

Paediatric optic neuritis: experience from a tertiary referral centre in Malaysia

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Abstract

Background: Optic neuritis typically presents with acute or subacute onset of mild or profound blurring of vision. There are very limited reports regarding optic neuritis in the paediatric population compared to adults from the South Asian region. We report a series of 7 cases of paediatric optic neuritis.

Methods: All optic neuritis cases aged less than 12 years old in 2016 were studied retrospectively.

Results: Out of 44 patients with optic neuritis, 7 of them were of paediatric age. The mean age was 9.9 years. All patients had sudden onset profound vision loss (range 3/60 to hand movement). Four patients had bilateral involvement, all had reduced colour vision. Three had underlying acute disseminated encephalomyelitis. All were treated with high-dose intravenous corticosteroids. Five patients made full recovery, one patient had partial recovery, and one patient had no visual recovery. Interestingly, none of them had multiple sclerosis (MS) or neuromyelitis optica (NMO) at the time of diagnosis.

Conclusion: Prognosis is generally good for isolated cases of paediatric optic neuritis. Outcome of cases secondary to ADEM depends on the degree and extent of demyelination. A diagnosis of chronic relapsing inflammatory optic neuropathy can be considered in recurrent cases that are steroid responsive. None of our cases had underlying MS or NMO during the study period.

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Optik neuritis pediatrik: pengalaman dari pusat rujukan tertiar di Malaysia

Abstrak

Latarbelakang: Optik neuritis adalah keadaan yang selalu hadir dengan permulaan subakut kekaburan mata yang melampau. Didapati tiada laporan berkenaan pediatrik optic neuritis di kalangan penduduk Asia Selatan. Kami melaporkan satu kes siri yang melibatkan tujuh pesakit pediatrik optic neuritis.

Kaedah: Semua kes optic neuritis yang berusia kurang dari 12 tahun dikaji secara retrospektif.

Keputusan: Terdapat empat puluh empat pesakit yang menghadapi optic neuritis, tujuh adalah golongan kanak-kanak. Min usia untuk mereka ialah 9.9 tahun. Kesemua pesakit datang dengan kehilangan penglihatan yang melampau secara megejut (dari 3/60 ke HM). Terdapat empat pesakit yang melibatkan kedua-dua mata. Kesemua mengalami pengurangan dari segi penglihatan warna. Tiga pesakit turut mengalami penyakit ensefelitis demielinasi secara akut (*acute disseminated encephalomyelitis* - ADEM). Semua pesakit telah dirawat dengan intravena kortikosteroid berdos tinggi. Lima pesakit mendapat penyembuhan yang sepenuhnya, seorang mempunyai penyembuhan separa dan seorang lagi tidak langsung mendapat pemulihan dari segi penglihatan. Menariknya, tiada seorang pun yang mendapat penyakit multiple sclerosis (MS) atau neuromyelitis optica (NMO) semasa diagnosis dibuat.

Kesimpulan: Kes optic neuritis pediatrik mempunyai prognosis yang baik. Hasil kejadian disebabkan yang oleh ADEM bergantung pada darjah dan keterukan demielinasi. Diagnosis keradangan optik neuropati yang berulang dan kronik (*chronic relapsing inflammatory optic neuropathy* - CRION) boleh dipertimbangkan sekiranya terdapat situasi yang berulang serta responsif terhadap steroid. Tiada satu pun kes kami yang mengalami MS atau NMO sewaktu kajian dilaksanakan.

Kata kunci: pediatrik optik neuritis, Malaysia

Introduction

Optic neuritis (ON) can be a potentially devastating condition. It usually presents with acute or subacute onset of blurring of vision, usually to a severe degree. There are limited data regarding ON in Malaysia, but in one retrospective study, the average age of onset was 21–30 years.¹ ON in children differs from adult-onset ON in some clinical features, aetiology, and prognosis.

ON in children is reported to have more bilateral involvement and greater visual acuity loss compared to adults.² Children tend to have disc oedema, with good visual prognosis.³ Contrary to adults, ON is often associated with recent immunization. The risk of subsequent development of multiple sclerosis (MS) is greater in older children seen in white matter lesions on magnetic resonance imaging (MRI).⁴

This retrospective chart review presents our observations of seven children seen over a 1-year period to mainly to illustrate the aetiology, clinical presentation, and outcome of ON. Its relationship to demyelinating conditions in the paediatric population is also explored.

Methods

This is a retrospective review of cases over a 1-year period (October 2015–October 2016) treated at the neuro-ophthalmology clinic in Hospital Kuala Lumpur (HKL), a tertiary referral centre located in an urban setting with a population of more than 1.5 million. The medical records of patients diagnosed with ON in children aged 12 years and below were traced. The minimum follow-up period was 3 years. The clinical presentation, aetiological factors, and outcome were analysed in each patient.

