

Neuromyelitis optica with simultaneous occurrence of optic neuritis and transverse myelitis

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ABSTRACT

Neuromyelitis optica (NMO) is an inflammatory demyelinating disease that preferentially affects the optic nerves and spinal cord. It has a worldwide distribution and distinctive clinical, neuroimaging and laboratory findings that distinguish it from multiple sclerosis. In most cases there is a long interval between the optic neuritis and myelitis but approximately 10 to 20% can have near simultaneous occurrence of both. We report a case of NMO presenting with symptoms and signs of optic neuritis and transverse myelitis which was later confirmed by neuroimaging and laboratory findings. The acute attack was treated with pulse therapy of corticosteroid and subsequently the patient was maintained on Azathioprine and tapering dose of oral steroid. This case highlights a neurological disorder that is increasing in prominence and may become more relevant in our region with increased diagnostic utility of antibody testing.

Keywords: Demyelination, optic neuritis, transverse myelitis, NMO IgG, aquaporin 4

INTRODUCTION

Demyelinating diseases of the central nervous system (CNS) are a common cause of neurological disability, usually affecting young adults. Multiple sclerosis (MS) is the most common form of CNS demyelinating disorder and is an immune mediated inflammatory disease that targets myelinated axons in the CNS, destroying the myelin and the axons to a variable extent. In most cases the disease

has a relapsing and remitting pattern characterised by short episodes of neurologic defects with complete or near complete resolution but a minority experience steadily progressive neurologic deterioration.¹

Demyelination can also result from infectious, toxic, metabolic and vascular processes. While most people with an autoimmune demyelinating disease are genetically predisposed to the development of myelin disruption, other causes of demyelination may occur sporadically. The autoimmune causes of demyelination include MS and its variants,

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neuromyelitis optica (NMO), acute disseminated encephalomyelitis (ADEM) and acute haemorrhagic leukoencephalopathy. Progressive multifocal leukoencephalopathy is an example of an infectious cause of demyelination, caused by the JC virus. Toxic or metabolic causes of demyelination include carbon monoxide, mercury intoxication, vitamin B12 deficiency, alcohol or tobacco amblyopia. Binswanger's disease is synonymous with vascular demyelination in patients with chronic hypertension.²

NMO, also known as Devic's disease is an uncommon idiopathic demyelinating disease of the CNS that preferentially affects the optic nerve and spinal cord. NMO has been reported in all continents and races but being more prevalent among black and Asian populations, where multiple sclerosis prevalence is usually low.^{2,3} We report a case of NMO and to the best of our knowledge this is the first case of NMO presenting to the Ophthalmology Department of RIPAS Hospital.

CASE REPORT

A 34-year-old Malay lady presented to the ophthalmology emergency clinic with a three day history of blurred vision in her left eye, starting in the upper half of the field of vision that became generalised within a day. There was no associated pain on eye movement. She also had numbness of the left side of the body with heaviness of the left upper and lower limbs. There were no symptoms of bladder or bowel dysfunction. She did not give a history of similar symptoms in the past and there were no relevant medical and family histories.

On ophthalmological examination, her visual acuity in the right eye was 6/6 and in the left eye was appreciation of hand movements only. Her gaze was orthophoric and extraocular movements were intact. There was also no nystagmus. Examinations of the lids, adnexae and anterior segment of both eyes were normal. Direct and consensual pupillary reflexes of the right eye were normal

