Case Report

Devic's disease – A case report

Kapil S Bainade[1], Veeranna A Kotrashetti[2], Vijay Baburao Sonawane[3], Amit J Vatkar[1], Saili Vishwanath Bunde[4]

From [1]Assistant Professor, [2]Professor and Head of Unit, [3]Associate Professor, [4]Junior Resident, Department of Pediatrics, Dr. D. Y. Patil University, Navi Mumbai, Maharashtra, India

ABSTRACT

Devic disease (Neuromyelitis Optica – [NMO]) is a severe inflammatory demyelinating condition that targets astrocytes in the optic nerves and spinal cord. It is characterized by optic neuritis and transverse myelitis. The disease is very rare with an incidence of 0.05–0.4% and female predominance. NMO is easily misdiagnosed with multiple sclerosis (MS) as characterized by relapses. The best predictor to differentiate NMO from MS is the presence of serum antibody to Aquaporin-4 called as NMO-immunoglobulin G.

Key words: Demyelinating disorder, Devic disease, Multiple sclerosis, Neuromyelitis optica, Optic neuritis, Transverse myelitis

Devic's disease (also known as neuromyelitis optica [NMO]) is an idiopathic, severe, and demyelinating disease of the central nervous system that preferentially affects the optic nerve and spinal cord [1]. The exact incidence of NMO is not known but there is female predominance across all age groups. It is characterized by severe optic neuritis and transverse myelitis occurring either simultaneously or sequentially. When sequential, ON and TM may be separated by months or even years. Nearly 53–100% of pediatric NMO patients experience a relapsing course [2]. Other features of NMO include female preponderance, longitudinally extensive spinal cord lesions (>3 vertebral segments), and absence of oligoclonal immunoglobulin G (IgG) bands. In spite of these differences from multiple sclerosis (MS), the relationship between NMO and MS has been controversial. However, since the discovery of NMO-IgG or aquaporin-4 antibody (an NMO-specific autoantibody to AQP4, the dominant water channel in the central nervous system densely expressed on end-feet of astrocytes) unique clinical features, magnetic resonance imaging (MRI) and other laboratory findings in NMO have been clarified further. Revised pediatric consensus criteria for NMO require the presence of optic neuritis and transverse myelitis with at least two of the following supportive features: MRI evidence of a contiguous spinal lesion at least three spinal segment in length, brain MRI not meeting the diagnostic criteria for MS and NMO-IgG seropositivity [3]. The presence of two of the three supportive criteria has 99% sensitivity and 90% specificity to distinguish NMO from MS [1]. Laboratory investigations include cerebrospinal fluid (CSF) analysis which shows marked pleocytosis (>50 leukocytes/μL) with a neutrophilic or lymphocytic predominance. CSF oligoclonal bands can be seen. NMO-IgG is positive. Acute attacks are usually treated with intravenous corticosteroids. If symptoms progressed despite steroid therapy intravenous immunoglobulin (IVIg) and/plasmapheresis is usually administered. Long-term immunosupression is generally used to prevent relapses and disability accrual given the aggressive nature of this disease. Azathioprine, repeated IVIg or plasmapheresis, rituximab, cyclophosphamide, mycophenolate mofetil, and ofatumumab, can be used in children with NMO.

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CASE REPORT

We report a 10-year-old female child who presented with progressive weakness in the lower limbs which was initially unilateral, later progressed bilaterally, blurring of vision in the left eye and difficulty in voiding urine since 2 days. She had been previously well with no known chronic medical condition. There was no recent history of vaccination or any history of drug consumption. The patient was vitally stable. On examination, left pupil was sluggishly reacting to light, all the deep tendon reflexes were brisk, abdominal reflex was absent, power in bilateral lower limb was 2/5, and power in upper limb was 5/5. Ophthalmic evaluation revealed left-sided RAPD, disc pallor (Fig. 1), and impaired color vision. Complete blood count (CBC), CSF routine, and CSF IgG were normal. MRI brain showed subcentimeter sized discrete areas of altered intensity appearing hyperintense on fluid-attenuated inversion recovery (FLAIR) and T2-weighted (T2W)

Correspondence to: Dr. Saili Vishwanath Bunde, 801, Shree Sai Deep Apt, Near Bhagirathi Bungalow, Bhusar Ali, Kalwa, Thane - 400 605, Maharashtra, India. E-mail: Sailibunde28@gmail.com

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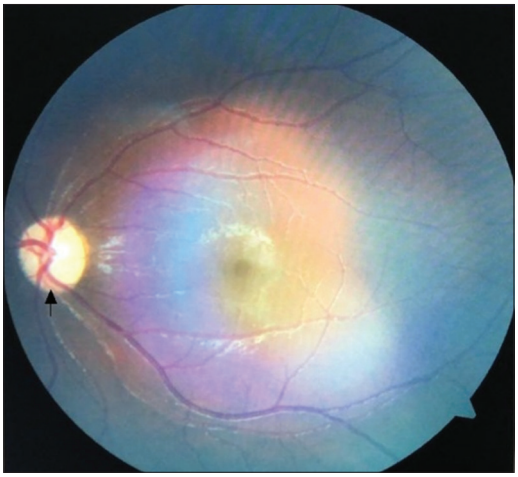