Results

A total of 44 cases of optic neuritis were seen, and seven (15.90% prevalence) were found to be in the paediatric age group. Table 1 shows the patients' clinical data and investigations. The mean age of the patients was 9.86 years. The most common symptoms were sudden onset bilateral blurring of vision with pain on eye movement. All affected eyes had reduced colour vision. Six patients had papillitis, while only one patient showed retrobulbar involvement.

Common risk factors include a preceding episode of infection, which can be as trivial as a history of upper respiratory tract infection (URTI) 2 weeks prior to onset of symptoms or ongoing sinusitis, or can be more disease-specific, namely, acute disseminated encephalomyelitis (ADEM). One patient had a history of URTI, whilst another patient had ongoing sinusitis. Three patients had ADEM; the cause for the other two patients was unknown.

Table 1. Summary of clinical features and investigations in children with optic neuritis

Case	Age/ Sex	Eyes	Associated symptoms	Colour vision	Disc appearance	Imaging	CTD/LP
1	7/F	BE	Headache	R: 3/15 L: 1/15	Hyperaemic, swollen bilateral discs	Optic sheath enhancement over coronal section	-
2	12/M	RE	Pain on eye movement	R: 0/15 L: 15/15	Hyperaemic swollen right disc	R ON enhancement, possible L thalamic, midline mamillary signal abnormality, possible AQP4 demyelination. Repeat MRI 6 months later: normal	-
3	11/F	BE	Unable to differentiate colours, pain on eye movement, neck and shoulder pain, severe headache	R: 1/15 L: 0/15	Bilateral discs not swollen, normal in appearance	Multiple T2 hyperintense areas in bilateral cerebellum, parietal, occipital, vertex region, suggestive of ADEM. Bilateral ON normal.	-
4	12/M	BE	Pain on eye movement	BE: 0/15	Hyperaemic, swollen bilateral discs	Normal, no evidence of demyelination	CTD: normal LP: normal, negative oligoclonal band
5	11/M	RE	Nil	R: 0/15 L: 15/15	Mildly swollen right disc	R intraorbital ON slightly swollen. Hyperdensity in L frontal sinus.	-
6	10/F	LE	Nil	BE: strong deutan	Left disc swollen, hyperaemic	White plaque-like lesion in occipitoparietal area, suggestive of ADEM.	
7	6/F	BE	Fever, vomiting, headache	R: 0/15 L: 1/15	Bilateral swollen discs	Multiple T2 hyperintense lesions involving deep and subcortical white matter, lentiform nuclei bilaterally, R thalamus and bilateral ON showing ADEM.	CTD: normal LP: normal, negative oligoclonal band

F: female; M: male; BE: both eyes; R: right; L: left; ON: optic nerve; ADEM: acute disseminated encephalomyelitis; CTD: connective tissue disease; LP: lumbar puncture

Table 2. Diagnosis, risk factors, treatment, and initial and final visual acuity

Case No.	Diagnosis	Initial VA	Risk factors/ comorbidities	Treatment	Final VA
1	Isolated bilateral ON secondary to viral URTI	R: 3/60 L: 3/60	Viral URTI	IV Methylprednisolone	RE: 6/6 LE: 6/6
2	Steroid-dependent ON 2 episodes of recurrences	R: CF L: 6/9	Epilepsy	IV Methylprednisolone	R: 6/6 L: 6/7.5
3	Bilateral ON 2' ADEM	R: 2/60 L: CF	ADEM	IV Methylprednisolone	R: 6/6 L: 6/6
4	CRION	R: CF L: CF	Nil	IV Methylprednisolone, no immunomodulators given	After 7 episodes R: 6/12 L: 6/24
5	Right ON 2' acute sinusitis	R: HM L: 6/9	Sinusitis	IV Methylprednisolone	R: 6/6 L: 6/6
6	ON 2' ADEM	R:6/6 L: HM	ADEM	IV Methylprednisolone	R: 6/6 L: 6/6
7	Bilateral ON 2' ADEM	R: 3/60 L: CF	ADEM	IV Methylprednisolone	R: NLP L: 2/60

ON: optic neuritis; URTI: upper respiratory tract infection; ADEM: acute disseminated encephalomyelitis; CRION: chronic relapsing inflammatory optic neuropathy; VA: visual acuity; R: right; L: left; CF: counting fingers; HM: hand movement; NLP: no light perception

None of the children had neuromyelitis optica (NMO), as all patients were negative for anti-aquaporin 4 on blood investigation. None of the patients had evidence of MS on imaging studies. The imaging studies of five patients showed ON, while the other two did not. All patients were admitted and treated with high-dose steroid based on Optic Neuritis Treatment Trial (ONTT) criteria. Five patients regained their baseline visual acuity while two did not due to multiple recurrences and ADEM with severe demyelination. Diagnoses, risk factors, initial and final visual acuity, and treatment are noted in Table 2.