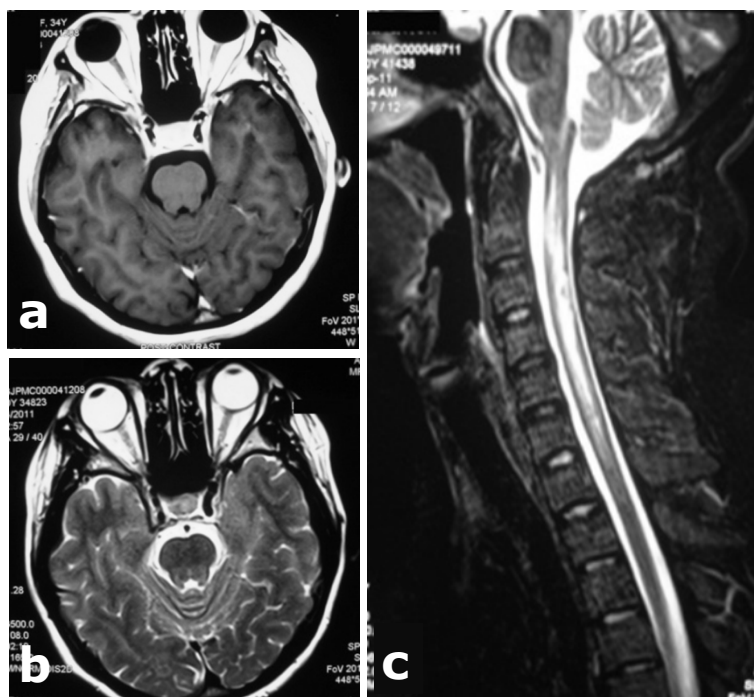


Fig. 1: a) An axial MRI (T1 weighted) image showing normal scan and no evidence of a space occupying lesion, b) An axial MRI (T2 weighted) imaging showing no space occupying lesion and, c) A sagittal MRI (T2 weighted) image of the spine showing hyperintense lesion extending from C3 to C5 levels consistent with demyelination.

whilst she had an afferent pupillary defect in her left eye. The intraocular pressures were 14mm Hg in both the eyes. Colour vision assessment using the Ishihara's chart was normal for the right eye but was not applicable in the left eye due to the poor vision. In view of the low vision, afferent pupillary defect and normal disc appearance, a diagnosis of retrobulbar neuritis was made in the left eye.

A neurologist's opinion was sought due to the associated neurological symptoms. Neurological examination revealed motor power of grade 4/5 in the left upper and lower limbs and grade 5/5 in the right side. The muscle tone and bulk were normal on both sides. She had left sided sensory impairment involving light touch. Reflexes were weakly elicitable and there were no cerebellar signs. Romberg's test for proprioception was negative. Other cranial nerves were normal. A provisional diagnosis of primary demyelinating disorder of the CNS was made, based on the signs and symptoms.

A computed tomography (CT) scan of the brain did not reveal any space occupying lesion (Figure 1a). After baseline investigations that include full blood count, urea and electrolytes, blood sugar evaluation and a chest radiograph, she was started on intravenous methylprednisolone 1gm daily for five days followed by oral prednisolone at a starting dose of 60mg/day and slowly tapering. Magnetic resonance imaging (MRI) of the brain and spinal cord was done and did not reveal any pathological enhancement in the brain parenchyma in T2 or FLAIR images. The post contrast T1 imaging of the brain also did not show any enhancing lesion. The optic nerves showed normal signal with no focal



Fig. 2: Fundoscopy showing mild temporal pallor of the neuroretinal rim consistent with optic atrophy.

enhancement in the above mentioned images. However, there was a hyper intense lesion in the spinal cord extending from C2 to C5 levels with no contrast enhancement (Figure 1c). The lesion was located in the dorsomedial tracts and did not show any mass effect.

Cerebrospinal examination was unremarkable and was negative for oligoclonal band IgG. The results of the autoimmune panel were as follows: ANA – speckled 1:40, anti DNA, anti Ro, anti La, anti-Smith, anti RNP, anti Scl-70 & RA factor were all negative. Based on the investigations a diagnosis of NMO was made. While on methylprednisolone her visual acuity improved gradually along with the neurological symptoms.

On review after a month, her visual acuity in was 6/6 in each eye. The left eye demonstrated colour desaturation and reduced brightness appreciation. Relative afferent pupillary defect persisted in the left eye showing a certain amount of permanent loss of optic nerve function. The left optic disc revealed mild temporal pallor of the neuroretinal rim (Figure 2). The visual evoked potential showed prolonged latency of P₁₀₀ (121 msec)

in the left eye and normal latency in the right eye (105 msec). She is currently under regular follow up in the ophthalmology and neurology clinics and is on Azathioprine 150 mg daily along with tapering dose of oral steroid at the time of writing.