Figure 1: Left-sided optic disc pallor

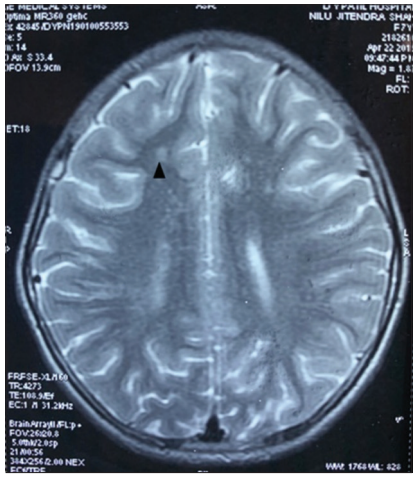

Figure 2: T2-weighted sequence showing hyperintense lesion

(Fig. 2) in subcortical white matter of bilateral frontal lobes. MRI spine showed multiple discrete and confluent T2W hyperintense lesions in intramedullary location of cervico dorsal spine up to D7. Serum NMO antibodies (Aquaporin 4) were positive. Considering all the above findings, NMO was diagnosed. Child was started on Inj methylprednisolone pulse therapy for 5 days and had complete resolution of symptoms. Patient was shifted to oral steroids and was discharged. During follow-up, the patient was recovering with no new symptoms; hence, steroids were tapered. Eight months later, the child returned to our hospital with loss of vision in left eye, weakness in bilateral lower limbs, and difficulty in voiding urine. Power in lower limb was 2/5 and knee and ankle reflex was brisk. MRI brain and spine was repeated. MRI brain showed multiple hyperintense areas in the frontoparietal region on FLAIR (Fig. 3a) and T2W (Fig. 3b) and no enhancement on contrast study (Fig. 3c). MRI spine showed multiple discrete and confluent T2W hyperintense lesions in the intra medullary location of cervico dorsal spine showing enhancement on post contrast study (Fig. 4a and b) largest contiguous spreading from C3 to D4. Compared to the previous MRI brain and spine, the lesions in the brain had increased. No significant changes were seen in the spine. Inj methylprednisolone pulse therapy at 30 mg/ kg/day was given for 5 days, followed by oral prednisolone at 2 mg/kg/day in tapering dose and azathioprine (immunomodulator) at 2 mg/kg/day was started for the patient. At present, the patient is on tablet prednisolone at 0.5 mg/kg/day and tablet azathioprine at 2 mg/kg/day. CBC, LFT, and RFT testing was done every weekly to look for leucopenia and azathioprine toxicity initially and now the patient is asked to repeat investigations every monthly. She has been stable since initiation of this treatment along with physiotherapy and has not suffered any more relapse since then.

DISCUSSION

Acquired demyelinating disorders of CNS are being increasingly recognized and diagnosed worldwide. NMO is a rare demyelinating disease characterized by monophasic or polyphasic episodes of optic neuritis and transverse myelitis. The NMO is also known under the name of Devic's disease, by the name of Eugène Devic who was the first one who identified the symptoms in 1894. It mainly affects the brain and the spinal cord. The viral and bacterial infections preceding or accompanying the NMO are a known phenomenon. The influenza-like illness that precedes the onset of neurological disease has been reported in about 25–30% of cases [4].

NMO shares a number of clinical and radiological features with MS [5-7]. The groundbreaking discovery of a novel, pathogenic autoantibody (termed NMO-IgG or AQP4-Ab) in a subset of patients by Dr Lennon and colleagues in 2004 [8,9], has led to a tremendous increase in interest in NMO. NMO-IgG/AQP4 antibody-positive NMO is now considered a disease entity in its own right rather than a subtype of MS. Population-based studies over the past two decades report the prevalence and incidence of NMOSD in different populations worldwide. One relevant finding is the varying prevalence observed in different racial groups. Consistently, the prevalence of NMOSD among Whites is ~1/100,000 population, with an annual incidence of <1/million population. Among East Asians, the prevalence is higher, at ~3.5/100,000 population, while the prevalence in Blacks may be up to 10/100,000 population. In India, there is a dearth of epidemiological data for demyelinating disorders. A population-based survey in urban Mangalore has shown a prevalence of 2.6/100,000 for NMO [10]. The spectrum of NMO disorders is likely to constitute approximately 20% of all demyelinating disorders in India [11].

NMO can occur in children, but pediatric NMO needs specific consideration due to possible poor visual and motor outcome [1]. Female predominance is seen, with female comprising over two thirds of patients. Within 5 years of disease onset, more than 50% of the patients with relapsing NMO are blind in one or both eyes. Likewise our patient had dimension of vision as a result of one attack within a year.

