

Optic neuritis associated with chronic inflammatory demyelinating polyneuropathy in a child - a case report

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Abstract

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an autoimmune disorder predominantly affecting the peripheral nervous system (PNS), characterised by muscle weakness and sensory disruption which may involve all four limbs [1]. CIDP affecting children is uncommon, with a large scale review in 2013 noting 143 documented cases described in the literature [2]. Central nervous system involvement has previously been described; however, optic neuropathy is an extremely rare manifestation of CIDP, with only a small number of cases previously reported (both unilateral and bilateral) in adult patients [3, 4, 5]. This report details a child who developed optic neuropathy in association with CIDP.

Keywords: Chronic inflammatory demyelinating polyneuropathy (CIDP), Optic neuritis.

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Case Report

A previously fit and well 11-year-old boy presented with lower limb weakness, noting that 'footballs are harder to hit'. He noticed this following a minor right foot injury sustained playing football at school. His symptoms progressed and he developed bilateral lower limb pain on movement. He attended his local hospital where he was diagnosed with a non-specific sports-related injury and discharged.

A month later, he developed episodic headaches, reduced mobility, an unsteady gait, frequent falls and slurred speech. He was admitted to hospital for further investigations. MRI (magnetic resonance imaging) scans of his brain and spine were reported as normal. Blood tests (renal and liver function test, C-reactive protein, glucose, HIV, Hepatitis B and Hepatitis C) were essentially normal; an ESR (erythrocyte sedimentation rate) of 70 and a mild microcytosis were noted, although his Hb and differential blood cell counts were normal. He was subsequently referred to the child and adolescent mental health service.

He continued to deteriorate, developing weakness in his hands and swallowing difficulties. He lost ambulation, requiring assistance to transfer and mobilise indoors. Examination showed bilateral horizontal nystagmus on abduction, past-pointing, intention tremor, reduced power in hands

and fingers, loss of movement in ankles and toes in addition to absent knee, ankle and biceps reflexes. Lumbar puncture and blood tests were negative for ANA (antinuclear antibodies), ANCA (anti-neutrophilic cytoplasmic autoantibodies), ganglioside antibodies, VLCFA (very long-chain fatty acids), serum electrophoresis, white cell ubiquitome, and heavy metals. Leukocyte enzymes, in addition to serum/urine GAMT (guanidinoacetate methyltransferase) and purines, were all normal.

EMG (electromyography) nerve conduction studies demonstrated severe demyelinating sensorimotor polyneuropathy in keeping with chronic inflammatory demyelinating polyneuropathy (CIPD), with likely bulbar involvement based on the clinical history. Contrast MRI scans of the brain and spine demonstrated newly identified thickening and enhancement of bilateral cranial nerves II, V, VII and cauda equina nerve roots, in keeping with CIDP (Figure 1 & Figure 2). During this admission, he complained of 'blurry' right eye vision, but eye examination demonstrated normal extra-ocular motility, normal colour vision (Ishihara plates) and normal disc appearances bilaterally. Left eye VA (visual acuity) was normal at 0.0 (LogMAR), but his right eye VA was subnormal at 0.3 (LogMAR) and a right infero-temporal visual field defect was identified by confrontation visual field testing.



Figure 1 Post-contrast T1 weighted sagittal spine imaging demonstrates surface thickening and enhancement of the conus medullaris and the nerve roots of the cauda equine.