DISCUSSION

NMO is an inflammatory, demyelinating syndrome of the CNS, characterised by severe attacks of optic neuritis and myelitis, which commonly spare the brain in the early stages.^{4,5} Although the association of myelitis with optic neuritis was reported as early as 1872, and later by Allbutt and Erb's in 1879, it was Devic and Gault who proposed that this was a distinct clinical entity in 1894.⁵ Historically, the interval between the optic neuritis and transverse myelitis is significantly longer in most cases, sometimes as long as several years.⁶ A majority of patients have relapsing episodes of myelitis and optic neuritis.^{3,7} Approximately 10 to 20% can have a monophasic course i.e. near simultaneous occurrence of optic neuritis and myelitis. Our case is interesting as it is the first one seen at RIPAS hospital presenting simultaneously with optic neuritis and myelitis.

NMO has a worldwide distribution and is relatively common in the non-white population especially east and Southeast Asians and West Indians. It is more common in African-Americans compared with Caucasian Americans. The frequency of NMO has been reported as 36% of MS cases in Hong Kong, 43% in Taiwan, 40% to 57% in Japan, 11 to 42% in India, 7% in Korea and 13 to 20% in Philippines.^{2,4} NMO is up to nine times more prevalent in women than men with a median age of onset around 40 years.⁴ Earlier, NMO was

considered as a variant of MS. Now it is recognised as a distinct entity with clinical, neuroimaging and laboratory findings distinguishing it from multiple sclerosis.^{5,6} Approximately 80-90% of patients with NMO have relapsing episodes of optic neuritis and myelitis. Relapses occur within 1-year in 60% of patients and within three years in 90%.^{4,7} It is reported that patients with nearly simultaneous optic neuritis and myelitis, like our patient, are less likely to relapse than patients with index events separated by weeks or months.⁴

Predictors of worse prognosis include, number of relapses in the first two years of activity, severity of the first attack and possible association with other autoimmune disorders or autoantibodies.⁷ NMO-IgG is a serum autoantibody which binds with autoantigen, aquaporin 4, which is the principal water channel involved in water homeostasis in the CNS, located in the foot process of astrocytes.^{2,4} NMO-IgG is 76% sensitive and 94% specific for clinically defined NMO.^{4,8} IgG oligoclonal bands in the cerebrospinal fluid that are frequently seen in multiple sclerosis (85%) are three fold less frequent in NMO (30%).^{4,9}

Our patient meets the proposed diagnostic criteria for NMO with two absolute criteria (optic neuritis and acute myelitis) and two of three supportive criteria. These include presence of contiguous spinal cord MRI lesion extending over ≥ 3 vertebral segments and MRI of the brain at the onset of the disease not meeting the diagnostic criteria for multiple sclerosis.^{2,10} Her NMO-IgG seropositivity, which is the third supportive criteria, is under evaluation. Intravenous corticosteroid therapy is commonly the initial treatment for acute

attacks of optic neuritis or myelitis.^{2,4} It has been reported that relapses resistant to corticosteroid therapy are not uncommon, mainly among patients who are seropositive for NMO-IgG.² Maintenance therapy with immunosuppressive to reduce the serum antibody levels along with oral steroids reduce the frequency of relapses.^{4,11} Our patient is currently on Azathioprine and tapering dose of oral steroid. She is under regular follow up to watch out for relapses.

Research in the field of NMO include evaluating the effectiveness of Mitoxantrone and Rituximab in the therapy of NMO. Others treatment includes autologous haematopoietic stem cell transplant in NMO, and plasma exchange in the management of acute severe attack refractory to intravenous methylprednisolone.¹²

In conclusion, NMO is a distinct clinical disorder that can be identified from other demyelinating disorders of the CNS by a combination of clinical, neuroimaging, serological and pathological characteristics. Improvement in patient outcome will depend on early diagnosis, aggressive management of relapses and early and effective immunosuppression.

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