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Case Report

Neuromyelitis optica in a paediatric patient: a case report

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ABSTRACT

Neuromyelitis optica is a multifocal demyelinating disease of the central nervous system that predominantly affects the spinal cord and optic nerves, with variable clinical features including motor weakness in limbs, bowel and bladder affection and loss of vision. The disease is characterized by poor or no recovery. Magnetic resonance imaging (MRI) of spine with contrast shows hyperintense lesions involving contiguous segments with a normal MRI brain. CSF studies shows anti aquaporin 4 antibodies. Visual evoked potential of eyes shows marked reduction of optic nerve function. We report a case of eight year old girl who presented with diminished vision in eyes (right >left) and weakness in all four limbs. Clinical features and investigations were suggestive of NMO. She was treated with inj. methylprednisolone for 5 days followed by oral prednisolone in tapering dose for 6 weeks. The child improved of hemiparetic gait and power in the left side. Vision in the left eye did not deteriorate further. Repeat MRI showed the resolution of previous spinal lesions. Follow up of the child over seven years has multiple admissions due to relapses. In the third admission child was given again 5 days of inj. methylprednisolone followed by azathioprine for two months. On the seventh admission due to relapse, inj. rituximab 500 mg and inj. methylprednisolone 500 mg was given and repeated every 6 months. In the last follow up in June 2024, the child is clinically stable with improvement in gait and no further deterioration of vision and no bowel or bladder affection.

Keywords: Neuromyelitis optica, Follow up, Relapse, Methylprednisolone, Prednisolone, Azathioprine, Rituximab

INTRODUCTION

Neuromyelitis optica (NMO, Devic's syndrome) is a well-recognized inflammatory demyelinating central nervous system disease, typically characterized by severe bilateral optic neuritis and longitudinally extensive transverse myelitis.[1] Most patients have pathogenic autoantibodies in their serum against the astrocytic water channel-aquaporin 4 (AQP4).[2] AQP4 antibody positivity has now been found in a wider range of clinical and magnetic resonance imaging manifestations, leading to the broader concept of NMO spectrum disorders (NMOSDs).[3]

CASE REPORT

An eight-year-old girl was referred to our hospital with a history of gradually diminished vision in both eyes for four months with complete loss of vision in the right eye. She also had weakness in all the limbs which was more marked in the left side of the body with hemiparetic gait for three months. There was bowel and bladder involvement initially in the form of involuntary passage of stool and urine. There was no history of trauma, recent vaccination, weight loss, altered sensorium, or involuntary movements. On examination, the child had left hemiparesis. Ophthalmological examination showed loss of vision and absent direct light reflex in the right eye. Left eye vision was 3/60. The child was admitted and investigated.

Investigations

MRI spine with contrast shows hyperintense lesion in the spinal cord from C2-C7 and T7-T10 level (more than 3 spinal segments) suggestive of transverse myelitis

(Figures 1). MRI brain was normal. NMO IgG Antibody (Anti aquaporin 4 antibody) in the dilution of 1:10 which was strongly positive in the CSF study but did not show oligoclonal bands. Sputum examination for acid-fast bacilli and Mantoux test were negative. Serum LDH and uric acid levels were normal. VEP (Visual evoked potential) of the left eye shows normal latency and amplitude while in the right eye, flash VEP shows minimal response to bright flash stimulus suggestive of marked reduction in the optic nerve function. All the above findings and investigations fulfill the criteria of neuromyelitis optica.

Initial and immediate treatment inj. methylprednisolone 500 mg intravenously over 1 hour once daily for 5 days followed by oral prednisolone for 4 weeks and then gradually tapered over the next 2 weeks. There was clinical improvement in the form of regaining normal power in the left side, hemiparetic gait improved and vision in the left eye did not deteriorate further. She was again readmitted after 6 months with complaints of the left sided weakness with diminution of vision on the right side with neck pain for 20 days. She was again administered inj. methylprednisolone pulse therapy for 5 days followed by oral steroids, tapered over 6 weeks. She was then started on tab. azathioprine 2 mg/kg/day daily for 2 months. The child had multiple relapses for which she was given inj. methylprednisolone. On the seventh admission the child was started on a single dose of inj. rituximab 500 mg after a single dose of inj. methylprednisolone 500 mg. This treatment is continued every six months to date.

