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Case Reports

Neuromyelitis Optica (NMO) in Children: A Rare Case Report

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Abstract

Background: Neuromyelitis Optica (NMO) is a rare autoimmune disease that covers 20-30% of diseases related to autoimmune disorders and about 1% of demyelination diseases. NMO symptoms are vary between individuals, there are generally 2 main symptoms, transverse myelitis and optic neuritis. It requires good knowledge and understanding of this disease so that proper management can be given as early as possible so as to reduce the morbidity and mortality of the disease. This article reported a child with NMO disease based on The Consensus of the International Panel for NMO Diagnosis (IPND) 2015.

Case Presentation: An 8-year old boy with spastic tetra paresis, bilateral nervus opticus dysfunction, urinary retention, and allodynia et causa suspected NMO. Patient received therapy using high-dose intravenous methylprednisolone and showing a clinical improvement.

Conclusion: This patient was diagnosed NMO based on IPND 2015 with an unknown AQP4-Ab status accompanied by supporting clinical symptoms. The management of NMO with high-dose intravenous methylprednisolone in this patient provides a meaningful response to the clinical improvement of the disease.

Keywords:

Autoimmune; methylprednisolone; neuromyelitis Optica

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INTRODUCTION

Neuromyelitis optica (NMO), also known as Devic's disease or Devic's syndrome, is an inflammatory autoimmune disease in the central nervous system (CNS) that commonly attacks the optic nerve and spinal cord. NMO is a rare disease, covering 20-30% of diseases related to autoimmune disorders and about 1% of demyelination diseases.¹⁻⁷

NMO is a complex disease caused by interaction between genetic host and environmental factor. The major immunological characteristic of NMO is the antibodies against aquaporin 4 (AQP4-Ab), which is the main water channel in the brain. However, the absence of seropositive AQP4-Ab in some cases of NMO raise the suspicion that NO can be caused by other mechanisms, such as connective tissue disorder, paraneoplastic disorder, or infectious disease. This is strong evidence supporting the hypothesis that NMO has heterogeneous etiopathogenetics.⁸⁻¹²

NMO symptoms vary between individuals, generally there are 2 main symptoms, transverse

myelitis (TM) and optic neuritis (ON). NMO is often misdiagnosed with multiple sclerosis (MS) because it has similar clinical presentation. Transverse myelitis on NMO tend to be more severe than MS. Likewise, ON in NMO and MS have nearly identical clinical presentation, but demyelination in NMO is more severe and destructive than MS, so determining the right diagnosis is very important.^{6-9,13,14}

Acute phase therapy includes the administration of high-dose intravenous corticosteroid in the early phase, followed by plasma exchange and other immune suppressive drugs to prevent the relapse. Early treatment is very important to minimize the damage and loss of axon in the inflammatory process of NMO.^{13,14}

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This requires good knowledge and understanding of this disease so that proper management can be given as early as possible so as to reduce the morbidity and mortality due to this disease. This study will describe an 8-year-old boy with NMO disease in Dr. Kariadi Hospital.

CASE REPORTS

An 8-year-old boy came to the Emergency Room (ER) of Dr. Kariadi Hospital, Semarang, Indonesia with the main complaint of weakness of the four limbs for 13 days before entering the hospital. He was admitted suddenly weak in the right leg and left arm which were then followed by weakness in the left leg and right arm. Weakness started from the tip of the arm and leg, slowly rises to the top. Both eyes were blurred and pain around the eyeballs when glancing. The patient said that the body felt pain in all over the body and the pain was increased when the body was touched. The patient complained that he was difficult to urinate, and had to push first so that he could urinate. There was no abnormality in defecation. Previously, he was hospitalized in private hospital Tegal for 7 days without any improvement, then he referred to Dr. Kariadi Hospital in Semarang.

Physical examination in the ED revealed blood pressure 100/70 mmHg, pulse rate was 98 times per minute, breathing rate was 22 times per minute, body temperature was 36.5°C, and body weight was 43 kg. Neurological examination results were: GCS was E4M6V5, numeric rating scale (NRS) pain scale was 3-4, dysfunction of bilateral optic nerve with visual acuity of both eyes were 1/60 (with correction), normal result of visual field and colour vision, and spastic tetra paresis with motor strength were 3, allodynia, and urinary retention. The results of blood tests showed leukocytosis (16,600/ μ L). ECG examination showed normal sinus rhythm. Chest radiograph showed the normal heart and lung. Cervical X-rays showed good curvature, intervertebral discs within normal limit. Patients were diagnosed with spastic tetra paresis, bilateral nervus opticus dysfunction, urinary retention, and allodynia et causa suspected NMO with differential diagnosis of multiple sclerosis (MS).

The treatment regimen consisted of RL infusion of 12 drops per minute, intravenous methylprednisolone 125 mg/12 hours, intravenous ranitidine 150 mg/12 hours, oral paracetamol 500 mg/8 hours, and oral vitamin B1-B6-B12 1 tablet/8 hours.