Discussion

Paediatric ON is a rare medical condition. Annual incidence was 1.04 (95% confidence interval [CI], 1.01–1.07) per 100,000 pediatric individuals and 3.29 (95% CI, 3.28–3.30) per 100,000 adults.⁵ The constellation of signs and symptoms leading to a diagnosis of ON include visual acuity loss, presence of pain on activity of the extrinsic eye muscles, relative afferent pupillary defect, dyschromatopsia, and swelling of the optic nerve head in anterior ON and normal appearance of the nerve in retrobulbar ON. In this retrospective chart review, the mean age of presentation was 9.8 years old, with bilateral presentation compared to unilateral in adulthood. They also tended to have papillitis rather than retrobulbar involvement, with profound blurring of vision of 6/60 or worse. This finding is in agreement with Shatriah *et al.*, who compared paediatric ON in Asian countries.⁶

Although the exact mechanism is unknown, the proposed pathophysiology for ON is immune-mediated, delayed-type IV hypersensitivity reaction from a peripheral activation of T-cells that cross the blood brain barrier and causes destruction of the myelin sheath involving axonal degeneration and death of neural cells. Precipitating risk factors include autoimmune diseases such as systemic lupus erythematosus, infectious or parainfectious causes (tuberculosis), syphilis, inflammatory (sinusitis, gum infection, URTI), post-vaccination immunological response, and post-vaccination states. In this chart review, two of seven patients had risk factors, which were sinusitis and viral URTI.

MRI of the brain and orbit may be performed to confirm diagnosis, which includes enhancement and enlargement of the optic nerve and retro-orbital fat streakiness. Of the seven patients, six showed classical findings of ON on imaging while one patient did not. MRI of the brain was not done for all cases, only when significant changes were found needing further detailed examination of soft tissue to rule out demyelinating diseases. Global and longitudinal enhancement of the nerve is the typical pattern seen in ON and its extension has been seen to correlate with visual impairment and with visual prognosis.⁷ Of the seven patients, five showed good visual recovery while the other two remained visually impaired: one due to extension of severe demyelination as shown in imaging studies, while the other due

to multiple attacks of neuritis secondary to chronic relapsing inflammatory optic neuropathy (CRION). Recurrent attacks of ON may cause poor visual acuity outcome due to progressive loss of the myelin sheath after repeated episodes of inflammation.

The aetiology for most of the children in this retrospective chart review was idiopathic, similar to earlier reports from Singapore, China, and India.⁸ Although the aetiology of ON is usually idiopathic, it is commonly associated with demyelination, including MS, NMO, and ADEM. In our observation, three of the seven children had ADEM, but none had any other demyelinating conditions. In the literature, many children with single or recurrent episodes of ON following ADEM had myelin oligodendrocyte glycoprotein antibodies.⁹ In ADEM, there is a tendency for longer intervals between attacks (more than 5 years), unlike in children with MS.¹⁰

Treatment of ON generally is based on the ONTT criteria since there are no clinical trials on paediatric ON to date. Based on ONTT, intravenous high-dose steroids can hasten visual recovery within the first week but does not affect long-term outcome. Current management of paediatric ON involves intravenous methylprednisolone (4–30 mg/kg per day divided in three doses per day) for 3 or 5 days, depending on visual recovery, followed by a more prolonged, tapered course of oral corticosteroid to avoid recurrence, which is rather common in this age group.

Paediatric ON generally has a good prognosis. Over a few weeks after an insult, resolution of inflammation and visual recovery occurs while remyelination takes place, although this process is usually not complete. As seen in the cases above, only two children had poor recovery, one due to severe demyelination in ADEM while the other had repeated episodes of neuritis. This is due to the aftermath of persistent demyelination and axonal loss, as well as rearrangement of sodium channels over demyelinated segments, which improves conduction but can make surviving axons prone to damage.¹¹ However, in cases which are recurrent, the prognosis is poorer. Recurrence is defined by new symptoms happening more than 2 weeks after the first presentation.¹²

In conclusion, prognosis is generally good for isolated cases of paediatric ON. However, the outcome for cases secondary to ADEM depends on the degree and extent of demyelination. A diagnosis of CRION can be considered in recurrent cases that are steroid responsive.

Declarations

Ethics approval and consent to participate

Given this was a retrospective study based on reviewing medical charts, ethics approval was not required.

Competing interests

None to declare.

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