The diagnosis of NMO is based on clinical symptom. The main symptoms are loss of vision and spinal cord function. Optic neuritis may manifest as decreased visual acuity, visual field defects or loss of color vision. Spinal cord involvement may lead to muscle weakness, decreased sensations, loss of bowel, and bladder control. Our patient had decreased visual acuity, loss

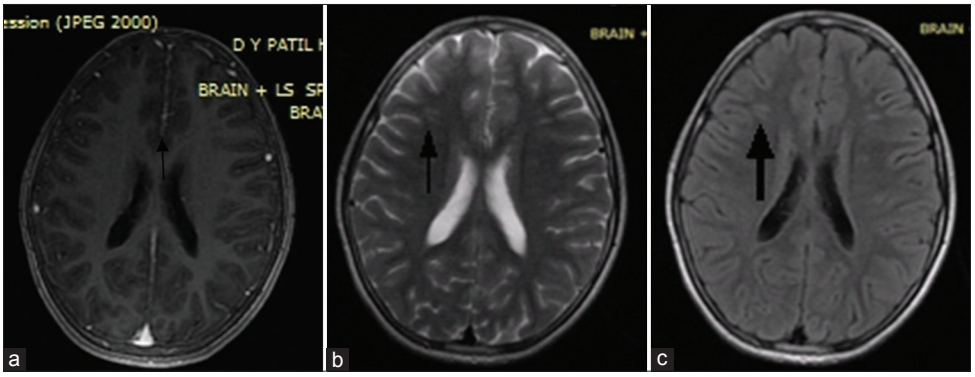

Figure 3: (a-c) Hyperintense areas in frontal lobe on fluid-attenuated inversion recovery and T2-weighted and no enhancement on contrast study

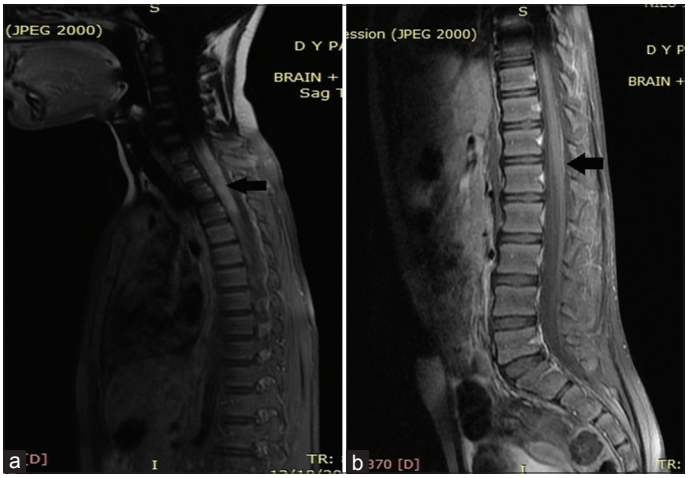

Figure 4: (a) Hyperintense lesions in cervicodorsal spine on T1-weighted, (b) Contrast

of color vision, and muscle weakness. There was no sensory or autonomic involvement.

Diagnostic criteria of NMO include the presence of acute optic neuritis and myelitis with at least two of the three supportive criteria, which consist of spinal cord MRI lesion extending over three vertebral segments, brain MRI lesion, which does not meet the diagnostic criteria for MS and NMO-IgG seropositive status [1]. Detection of aquaporin four antibodies distinguishes it from other demyelinating disorders which were positive in our case.

Brain MRI that was performed in patients with NMO reveals that gray matter is more affected than white matter unlike MS which affects only white matter [12]. Spinal cord lesions are usually large, extending over three vertebral segments in about 85–90% of patients and are mostly located in the cervical and upper thoracic region [1,13]. CSF examination plays an important role is making the diagnosis of NMO. It characteristically shows pleocytosis >50·10^6 WBC/L in patients with NMO [1,6]. However, this profile is not specific and is usually present in about 10–20% of the patients [7]. Our patient's CSF analysis did not show significant pleocytosis. Oligoclonal bands of IgG in the CSF are frequently seen in MS and these are detected in 15–30% of patients with NMO [14]. Oligoclonal bands were negative in our patient's CSF examination.

There is no proven treatment protocol either in the acute attacks or in the long-term remissions in NMO. Children have good outcome but some are left with severe visual and motor impairment. Intravenous corticosteroid therapy is the commonly preferred initial treatment for acute attacks [7]. Immunosuppressive therapy (oral azathioprine, associated or not with oral steroids; IVIg; and rituximab) is an accepted method to provide clinical remission of corticosteroid resistant NMO [15]. Our patient was treated with corticosteroid pulse therapy, followed by low dose corticosteroid and azathioprine. The patient responded well after starting azathioprine. The last follow-up of our patient showed improved vision and neurological examination was normal. Prognosis in pediatric patient is good. Regular follow-up is advised.

CONCLUSION

NMO should be differentiated from other childhood demyelinating disorders including acute disseminated encephalomyelitis (ADEM) and MS, especially when there is a high suspicion of optic neuritis.

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