· Case report ·

Successful treatment of an early recurrence of neuromyelitis optica in a child

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Received:2010-10-08 Accepted:2011-03-06

Abstract

• AIM: To report unusual presentation and good outcome of neuromyelitis optica(NMO) in a child.
• METHODS: Case Report.
• RESULTS: An 8-year-old girl presented with 5-day history of sudden bilateral visual deterioration followed by left lower limb weakness. Visual acuity was perception to light in both eyes. Funduscopy revealed bilateral hyperaemic swollen optic discs. MRI of brain and spine revealed enhancing white matter lesions in the right frontal lobe and spinal cord at C5 level. She was diagnosed NMO and treated with intravenous methylprednisolone and tapering doses of oral prednisolone as maintenance therapy. Symptoms gradually improved 1 month after treatment. However, she presented with similar presentation 1 week after stopping oral prednisolone. MRI of brain and spine were reviewed and showed enhancing lesion in the right frontal lobe and longitudinal segment of spinal cord from C3 to C5 level. She was promptly given intravenous methylprednisolone for 5 days followed by prolonged tapering of oral prednisolone over 6 months period. After 2 months, she was able to walk and attend activities of school. Visual acuity was improved to 6/10 in both eyes and neurological examination was normal. There was no recurrence during the next year. Final visual acuity was 6/7.5 in the the right eye and 6/10 in the left eye.
• CONCLUSION: The diagnosis of NMO should be kept in mind although it is unusual presentation in child presented with bilateral visual loss and unilateral lower limb weakness. Early diagnosis and treatments would yield good outcome to the patient.

• KEYWORDS: neuromyelitis optica; optic neuritis; myelitis; children
DOI:10.3969/j. issn. 1672-5123. 2011. 05. 003

Chiang WS, Thomas T, Leslie Wong TW, Ghani SA, Ibrahim M. Successful treatment of an early recurrence of neuromyelitis optica in a child. *Guoji Yanke Zazhi(Int J Ophthalmol)* 2011;11(5):760-764

INTRODUCTION

Neuromyelitis optica (NMO), also known as Devic's disease, which is a rare autoimmune disorder, primarily affects the optic nerves and spinal cord resulting in optic neuritis and myelitis. It may also affect the brain[1]. The main presentations of NMO are loss of vision and weakness of limbs. They can occur independently or simultaneously or in close temporal succession[2]. There are variants of NMO in clinical presentations. It may resemble multiple sclerosis (MS) or acute disseminated encephalomyelitis (ADEM). Therefore, it is challenging to make the diagnosis. Devastating complications and permanent neurological deficit will occur if this diagnosis is neglected.

CASE REPORT

An 8-year-old Kadazan girl presented with sudden bilateral loss of vision for 5 days followed by left lower limb weakness. There was no associated headache, nausea, vomiting, altered bowel habit and urinary symptoms. There was no history of trauma, recent sinusitis and upper respiratory tract infection. Systemic review and family history were unremarkable. She was conscious and alert during examination. Vital signs were stable. There was no sign of respiratory distress. Visual acuity was perception to light and relative afferent pupillary defect was negative in both eyes. Anterior segment examination and intraocular pressure(IOP) were normal. Funduscopy showed bilateral hyperaemic optic discs swelling with dilated and tortuous veins (Figure 1). Neurologically, the left lower limb motor power was 4/5 and sensation was reduced. Other cranial nerves assessment was normal. There was absence of cerebellar sign.

CT showed orbit and brain were normal. However, MRI of brain and spine revealed enhancing solitary lesions in the right frontal lobe and posterior spinal cord at C5 level (Figure 2,3). There were hypointense lesions on T1 weighted, hyperintense on T2 weighted, no suppression on fluid attenuated inversion