He commenced IVIG (intravenous immunoglobulin) with a significant improvement in limb power and mobility noted over the following seven days; however, his progress slowed after this period. Two months later he presented to an ophthalmology outpatient clinic complaining of a significant deterioration in his right eye vision. On examination, his left eye VA measured 0.06 (LogMAR), but his right VA had deteriorated to light detection in all four quadrants only, with a right RAPD (relative afferent pupillary deficit). Discs remained normal in appearance. He underwent a brain MRI which again demonstrated enhancement of cranial nerves III, V, VII and VIII, but this was not significantly different from the previous MRI. Although clear optic nerve involvement was not demonstrated on MRI, the visual electrophysiology findings at the time showed marked, generalised post-retinal, visual pathway dysfunction, affecting the right eye pathway more than that of the left eye. Indeed, flash and pattern VEPs (visual evoked potentials) from the right eye were non-detectable. From the left eye, the flash VEP was markedly small, but a near normal pattern VEP from the left eye showed preservation of the left eye's macular pathway. The PERG (pattern electro-retinogram) p50/n95 amplitude ratios from either eye were normal. This indicated normal retinal ganglion cell function for each eye, and localised the site of dysfunction to post-retinal ganglion cell axons that form the optic nerve. In view of his slow overall progress with IVIG therapy over the next weeks, he was started intravenously on methylprednisolone. An ophthalmology

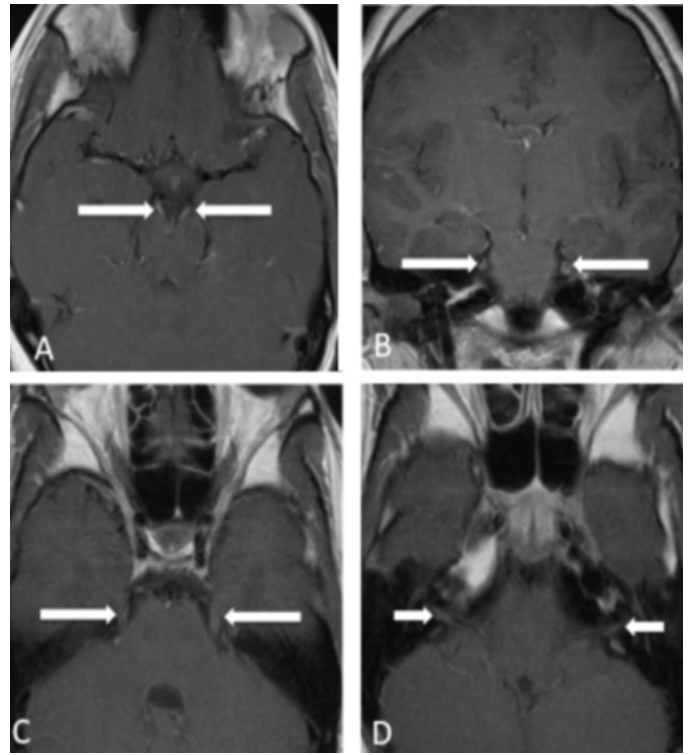


Figure 2 Axial and coronal enhanced brain images demonstrate cranial nerve thickening and enhancement involving cranial nerves III (A), V (B and C), VII and VIII (D).

clinic review at this time found the right eye VA had deteriorated to 'no perception of light' and the left eye VA had deteriorated to 0.3 (LogMAR). The right-sided RAPD remained. Some temporal pallor of the left optic disc was noted. Kinetic perimetry showed an inferior field deficit in the left eye. Over the next two months there was a clinical improvement in his right eye vision, with right eye VA 0.6 (LogMAR), but he complained of a further deterioration in his left eye vision, VA 0.58 (LogMAR). VA of either eye did not improve with a pinhole which excludes uncorrected refractive error. Colour vision tests were reduced bilaterally,

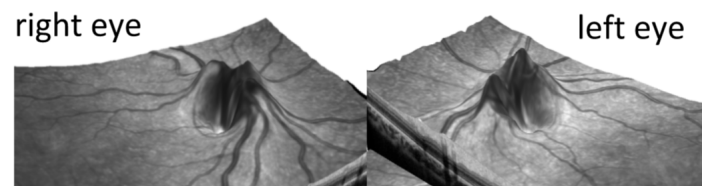


Figure 3 Spectralis OCT images week 40. The 3D plots show some bilateral optic disc swelling, LE more than RE.

ally, but he was more confident with his right eye. A left relative afferent pupillary defect was identified. Both discs were recorded as normal. Repeat electrophysiology testing showed reduction in PERG N95 amplitudes of each eye, indicating involvement of the retinal ganglion cells bilaterally. The left eye PVEPs (pattern visual evoked potentials) had

deteriorated with significantly increased latency in keeping with conduction dysfunction (e.g. P100' to 100' checks @ 153 ms), yet PVEPs from the right eye showed some recovery, albeit being slightly delayed (P100' to 100', 50' 25' checks @ 120 ms) with a small amplitude.