Fundus colour examination (figure 1) showed that both optic discs were firmly bounded with CDR of 0.3-0.4, no glaucomatous excavation, arterial-venous ratio and vessels structure within normal limit, and neither retinal bleeding nor retinal detachment were present. Head MRI with contrast showed a normal result (figure 2). No visible thickening, irregularity, changes in signal intensity, or pathological contrast enhancement in both optic nerve. There were no retro-bulbar mass, no intracranial space occupying lesion, no infarction, bleeding, or signs of increased intracranial pressure. The whole spine MRI with contrast (figure 3) showed no lesions or masses in the spinal cord, and within intra or extra dural of the spine.

During 16 days of treatment, the patient's condition was improved in neurological status, motor strength of the upper limb was 5 and lower limb was 4, and visual acuity of both eyes improved to 6/6. The pain in the body and the eyes were reduced, and urinary function was improved as well. After 6 days of treatment, methylprednisolone injection was tapering off and continued with oral methylprednisolone.



Figure 1. Fundus colour examinations showed normal results

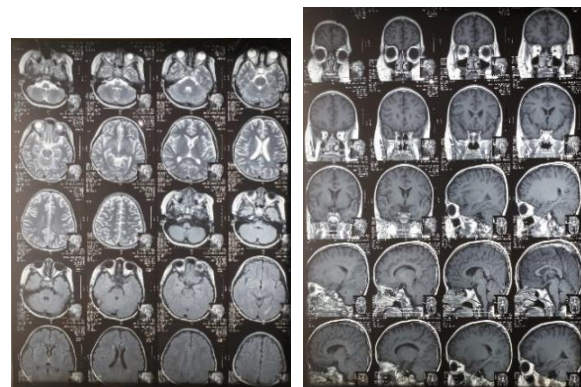


Figure 2. Head MRI results with contrast showed normal results

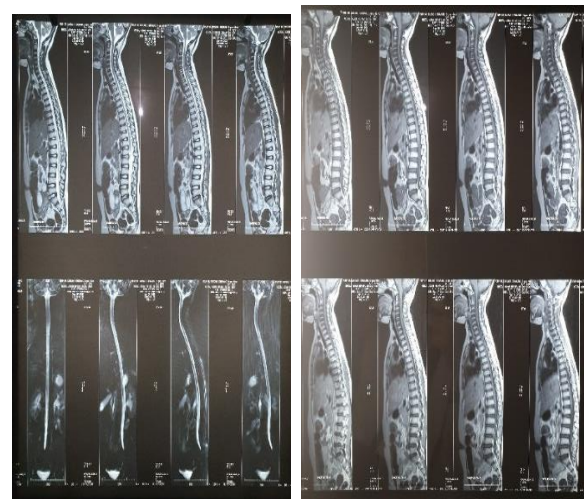


Figure 3. Whole spine MRI results with contrast showed normal results

DISCUSSION

NMO is a rare disease. NMO can affect men and women, in the age of 3-80 years. In preadolescent children, there are no gender predilection. But after the adolescence phase, women dominate around 70-90% of all individuals affected by this disease.^{1-11,14} In Europe, NMO is very rare in the pediatric population, a cohort study in pediatric patients in Germany shows an age range from 5-14 years.¹³ Population-based studies in Europe and Asia reported that incidence and prevalence of NMO ranges from 0.05-0.4 and 0.52-4.4 per 100,000.¹⁵ There were no differences in incidence and prevalence of NMO in Asia compared to others; although ethnicity, genetic, and environmental factor may influence on disease phenotype and clinical outcome.¹⁵⁻¹⁶

findings on ocular examination, and is caused by a direct autoimmune reaction in the optic nerve.^{18,19} Clinical manifestations of optic neuritis include symptoms and signs of a sharp decrease in visual acuity, mild pain around or behind the eyeball, impaired visual field, decreased contrast sensitivity, impaired color vision, pupillary abnormalities, and fundal findings is the form of lesion near the optic nerve papillary.²⁰⁻²²

MRI is the main modality examination for the diagnosis of NMO, which will indicate an inflammation signs of the brain and spinal cord, which appears as a white area. Spinal MRI of patient showed no sign of inflammation in 3 or more segments of the spinal cord (longitudinally extensive transverse myelitis), where as in brain MRI there was also no picture of lesions typical of NMO which are usually located in the hypothalamus,

Table 1. The International Panel for NMOSD Diagnosis 2015^{14,25}

Diagnosis with AQP4-Abs

- at least one core clinical characteristic
- positive AQP4-Abs with best available method
- exclusion of alternative diagnosis (e.g. sarcoidosis, neoplastic/paraneoplastic, vascular, chronic infection)

Diagnosis without AQP4-Abs/unknown status

- at least two core clinical characteristics resulting from one or more clinical attacks and fulfilling the following:
 - a. at least one of optic neuritis, LETM, APS
 - b. dissemination in space (2/more different core clinical characteristics)
 - c. fulfillment of additional MRI requirements as applicable
- negative for AQP4-Abs with best available method, or testing unavailable
- exclusion of alternative diagnoses