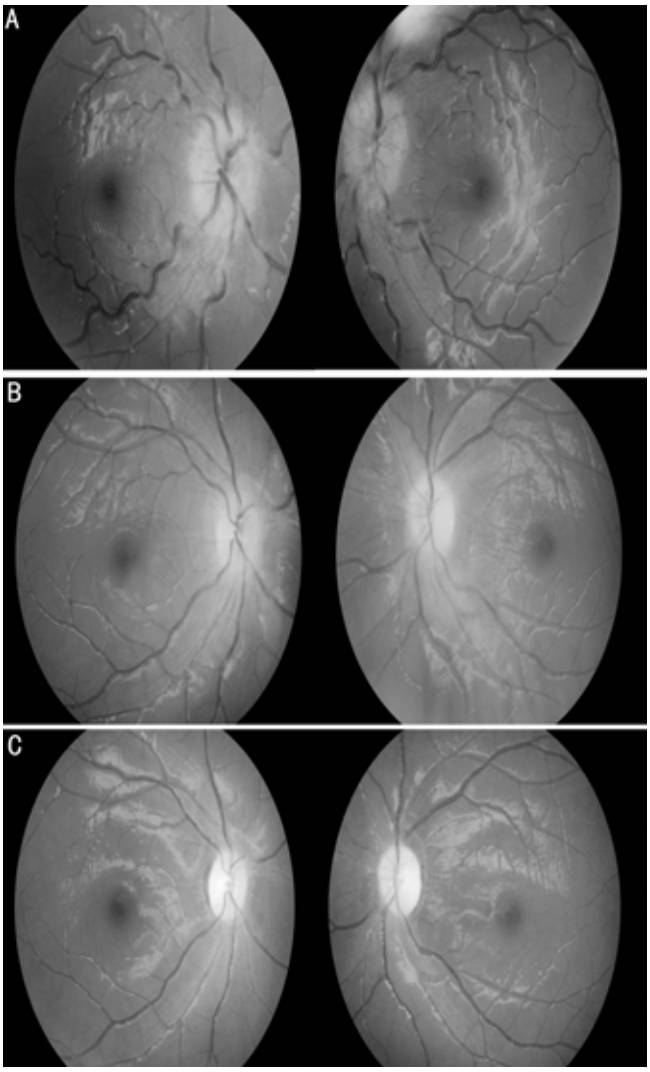

Figure 1 Fundus examination A: Bilateral hyperaemic optic discs swelling with dilated and tortuous veins; B: Bilateral decreased hyperaemic optic discs swelling after 2 weeks; C: Bilateral pale optic discs after 2 months.

recovery (FLAIR) but enhanced post gadolinium. Tuberculosis, syphilis and connective tissue diseases were negative. Erythrocyte sedimentation rate (ESR) and chest X-ray were normal. Mantoux test and VDRL were negative. Sputum and gastric lavage for acid fast bacilli were not detected. Connective tissue diseases screening which included rheumatoid factor, C3, C4, ANA, and dsDNA was negative. Blood investigation such as full blood count, blood urea serum electrolytes and random blood sugar were within normal limit. Lumbar puncture for cerebrospinal fluid (CSF) analysis was unremarkable. She was diagnosed with neuromyelitis optica based on clinical features and MRI findings.

She was promptly treated with intravenous methylprednisolone 250mg for five days (q. i. d.) and then tapering doses of oral prednisolone over 1 month as maintenance therapy. Oral prednisolone was started with 1mg/kg daily. She was not able to continue her studies at school and perform daily activities at home because of her poor vision and left lower limb weakness. After 2 weeks, vision of both eyes was improved to 2/60 in the right and 1/60 in the left. Fundus examination showed bilateral decreased hyperaemic optic discs swelling (Figure 1). She gradually regained power to 5/5 and sensation in her left lower limb in 1 month.

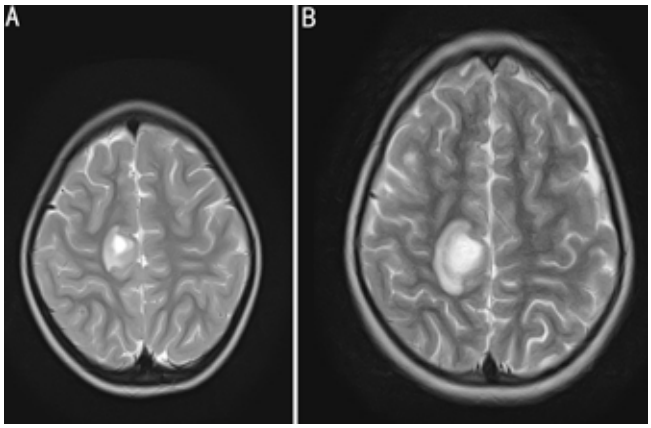

Figure 2 MRI of brain A: Solitary lesions in the right frontal lobe; B: Enhancing solitary lesion associated with perilesional edema in the right frontal lobe after stopping a 4-week tapering course of oral prednisolone.