Over the next three months his right vision continued to improve, but his left vision continued to deteriorate with VAS (visual acuity score) in the right eye being 0.12 and the left eye 1.40 (LogMAR). He continued to undergo close observation, in addition to receiving treatment with 50mg of prednisolone once daily, with lansoprazole for gastric protection. Visual electrophysiology, repeated one year after his first admission, showed some recovery of retinal ganglion cell function bilaterally with larger PERG amplitudes and improved P50/N95 ratios. The right eye PVEP had improved slightly, but the left eye pattern and flash VEPs had deteriorated further.

Two months later, right vision had improved to normal levels with the right eye -0.06(LogMAR) and there was some slow improvement in the left vision, with the left eye 0.44(LogMAR), with temporal pallor of the left optic disc. Serial OCT of the optic discs showed infero-temporal thinning of the peripapillary retinal nerve fibre layer (RNFL), which slowly progressed between July 2015 and May 2017 (Figure 3 & Figure 4).

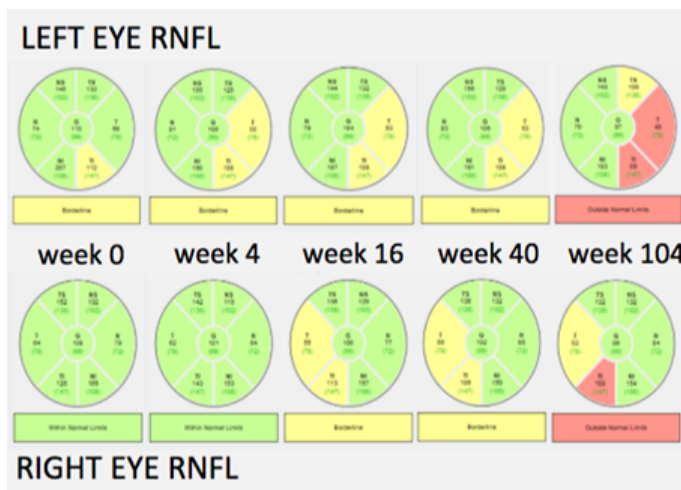


Figure 4 The RNFL thinning noted bi-temporally progressed between weeks 40 and 104, highlighted changing from yellow to red.

In May 2017 his VA was right eye -0.1 and left eye 0.1 (logMAR) with temporal disc pallor and left eye RAPD (longitudinal change in VA shown in (Figure 5). PERGs showed bilateral retinal ganglion cell dysfunction. PVEPs from the right eye were stable and from the left eye were improved, but showed evidence of macular pathway dysfunction affecting the left more than the right eye pathways.

During this time the patient's motor function has significantly improved. He is now independently ambulant and has returned to playing football. His hand function has also improved, but not returned to full strength as yet. He con-

tinues to have some motor deficit in his foot muscles, such that ankle dorsiflexion remains sub gravity. He is otherwise independent in most of his daily activities. He remains on monthly IVIG and oral prednisolone, but continues to show slow and steady improvement.

