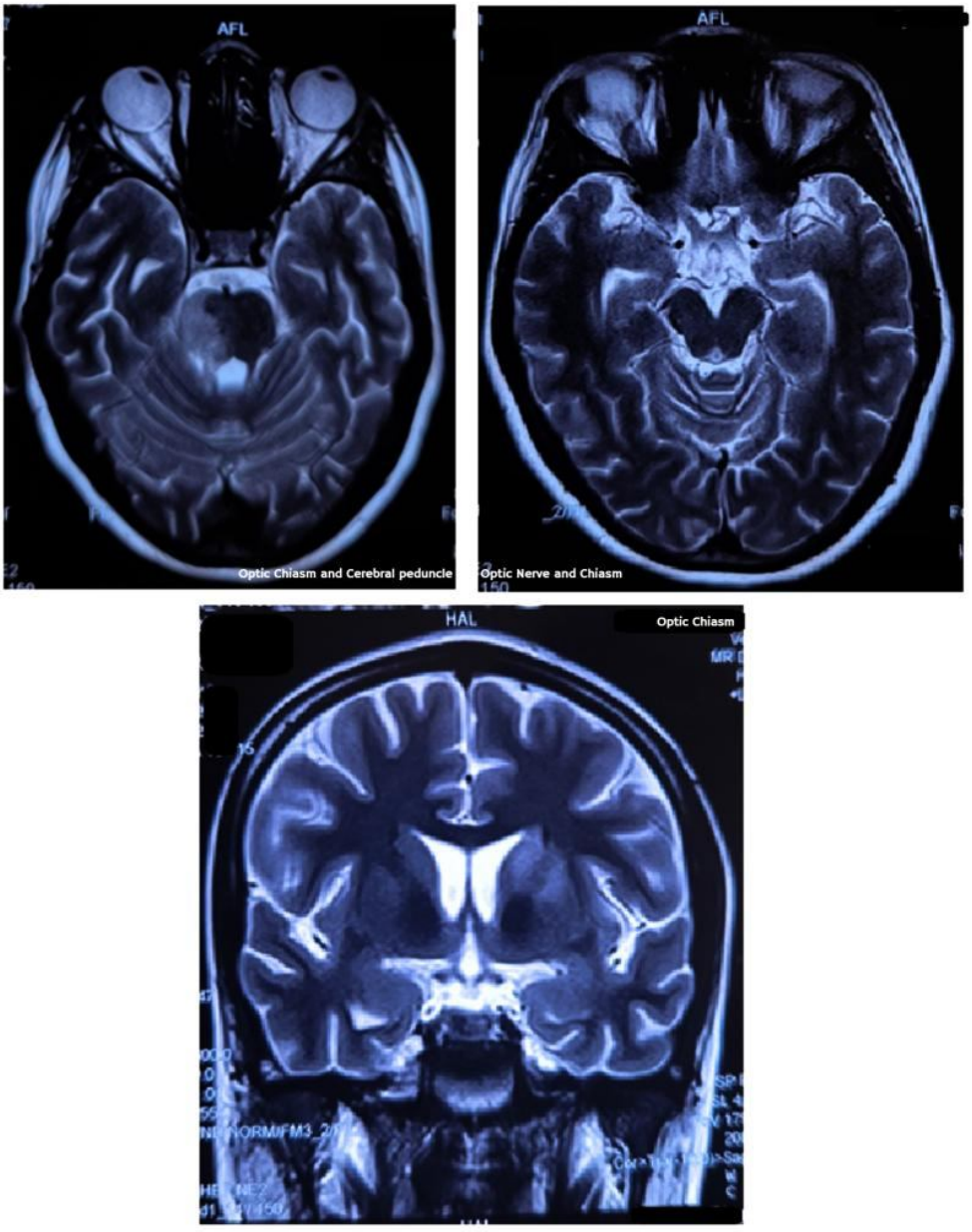

Figure 2: T2W images of axial and coronal sections of optic nerve and chiasma showing no radiological abnormalities

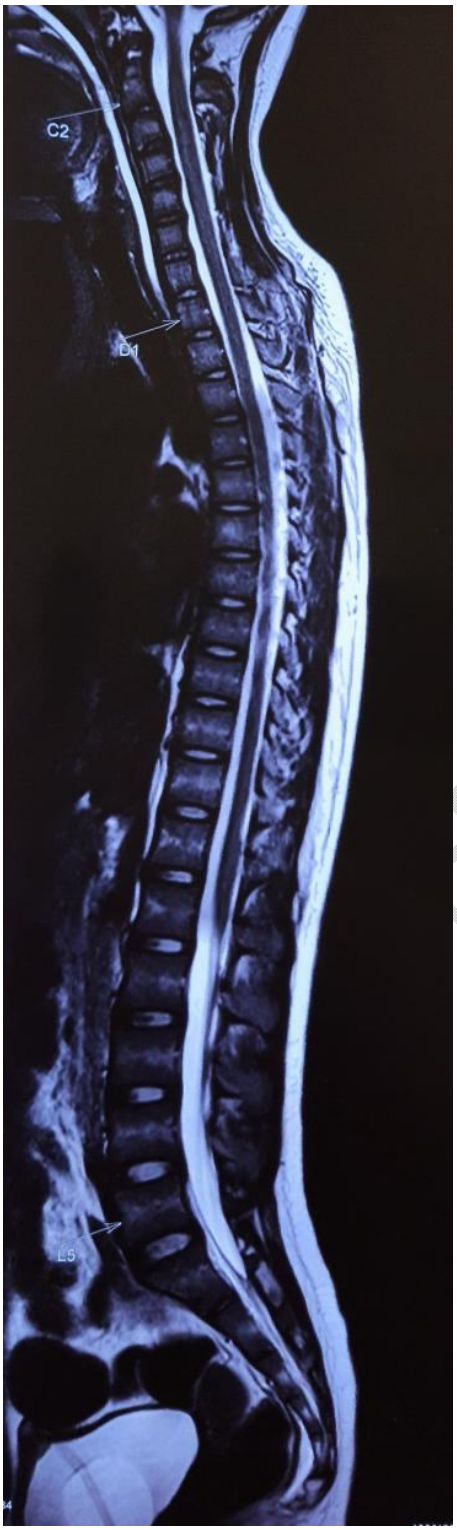

Figure 3: MRI Spine showing no spinal pathology