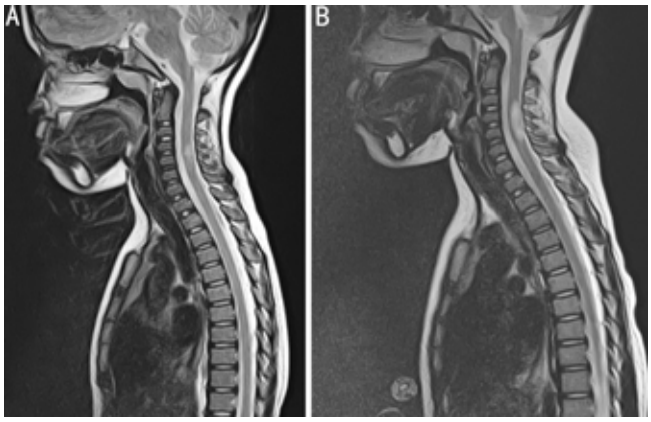

Figure 3 MRI of spine A: Spinal cord (C5 level) which appeared hyperintense on T2 weighted; B: Enhancing elongated lesion at C3-C5 level of spinal cord after stopping a 4-week tapering course of oral prednisolone.

However, similar symptoms appeared 1 week after stopping a 4-week tapering course of oral prednisolone. Visual acuity was hand movement in the right eye and 1/60 in the left eye. Funduscopy showed bilateral pale optic discs. Left lower limb motor power was reduced to 1/5. Sensation was reduced in left lower limb. MRI of brain, spine and orbit were done. MRI of brain showed enhancing lesion was associated with perilesional edema in the right frontal lobe whereas that of spine showed enhancing elongated lesion involving cervical spinal cord from C3 to C5 level measuring 2.8mm in length (Figure 2, 3). These were hypointense lesions on T1 weighted, hyperintense on T2 weighted, no suppression on FLAIR but enhanced post gadolinium. MRI of orbit was normal. A second course of intravenous methylprednisolone 250mg was promptly given, qid. After 5 days of intravenous methylprednisolone, she was given high dose oral prednisolone 2mg/kg daily. Oral prednisolone was scheduled to be tapered over 6 months period. After 2 months follow-up, visual acuity

in both eyes were improved to 6/10. She had residual minor deficits in colour vision. Fundoscopy showed bilateral pale optic discs (Figure 1). She regained full power and sensation of left lower limb. She was able to attend activities of school and perform daily living activities. Oral prednisolone was continued for another 4 months. Subsequently, she was regular visited at our clinic monthly. There was no recurrence for one year following . Final visual acuity was 6/7.5 in the right eye and 6/10 in the left eye. Humphrey visual field was not performed because she was not cooperative during examination. However, obvious visual field defect were not elicited in confrontation visual field test.

DISCUSSION

NMO is an immune mediated demyelinating disease of central nervous system leading to optic neuritis and myelitis. Clinical manifestation of NMO varies from one individual to another. Clinical presentation of our patient was rare. She was an 8 year-old girl, visual acuity was perception to light in both eyes simultaneously followed by left lower limb weakness without preceding prodromal viral illness. Age at onset of NMO which is 8 year-old is unusual . Minagar *et al*[3] revealed that NMO was commonly affected young individuals with an average age of 25- 27 years old and predominantly affected females with the ratio of 1.8∶1 to 1.4∶1, whereas Wingerchuk *et al*[4] revealed the median age at onset was 39 years old and the female to male ratio was 9∶1. This disease incidence is more common in Asians than Caucasians[5]. Lotze *et al*[6] conducted a retrospective study in 9 patients with NMO at Texas Children's Hospital from 2001 to 2007. All patients were female. Age at onset of youngest was 2 years old in one patient and initial attack of the median age in 9 patients was 14 years old. NMO commonly presents with visual impairment in optic neuritis or spinal cord dysfunction in myelitis visual impairment manifests as decreased visual acuity, visual field defects, or loss of color vision[7]. It can affect both eyes at one time or at different time. The typical of visual field defect is central scotoma. Other changes of visual field such as paracentral scotoma, altitudinal deficits and bitemporal hemianopsia are possible[8]. Spinal cord dysfunction can lead to muscle weakness, reduced sensation, paraesthesia, walking difficulty or loss in bladder and bowel control[7]. The muscle weakness can involve all four limbs. Myelitis with severe symmetric paraplegia, sensory loss, and bladder dysfunction are typical features in NMO[4]. Our patient with unilateral left lower limb weakness was not commonly presentation. The presentation of NMO is acute in onset and classically preceded by prodrome of viral like illness such as myalgia, malaise, fatique, running nose, cough and altered bowel habits. About half of patients with NMO had prodrome symptoms[2]. However, absence of prodrome symptoms did not exclude NMO.