Core clinical characteristics

- optic neuritis
- acute myelitis
- APS
- brainstem syndrome
- symptomatic narcolepsy or acute diencephalic syndrome with NMOSD-typical diencephalic MRI lesions
- symptomatic cerebral syndrome with NMOSD-typical brain lesions

Additional MRI requirements for NMOSD without AQP4-Abs/unknown status

- acute optic neuritis: normal or only nonspecific white matter lesions on MRI brain; or optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium-enhancing lesion extending over >1/2 optic nerve length or optic chiasm involvement.
- acute myelitis: MRI spinal cord demonstrating attack-associated lesion spanning ≥ 3 contiguous vertebral segments (LETM); or ≥ 3 contiguous segments of focal cord atrophy with previous history of acute myelitis
- APS: dorsal medulla/area postrema lesion on MRI brain
- acute brainstem syndrome: peri ependymal brainstem lesions.

APS: area postrema syndrome, AQP4-Abs: aquaporin-4 antibodies, LETM: longitudinally extensive transverse myelitis, NMOSD: neuromyelitisoptica spectrum disorder

NMO symptoms vary between individuals, there are generally 2 main symptoms, namely transverse myelitis (TM) and optic neuritis (ON). TM is an acute inflammatory process involving a focal area in the spinal cord with clinical characteristics of either acute or sub-acute development of signs and symptoms of neurological dysfunction of the motor, sensory and autonomic nerves in the spinal cord.¹⁷ In this patient, there was a sudden weakness of the limbs, gradually in the left arm and right leg followed by the left leg and right arm, in which the weakness were getting heavier gradually. Sensory involvement can be found in the form of allodynia where pain was felt throughout the body and pain increased when the body was touched. Impaired autonomic function is indicated by the presence of urinary or alvi retention. Both visual acuity in this patient was accompanied by ocular pain. Generally, ON was acute, severe visual disturbance without significant

corpus callosum, periventricular or brain stem.²⁴ LCS examination was not done due to the patient's condition impossible to do it. LCS examination of NMO usually showed pleocytosis (> 50 cell /mm³) with predominant neutrophil and an increase in protein (100-500 mg/dl). Although rare, oligoclonal bands can be found in NMO (15-30%) but this is more common in multiple sclerosis. Unfortunately, anti-AQP4 examination can not be examine in the Dr. Kariadi Hospital. In fact, AQP4-Ab examination of NMO cases was reported to had sensitivity of 76.7% and specificity of 99.8%.^{11-14,24}

The International Panel for NMO Diagnosis (IPND) revised the consensus about clinical diagnosis of neuromyelitis Optica spectrum disorder (NMOSD) in 2015 (Table 1). In accordance with the consensus, this patient could be included in an NMO diagnosis with an unknown AQP4-Ab status with supporting clinical symptoms. The main differential diagnosis in this patient

is MS. NMO and MS have very similar clinical features, but in this patient the course of the disease was monophasic and the findings on head and whole spine MRI with contrast are not typical for MS, therefore the diagnosis of this patient was NMO.^{14,25}

Patients received high-dose intravenous methylprednisolone therapy (125mg/12 hours) and tapering off for 6 days then continued with oral administration of methylprednisolone. Evaluation showed that there was clinical improvement. Visual acuity gradually improved, where at the beginning of treatment visual acuity of the right and left eye were 1/60 improved to 3/60, and at the end of visual acuity were 6/6. Motor strength also showed improvement in all four limbs. Evaluation of sensoric function showed an improvement in which patient who initially experienced pain throughout the body, at the end of the treatment there was a decrease in pain scale and no pain when light touch. Evaluation of autonomic function showed that the urinary function had improved.¹¹⁻¹⁴

Based on multicenter study of MS and NMO had been reported that intravenous methylprednisolone therapy was effective as first-line therapy in NMO but was more effective in MS patients compared to NMO.^{3,4} When the patient's condition did not improve or even worsened after corticosteroid therapy, it is recommended to do therapeutic plasma exchange (TPE) for 5-7 cycles. TPE has also been used concurrently or immediately after glucocorticoid therapy in progressive or refractory conditions. The results of a study showed that TPE as early as possible (≤ 5 days) is more beneficial than TPE delays in cases of NMO refractory to intravenous methylprednisolone.^{2-4,11-14} IVIG is another important therapy that can affect various immunomodulatory pathways and antigenic-recognition, including humoral and cellular immunity. Several immunosuppressive agents (steroid, azathioprine, rituximab, and mycophenolate mofetil) have also been accepted as long-term therapy for NMO patients.¹¹⁻¹⁴

CONCLUSION

This patient was diagnosed neuromyelitis optica (NMO) based on diagnostic criteria of the International Panel for NMO Diagnosis (IPND) 2015 with an unknown AQP4-Ab status, supporting by clinical symptoms. The management of NMO with high-dose intravenous methylprednisolone has meaningful response to the clinical improvement. After intravenous methylprednisolone for 6 days, steroid was tapering off and continued by oral methylprednisolone.

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