CASE REPORT

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Neuromyelitis Optica – Sometimes a Misnomer

Paromita Das, Nitasha Pasricha**, Pratap Singh***, MPS Chawla*****

Abstract

Neuromyelitis optica spectrum disorder is an autoimmune, demyelinating disease of the central nervous system. Characteristic clinical features include longitudinally extensive transverse myelitis and optic neuritis. Around 70 - 80 per cent cases are associated with aquaporin-4 antibodies. Treatment involves high-dose corticosteroids and immunosuppressants to prevent relapse. Here we present a case of seropositive NMO without optic neuritis.

Key words: Neuromyelitis optica, longitudinally extensive transverse myelitis, aquaporin-4, optic neuritis.

Introduction

Neuromyelitis optica is an autoimmune disorder of the central nervous system. It's prevalence in India is 2.6/ 1,00,000[1] and shows a high female preponderance. It is classified under the entity – NMOSD (neuromyelitis optica spectrum disorder). Earlier it was considered to be the optico-spinal variant of the more commonly encountered disease – Multiple sclerosis (MS). After the identification of aquaporin-4 antibodies in 2004, the two diseases were identified as separate entities[2]. However, aquaporin-4 antibodies are not universal to the disease, and are not found in 30 per cent cases of NMO, which are diagnosed based on the more stringent MRI criteria as elucidated by the 2015 International Diagnostic Criteria for NMO-SD. The core clinical characteristics include acute myelitis, optic neuritis, area postrema syndrome, brainstem syndrome, acute diencephalic syndrome and symptomatic cerebral syndrome[3]. On magnetic resonance imaging, longitudinally extensive transverse myelitis (LETM) which is defined as contiguous involvement of three or more spinal segments is specific for NMO compared to multiple sclerosis which presents as acute transverse myelitis. Similarly, optic neuritis in NMO is also longitudinally extensive and has a predilection for the posterior segment of the optic nerve and can be bilateral at presentation, whereas multiple sclerosis usually affects the anterior segment and is usually unilateral. Area postrema syndrome is the presenting feature in 12% of cases[4]. Neuromyelitis optica is rarely seen without the simultaneous or successive involvement of the optic nerve and the spinal cord. However, since the discovery of aquaporin-4 antibodies, presence of optic neuritis is not mandatory for diagnosis of NMO. Presence of any one of the core clinical characteristics along with aquaporin antibodies, clinch the diagnosis of NMO, after exclusion of other possible aetiologies. Our case highlights one such rare instance where neuromyelitis optica was seen without the presence of optic neuritis. We present a case of seropositive NMO without optic neuritis, from a tertiary care hospital in North India.

Case summary

Our case is a 38 years, right-handed female, who presented with gradually progressive, asymmetrical weakness of both lower limbs (right more than left), proximal weakness followed by distal weakness, and a sensation of gradual stiffening of both lower limbs. This was associated with sensory loss in the form of decreased touch, pain and temperature in both lower limbs compared to the upper limbs. There was no bladder or bowel involvement, no involvement of the muscles of eyelid, deglutition, speech or respiration and no diurnal variation. She had no band-like sensation over trunk, no visible wasting of any limb or any abnormal limb movement. There was no history of cranial nerve involvement. However, prior to the onset of weakness, she did not have any fever or respiratory or gastrointestinal infection or recent vaccination. She was recently diagnosed to have hypothyroidism and was on replacement therapy for the same. She had a past history of tuberculous meningitis for which she had taken a full course of ATT. She had no other co-morbidities. She followed a vegetarian diet. She had four normal vaginal deliveries with no bad obstetric history.

Clinical examination revealed normal higher mental function, no spinal deformity, normal visual acuity of 6/6 in both eyes, both pupils normal is size and reaction, no relative afferent pupillary defect, normal colour vision, normal visual fields in both eyes and normal fundus examination. There was clasp-knife rigidity in both lower limbs. Tone was also increased in both upper limbs with presence of Hoffman's

Post-Graduate Resident, **Senior Resident, ***Associate Professor, ****Professor and HOD, Department of Medicine, ABVIMS and Dr Ram Monahor Lohia Hospital, Baba Kharak Singh Marg, New Delhi - 110 001.