The actual etiology of NMO is uncertain. There were major progresses of researches in the past years to discover the NMO pathogenesis and diagnosis. The majority of patients with NMO have no affected relatives, and it is generally regarded as a non-familial condition[7]. There are researches on immune system's role in NMO. In NMO, the body's immune system attacks the myelin surrounding nerve cells. The attacks are believed to be mediated by antibodies called NMO-IgG. These antibodies target a protein of nervous system cells called aquaporin-4[7]. Aquaporin-4 is the most abundant water channel in the central nervous system. Areas containing high concentration of aquaporin-4 include spinal cord, optic nerve, hypothalamus, periventricular region and astrocytic foot processes at the blood-brain barrier. This distribution is consistent with the clinical location of lesions in NMO[7]. The inflammatory lesions in NMO is complement mediated demyelination in which the autoantibodies will cause B-cell dysregulation and complement-activation resulting in demyelination. These processes further lead to cavitation, necrosis and gliosis of nervous tissues[3]. They are different from MS pattern of inflammatory lesions in their prominent perivascular distribution[7]. There is association between NMO with autoimmune disease such as systemic lupus erythematosus. This further strengthen the evidence that NMO is an autoimmune disease[9]. There is the possibility that NMO is post viral infection related immune diseases. Based on the majority of patients with NMO were preceded with prodromal viral like illness [2].

NMO is a clinical diagnosis. However, there are variants of NMO that make the diagnosis difficult. There were various diagnostic guidelines that were discussed in recent years. In 2006, Mayo Clinic proposed a revised set of criteria for diagnosis of NMO. The new guidelines for diagnosis require two absolute criteria plus at least two of three supportive criteria[10]. The absolute criteria consist of optic neuritis and acute myelitis, whereas the supportive criteria consist of MRI brain, MRI spine and serum NMO IgG findings. The MRI brain finding does not meet the criteria of MS features whereas MRI spinal cord shows contiguous T2-weighted signal abnormality extending over 3 or more vertebral segments. Presence of periventricular plaques is the typical feature of MS in MRI brain. In MS, MRI shows spinal cord lesion rarely exceed one or two vertebral segments in length[11]. In supportive criteria, serum NMO IgG shows seropositive status in NMO. Serum NMO IgG is a specific test for NMO. However, some patients with NMO have seronegative NMO IgG. Lennon *et al*[12] conducted a study of NMO IgG in patients with NMO and MS in 2004. They found that NMO-IgG test was positive in 73% of 45 patients with neuromyelitis optica, whereas only 9% of 22 multiple sclerosis patients were positive. NMO-IgG were 73% sensitivity and 91% specificity for neuromyelitis optica. In our patient, she had clinical features of optic neuritis and myelitis. MRI of brain was not

the typical feature of MS and the reviewed of spine MRI showed three contiguous segments involvement of spinal cord extending from C3 to C5 level. Thus, she fulfilled this revised diagnostic critio of NMO. NMO-IgG was not done for her because her parents refused .

CSF analysis is not part of this revised diagnostic criteria, but it is useful to distinguish between NMO and MS. CSF pleocytosis ($>50\times10^6$ leucocytes/L) with high proportion neutrophils is indicative of NMO, whereas in MS it is always less than 50×10^6 leucocytes/L and has high proportion of lymphocytes. Oligoclonal bands of IgG in the CSF is detected in 85% of patients with MS and 15%-30% of patients with NMO[4]. Therefore, a normal CSF analysis doesn't exclude NMO.