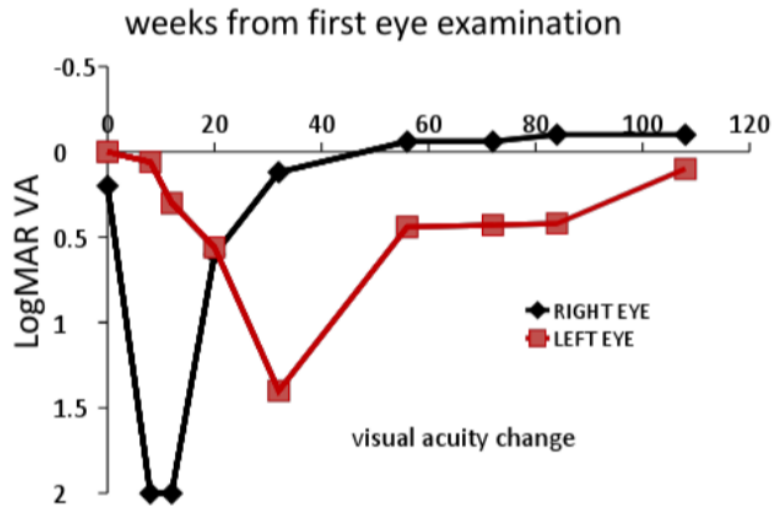


Figure 5 The changes of monocular high contrast LogMAR VA is plotted over time, black RE and red LE. [for reference LogMAR 0 = 6/6 =20/20 VA, and LogMAR 2 here depicts NPL]

Discussion & Conclusion

Optic neuritis in association with CIDP is an uncommon phenomenon. To the best of the authors' knowledge, despite previous case reports detailing this manifestation in adult patients, this is the first case to be described in a paediatric patient. However, McMillian et al., 2013 [2] make note of the difficulty in obtaining reliable sensory imaging in the majority of paediatric CIDP patients given their young age, and this may therefore lead to a failure to identify affected patients who do not present with overt clinical symptoms.

The recovery of right eye vision from NPL to -0.06 (LogMAR) was remarkable, but the recovery was protracted over a 12-month period. In spite of recovery of the central visual field, i.e. the macular pathway function, there was flash VEP evidence of bilateral generalised pathway dysfunction. During a one-year period of ophthalmic surveillance, right and left post-retinal macular pathways were asynchronously involved. Although no evidence of optic neuritis was seen on MRI, the PERGs and PVEPs suggested optic neuritis, and negative MRI findings have previously been reported in adult cases. It is uncertain whether the systemic treatment altered the relative severity of the left eye pathway involvement of the right eye.

The PERG N95 is a sensitive measure of ganglion cell function in the retina. Preservation of N95 in cases of optic neuritis is taken as a good prognostic indicator of visual recovery. The right eye PERG N95 was normal even when the

right eye PVEP suggested optic neuritis, presumably because the retinal ganglion cells were still functioning normally at the retinal end of the cell and the dysfunction was retrobulbar. Some months later at the zenith of bilateral vision loss the N95/P50 ratio of either eye diminished. In optic neuritis, this observation usually indicates irreversible ganglion cell dysfunction before optic atrophy is manifest. Atypically in our case, the PERG P50/N95 amplitude ratio recovered, as did right eye VA. The PERGs were altered during an episode of marked bilateral vision loss. It is possible that this episode was sufficiently transient for retinal ganglion cell function to be restored before cell death. The amplitude of the N95 depends upon the preceding P50. A reduction of N95, consequent upon reduction of P50, has been described in cases of acute optic neuritis of less than seven days onset [6]. In these circumstances, as the PERG P50 recovers, a delay in PVEP becomes apparent. Retrograde degeneration is thought responsible for subsequent or sustained loss of PERG N95. In our case the P50 amplitude did not diminish. The latest PERGs N95 however indicate bilateral retinal ganglion cell dysfunction and concomitantly there has been thinning of the RNFL bilaterally. This suggests a chronic degenerative process.

Treatment options for CIDP include IVIG, corticosteroid administration and plasma exchange; however, the optimal management of optic neuritis in association with CIDP has yet to be determined [6]. The subject of this case report initially presented with demyelination of the peripheral nervous system, which then progressed to ophthalmological manifestations prior to IVIG therapy. Following IVIG treatment, an initial positive response in peripheral symptoms was observed, quickly followed by a plateau phase; however, he continued to experience clinical deterioration vision/optic nerve function, even after the initiation of high dose corticosteroid therapy, hinting at differences in the underlying processes.

Competing interests

The authors have declared that they have no competing interests.

Author contributions

All the authors contributed to data collection and also critically reviewed the manuscript. The final version of the manuscript was approved by all the authors.

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