A Rare Variant of Neuromyelitis Optica

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Abstract

Absence of antibodies against Aquaporin 4 (AQP4) in the serum in a case of Neuromyelitis Optica (NMO) is rare. Although the AQP4 +ve variant of NMO is currently considered as a type autoimmune disease (autoimmune astrocytopathy or autoimmune astrocytic channelopathy), the cause of the AQP4 –ve variant is still unknown. Here we present a case of a 28 year old female who presented with sub-acute onset of central vertigo, nystagmus, diplopia and vomiting with recent exaggeration of symptoms and was subsequently diagnosed as case of AQP4 –ve Neuromyelitis Optica.

Devic’s disease or Neuromyelitis Optica (NMO) is an inflammatory disorder which is aggressive and characterized by recurrent attacks of optic neuritis (ON) and myelitis. The attacks ON is unilateral in some cases of NMO, while in other cases it can be bilateral as well and the attacks of myelitis severe and transverse both of which are rare in multiple sclerosis (MS). Besides, the myelitis in NMO is typically longitudinally extensive, and involves three or more contiguous vertebral segments. Also in contrast to MS, progressive symptoms do not occur in NMO.¹ In spite of the fact that differences exist between NMO and multiple sclerosis (MS), the relationship between NMO and MS has been controversial for a long time.² It is now recognized that in approximately half of the cases there are lesions that involve the hypothalamus thereby causing endocrinopathy, the lower brainstem presenting as interactable hiccoughs or vomiting due to the involvement of the area postrema in the lower medulla; or the cerebral hemispheres producing focal symptoms, encephalopathy or seizures.

Case Report

A 28 year old right handed Hindu housewife was admitted with the chief complaints of vomiting for one and half month, gradually increasing vertigo with nystagmus and generalized weakness for one month. The vertigo was more at upright postures than while supine. Her sensory modalities seemed to be intact. From a few days prior to admission her condition started worsening rapidly. Her walks now were not only interrupted by vertigo but began to require support with to and fro swaying of the body. Nystagmus and vertigo increased, vomiting persisted, she began to have hiccoughs, visual acuity decreased and she developed double vision. There was constipation and urinary retention with frequent small volumes of urine. Her history of past illness, personal or family history, or menstrual history revealed no significant facts.

On examination she was underweight (BMI: 16.45 kg/m²) and she had mild pallor. Examination of cranial nerve II revealed a visual acuity decreased to perception of hand movement with impaired color vision. Fundoscopy (Figures 1 A, B) revealed features of bilateral optic neuritis. Examination of the cranial nerve III, IV, and VI revealed grade III nystagmus and mild bilateral intranuclear ophthalmoplegia. Muscle tone was increased across all the joints in both the upper and lower limbs. The power was mildly reduced across all the major joints of both the upper and lower limbs in all ranges of motion with most of them being 4/5 with a power of even 4-5 noted in hip adduction and knee flexion. Abdominal reflex was bilaterally absent in all the three quadrants, and plantar was bilaterally extensor. The supinator jerk (2+/4), knee jerk (3+/4) and ankle jerk (2+/4) were all brisker than normal. All primitive reflexes were absent and sensory modalities intact. There was presence of truncal titubation. Finger - nose test, finger - finger nose test and heel - toe test were all mildly impaired and the patient had a broad based ataxic gait.

Laboratory investigations revealed normal blood counts, normal liver and kidney function tests. Serum electrolytes were mildly deranged (Na+: 129 meq/l and K+: 2.7 meq/l) which were subsequently corrected with replacement. Urine routine examination revealed normal values and so did her CSF studies. She was negative for HBS Ag, HCV Ab, HIV and ANA. Ultrasonography of the whole abdomen revealed normal findings. The non-contrast CT scan of the brain revealed no abnormality. MRI (Figure 2) of the cervical-dorsal spine (T2W sagittal and post gadolinium) revealed long segment T2 Hyperintensities in the dorso-lateral aspect of the spinal cord involving more than 3 segments from lower border of C3 vertebra up to the C6-C7 disc which are hyperintense on T2 and showed patchy enhancement. MRI (Figure 3) of the brain revealed altered signal intensities in the peri-aqueductal and right dorso-lateral medulla, which were hyper-intense on T2 and flair without any abnormal blooming or diffusion restriction and without any enhancement. Indirect ophthalmoscopy revealed acute optic neuritis. Repeat CSF was positive for oligoclonal band but repeated serum samples sent for AQP4 antibody turned out to be negative.

To diagnosis a case as NMO, it requires the presence of the absolute criteria, viz. 1) optic neuritis and 2) acute myelitis and two out of three supportive criteria, viz. 1) brain MRI not meeting the criteria for MS at the disease onset, 2) Spinal cord MRI with features of myelitis extending over three or more vertebral segments and 3) NMO IgG seropositive status.³

The patient had fulfilled both the absolute criteria and two out of the three supportive criteria required for

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the diagnosis of NMO except that she was AQP4 antibody negative. So she was finally diagnosed as a case of AQP4–ve neuromyelitis optica. Patient was treated with 1gm methyl-prednisolone for 5 days followed by tapering dose of oral prednisolone and discharged with 10 mg of oral prednisolone and 50 mg of azathioprine. The patient improved remarkably.

Discussion

NMO is a syndrome with diverse causes. Up to 40% of the cases have a systemic autoimmune disorder which is often systemic lupus erythematosus, Sjögren’s syndrome, perinuclear antineutrophilic cytoplasmic antibody (p-ANCA) – associated vasculitis, myasthenia gravis, Hashimoto’s thyroiditis, or mixed connective tissue disease. In other cases onset may be associated with acute infection with Varicella-Zoster virus, Ebstein–Barr virus, HIV or tuberculosis. Rare cases of NMO appear to be paraneoplastic and usually associated with breast lung and other cancers. NMO may often be idiopathic. It usually disables the patient over time and at times ending up with respiratory failure from cervical myelitis, permanent blindness and permanent paralysis of one or more limbs. AQP4 antibodies can be found in the sera of about two-third of the patients with a clinical diagnosis of NMO. However in the rest one-third patients, repeating the test using a different assay or CSF is helpful to clarify whether they in fact carry AQP4 antibodies.

Important pathological features of NMO include perivascular deposition of IgG and complement in the perivascular space, granulocyte and eosinophil infiltrates and hyalinization of the vascular walls. It is these features which distinguish NMO from other demyelinating diseases such as MS and acute demyelinating encephalomyelopathy.

Acute attacks of NMO can be treated with high-dose glucocorticoids (intravenous methyl-prednisolone 1-2 g/d for 5 – 10 days followed by a tapering dose of oral prednisolone). Plasma exchange has also been used in certain cases that do not respond to glucocorticoids alone. Natalizumab is highly effective in MS but may not be sufficiently effective for NMO. In case of relapses, treatment can be done with either mycophenolate mofetil (250 mg bid gradually increasing to 1000 mg bid), β cell depletion depletion with rituximab or a combination of glucocorticoids (500 mg intravenous methyl-prednisolone daily for 5 days; then oral prednisone 1 mg/kg/day for two months, followed by taper) plus azathioprine (2mg/kg/d started on week 3).

References