There are various options of treatment for NMO such as intravenous corticosteroids, plasmapheresis, intravenous immunoglobulin and immunosuppressive agents. The common immunosuppressive agents are oral prednisolone and azathioprine. Others such as rituximab, cyclophosphamide, mitoxantrone and mycophenolate mofetil are alternative immunosuppressive agens. In acute episodes of NMO, patients are treated with a course of high dosage intravenous corticosteroids such as methylprednisolone. Alternative effective treatments in acute attack of NMO are plasmapheresis or intravenous immunoglobulins if the patients do not respond well to intravenous corticosteroids treatment. Various regime of methylprednisolone were studied in previous literatures. Sellner *et al*[8] recommended intravenous methylprednisolone 1g for 3-5 days as first line therapy, followed by tapering of oral prednisolone. Early initiation of plasmapheresis is recommended in steroid unresponsive relapses. Besides this regime, there is another regime that consists of combination of corticosteroids and immunosuppressive agents. Mandler *et al*[13] recommended intravenous methylprednisolone 500mg/d, b. i. d. for 5 days and then continued with oral prednisolone 1mg/(kg·d) for 2 months and slowly tapered to 10mg every 3 weeks. Immunosuppressive agent such as azathioprine 2mg/(kg·d) was added after 3 weeks of oral prednisolone[13]. There were good outcomes in both regimes. However, response of treatment varies individually depend on the severity of NMO. In our patient, she has an early recurrence of NMO, she was given intravenous methylprednisolone 250mg, q. i. d. , for 5 days followed by oral prednisolone 2mg/kg·d and tapered over 6 months. She responded to this regime well with good outcome. It is important to follow up the patients regularly post-treatment of corticosteroids because some patients have relapses on withdrawal of the corticosteroids[3].

NMO can be monophasic or relapsing course. About 80%-90% NMO is relapsing[4]. The median time to second attack is 7 months[6]. However, rapid recurrence after initial treatment is unusual. Our patient had early recurrence about 5 weeks after the initial treatment . About 60% of patients with NMO have a relapse within one year and 90% within 3 years[2]. It differs with MS that commonly in relapsing-remitting course[14]. Prevention of NMO attacks with immunosuppressive agents is debatable. There are no randomized controlled trials that have established the effectiveness of treatments for the relapse prevention. Generally, maintainence immunosuppressive therapy is a strategy for reducing relapses of NMO. Sellner *et al*[8] recommended combination of oral azathioprine [2. 5-3g/(kg·d)] and prednisolone (1mg/kg·d or alternate day) as first line therapy for prevention of relapse. However, the optimal treatment duration is not determined yet. If patient develops steroid dependence for clinical remission, alternative immunosuppressive treatment such as cyclophosphamide (7-25mg/kg every month over a period of 6 months), mitoxantrone ($12mg/m^2$ every 3 months for 9 months) or mycophenolate mofetil (1-3g/d) are considered[8].

Generally, the prognosis of NMO is good in early treatment. However, residual neurological deficit may persist. Our patient had good outcome with final visual acuity of 6/7. 5 in the right eye and 6/10 in the left eye. She had no permanent neurological deficits of limbs and no recurrence after a year following. Individuals may present as isolated optic neuritis or isolated myelitis in early presentation. Therefore , it is crucial to consider NMO as part of the differential diagnosis of optic neuritis or myelitis in a child even it is rare. Prompt diagnosis, with immediate and appropriate treatments will help to improve vision and prevent disability.

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儿童早期复发型视神经脊髓炎的成功治疗 1 例

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摘要

目的:报告罕见的儿童早期复发型视神经脊髓炎的成功治疗 1 例。

方法:病例报告。

结果:患者,女,8 岁,卡达山族,突发性双眼视力下降 5d 后,出现左下肢肌力减弱症状。发病时,患者双眼视力为光感,伴双眼视盘充血水肿。脑部与脊髓 MRI 显示:右额叶及颈 5 水平脊髓后部有白色增强信号的病变,诊断为视神经脊髓炎,给予静脉注射甲基强的松龙冲击治疗,随后转为口服泼尼松龙维持治疗。1mo 后症状逐渐缓解。然而,停止口服泼尼松龙 1wk 后症状复发。复查脑脊髓 MRI 显示:在脑部的同样区域以及脊髓颈 3 到颈 5 段仍有持续的炎症存在,遂立即给予甲基强的松龙冲击治疗,并口服激素延缓减量。2mo 后,患者已经可以行走并参与学校活动,此时双眼的视力提高到 0.6,但还残留少量的色觉损害,下肢神经检查也正常。口服递减药量的泼尼松龙维持治疗持续 4mo,随访 1a 没有复发。最终,患者视力恢复到右眼 0.8,左眼 0.6。

结论:对于突发性双眼视力下降伴随肢体肌力减弱的儿童患者,必须对视神经脊髓炎有所警惕。早期诊断及治疗有利于患者的康复。

关键词:视神经脊髓炎;视神经炎;脊髓炎;儿童