Corresponding Author: Dr Nitasha Pasricha, Senior Resident, Department of Medicine, ABVIMS and Dr Ram Monahor Lohia Hospital, Baba Kharak Singh Marg, New Delhi - 110 001. Phone: 8448870267, E-mail: nitashapasricha2404@gmail.com.

and Wartenberg's sign. Power was 4/5 across joints of upper limb and 1/5 across hip, knee and ankle joints of right lower limb, and 3/5 in left lower limb. Deep tendon reflexes were brisk throughout with presence of sustained ankle clonus. Abdominal reflex was absent bilaterally, and bilateral planters were extensor. There was loss of pain and temperature sensations along with impaired vibration and position sense up to the level of the anterior-superior iliac spine on both sides. However, there was no sensory involvement of the upper limb. Lhermitte's sign was present on examination. Cerebellar, autonomic functions were normal. Gait could not be evaluated in our patient as she was unable to bear weight in lower limbs.

Based on history and examination, a provisional diagnosis of spastic quadriparesis due to cervical myelopathy was made, and baseline laboratory investigations were done. Blood investigations revealed normocytic, normochromic anaemia (haemoglobin: 7.4 gram/deciliter), total leucocyte count of 9,700 per microliter, platelet count of 250,000 lac per deciliter, normal ESR, normal kidney function test, normal liver enzymes, normal vitamin B12 and folate levels. Lipid profile showed hypertriglyceridaemia (triglyceride: 260 milligram/deciltre). HIV, hepatitis B, hepatitis C, VDRL serology were non-reactive. Thyroid function test revealed primary hypothyroidism: TSH: >100 IU/l (high), free T3: 0.46 nanogram/deciliter (low) and free T4: 3.31 microgram/deciliter (low). Anti-TPO antibody was within normal limits. Chest X-ray and non-contrast CT scan of head were within normal limit. Cervical spine X-ray revealed straightening of cervical lordosis. X-ray of thoracic spine was within normal limits.

Contrast-enhanced MRI (CE-MRI) of whole spine with focus on cervical spine was done. It revealed long segment T2-hyperintense intramedullary signal extending from C6-D8 vertebral levels causing its mild expansion with patchy enhancement at D5-D6 level (Fig. 1). This was suggestive of longitudinally extensive transverse myelitis (LETM) in our patient. CE-MRI brain was within normal limits.

Differential diagnosis of LETM includes NMOSD, idiopathic, systemic lupus erythematosus (SLE), Sjogren's syndrome, spinal tumours, dural arterio-venous fistulas, acute disseminated encephalomyelitis (ADEM), and multiple sclerosis[5]. Accordingly, further work-up was done. Cerebro-spinal fluid analysis showed cell count of 5 cells, all mononuclear; protein: 122 mg/dl; sugar: 66 mg/dl; ADA: 0.84 IU/l (normal < 5 IU/l); IgG index – normal. Serum aquaporin 4 IgG was positive. Serum MOG antibody was negative. Serum ANA, anti-Ro antibody, anti-La antibody, APLA profile were negative. So, a final diagnosis of LETM due to neuromyelitis optica was made. She was started on injection methylprednisolone 1 gram intravenous daily for five days, followed by tablet prednisolone 40 mg once daily

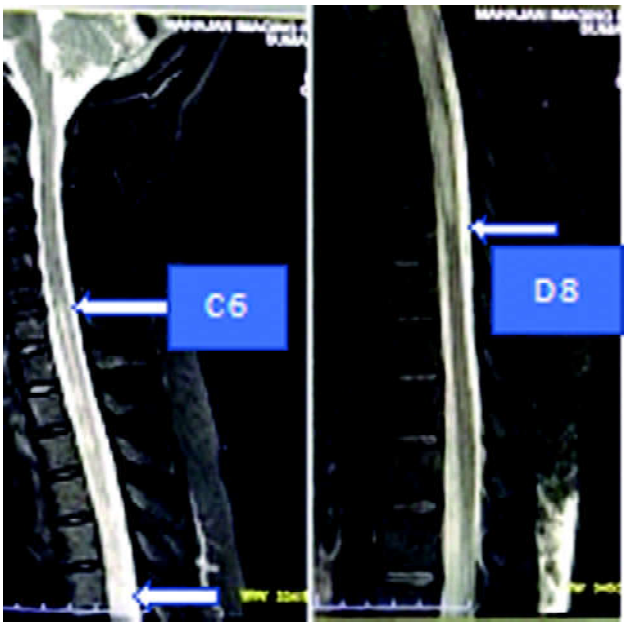

Fig 1: *CEMRI spine showing longitudinally extensive transverse myelitis from C6-D8 level.*

and tablet azathioprine 50 mg twice daily. Physiotherapy of both lower limbs was also initiated during hospital stay. Rehabilitation measures during the recovery period like use of crutches while walking, and avoiding physical exertion, were explained to the patient and her family members. She had no optic involvement during her course of stay in hospital and Visual-evoked potential study was normal in both eyes (Fig. 2). She improved symptomatically, gradually regained motor power in both her lower limbs and was able to walk with support. She was discharged after three weeks of oral steroids with plan to follow-up closely for relapse of myelitis and/or new onset optic neuritis while simultaneously optimizing the dose of immunosuppressant.