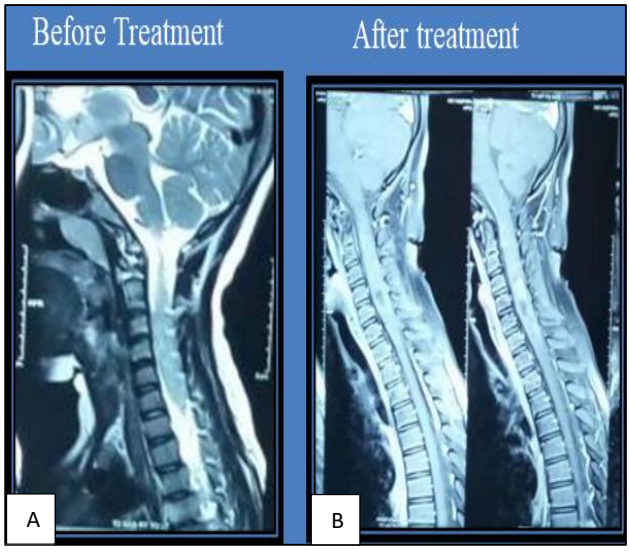

Figure 1 (A and B): Repeat MRI-suggested resolution of previous spinal lesion.

The treatment of NMOSD is primarily immunosuppressive. In the acute phase, high-dose Methylprednisolone, plasma exchange, or intravenous immunoglobulin (if not better with steroids) are used to control inflammation for rapid recovery.[4] However, the course is punctuated by severe clinical relapses with rapid and permanent disability. Aggressive long-term treatment is essential. Immunosuppressive agents such as azathioprine (AZA) and mycophenolate mofetil (MYC) have been reported to reduce relapse risk and preserve neurological function.[4-8] Recently, rituximab, a monoclonal antibody to CD20, has been found to be effective in several reports and small uncontrolled studies.[9] We present our experience with the use of rituximab in our Indian paediatric patient.

DISCUSSION

In patients with NMOSD, repeated and severe clinical relapses lead to rapid accumulation of disability. This can be in the form of permanent blindness, loss of ambulatory function, and sphincter involvement.[1] Up to half of NMO-diagnosed patients become wheelchair-bound or functionally blind in 5 years of disease onset.[10] Disability is directly related to the number of relapses, which add to the burden of destructive multifocal inflammatory lesions. Thus, aggressive immunosuppressive therapy to reduce the relapses is the mainstay of NMOSD treatment. Studies demonstrated a reduced relapse rate and disability over the treatment period.[5-8] In our child there is no deterioration of ambulatory function after initial marked improvement in 2017. The vision in the left eye remained static with no deterioration.

Recently, there have been several uncontrolled studies from different countries for treating NMO using rituximab.[9] In 2005, Cree et al reported the first open-label study evaluating rituximab in eight NMO patients.[11] They showed a significant reduction in relapses as well as improvement in disability (as measured by expanded disability status scale score) in their patients. A retrospective multicenter analysis of 25 NMO patients in 2008 and two in 2011 (10 and 23 patients) showed a similar reduction in relapses as well as disability.[12-14] Overall, they suggest that rituximab is associated with reduced relapse rate, even in patients with particularly active disease despite other therapies. The current study in Indian patients also demonstrates a marked beneficial effect of rituximab treatment on patients with NMOSD. In our child, we started rituximab in May 2021 due to three relapses with neurological deterioration in gait despite treatment with inj. methylprednisolone followed by oral prednisolone.

The evaluation of sustained efficacy and long-term tolerability of rituximab is important. This was supported by a 5-year follow-up retrospective case series of 30 NMOSD patients published in 2013.[15] This study included patients on long-term rituximab treatment and the mean duration of treatment was 4 years, 4 months, also suggesting long-term efficacy. In 2015, another retrospective analysis of 32 patients explored the response to rituximab in treatment-naïve NMO, with favorable results. Rituximab has been predominantly used in NMO patients as immunosuppressive therapy to

prevent relapses, especially in those who do not respond well to other drugs such as AZA and mycophenolate. It is also being increasingly used as a first-line drug in patients with severe forms of NMO.[16] In our child, we have completed 6 doses of inj. rituximab 500 mg every 6 months. The child was also given inj. methylprednisolone 500 mg before inj. rituximab each time.

The long-term use of rituximab has shown a reasonable safety profile. It carries a very minor risk of progressive multifocal leukoencephalopathy, malignancies, and severe infections.[17] Overall, in other NMO studies mentioned before, rituximab showed an acceptable safety profile. This is also consistent with the data available on long-term use of rituximab in rheumatoid arthritis patients.[17] Despite these studies, more data about rituximab's long-term safety still needs to be collected over time. In our child, we will continue to have a long-term follow-up to monitor relapses and adverse effects due to Rituximab.

CONCLUSION

Neuromyelitis optica in paediatric patients is rare. Relapses and clinical deterioration are common features in NMO patients. Follow-up over a period of seven years in our case who had the initial manifestation at the age of eight years had multiple relapses despite pulse methyl prednisolone, oral prednisolone and azathioprine. A single dose of rituximab therapy 500 mg with methyl prednisolone 500 mg every six months since 2022 has prevented further relapses in our child. Multicentric studies with more number of paediatric cases, followed up for a longer duration will be the cornerstone in the management of paediatric NMO.

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