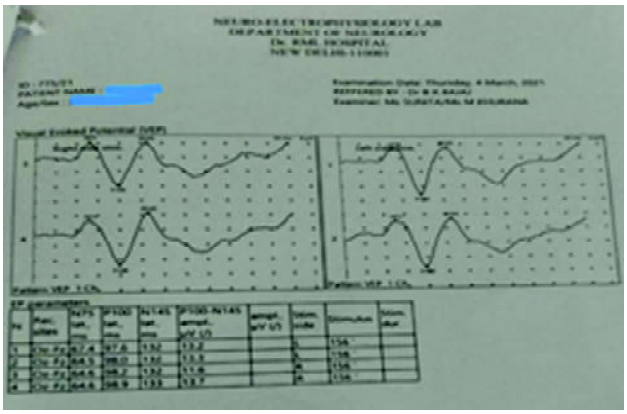

Fig 2: *Visual-evoked potential study showing normal P_{100} latency in both eyes.*

Discussion

Neuromyelitis optica is a demyelinating disease of the central nervous system. According to 2015 Internatinal diagnostic criteria for NMO-SD[3], seropositive NMO requires the presence of at least one core clinical characteristic among the following – optic neuritis, acute myelitis, area postrema syndrome, brainstem syndrome, acute diencephalic syndrome, symptomatic cerebral syndrome, along with presence of aquaporin-4 IgG antibody and exclusion of alternative diagnosis. Seronegative cases account for upto 30 per cent of NMO and they require more stringent criteria – presence of at least two core clinical criteria which must include acute myelitis with LETM or optic neuritis or area postrema syndrome with evidence of dissemination in time and space. Aquaporin-4 is widely distributed in the body with highest concentrations in the foot process of the astrocytes of the brain and spinal cord[6] which accounts for the classical clinical presentation of myelitis and optic neuritis. Antibody directed against this antigenic target causes compliment mediated lysis of the astrocytes which then leads to the widespread demyelination. NMO can be primary or secondarily associated with other autoimmune conditions like SLE, Sjogren's syndrome, etc., presence of aquaporin-4 antibody with LETM confers a risk of relapse of fifty per cent within 12 months[7]. The disease follows a relapsing course and seropositive cases are associated with higher degrees of relapse. NMO without optic neuritis is rarely encountered, as previously reported Flores-Alfaro *et al* in BMJ Case Reports CP 2019.

In our case, the presence of longitudinally extensive transverse myelitis along with the presence of aquaporin-4 antibodies clinched the diagnosis of NMO. However, it is worthwhile to note that around 30 - 40% cases will be seronegative NMO.

Standard treatment in the acute phase involves pulse methylprednisolone one gram for five days followed oral prednisolone at the rate of 1 mg/kg which is gradually tapered off. If no improvement is seen within days of administration of steroids, plasma exchange should be initiated. Some data support plasma exchange as first line therapy for relapse.

In the absence of treatment, fifty per cent patients are wheelchair bound or blind within the first five years of diagnosis, and there is a thirty per cent mortality rate[8]. This makes it imperative to promptly diagnose and initiate long-term immunosuppression for these patients to reduce both mortality and morbidity associated with NMO. Long-term immunosuppression is initiated at the first attack of seropositive NMO. Most commomly used agents are mycophenolate mofetil and azathioprine. The choice of agent depends on the age of the patient with azathioprine being selected in younger females. B-cell depleting therapy rituximab is given a second line therapy.

Learning points

1. Neuromyelitis optica is a distinct disease entity from multiple sclerosis and can have involvement of parts of central nervous system other than spine and optic nerve.
2. Rare instances of sparing of optic nerve in NMO have been reported, thus questioning the nomenclature of the disease.
3. NMO antibody (aquaporin-4) has a proven role in diagnosis of this disease, and criteria of diagnosis differ based on presence or absence of these antibodies.
4. Spinal cord involvement in the form of longitudinally extensive transverse myelitis is specific for NMO, and useful differentiating point from multiple sclerosis where it is more classically single segment involvement.

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