Macular oedema in Charcot-Marie-Tooth disease

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Abstract
Charcot-Marie-Tooth disease is a rare, inherited neuromuscular disorder which is seldom associated with ocular features. We present the first reported case in the English literature of unilateral macular oedema in a child with Charcot-Marie-Tooth disease and no underlying metabolic or vascular disorders.

Keywords: Charcot-Marie-Tooth, macular oedema, ocular features

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Introduction
Charcot-Marie-Tooth (CMT) is an inherited neuromuscular disorder, not typically associated with metabolic derangements. Professor Jean Martin Charcot and Pierre Marie, both of France, published the first description of CMT in 1886, in a patient presenting with muscle weakness and wasting in the legs. He called the disease peroneal muscular atrophy. Howard Henry Tooth described the same disease in his Cambridge dissertation, also in 1886, but called the disease peroneal progressive muscular atrophy. Tooth explained the symptoms to be as a result of a neuropathy, rather than myopathy. CMT presents in two forms: CMT1 and CMT2. CMT1 is a disorder of peripheral demyelination, which leads to uniform slowing of conduction velocity in motor and sensory nerves. CMT1 is predominantly inherited in an autosomal dominant fashion. CMT2 is primarily an axonal disorder and not demyelinating in nature.

CMT1 is known to be associated with the following ocular features: impaired accommodation, anisocoria, tonic, Argyll Robertson and Horner’s pupils. It can also present with glaucoma and cataracts. Other studies have reported external ophthalmoplegia, bilateral vitritis, optic neuropathy, primary optic atrophy, macular degeneration and retinitis-pigmentosa-like electroretinography tracings. After a search of the English literature, to date, this appears to be the first report of macula oedema in a child with CMT.

Case study
An 11-year-old girl was referred to the Red Cross War Memorial Children’s Hospital in Cape Town, South Africa, with a one-month history of occasional headaches and reduced vision in the left eye. At age 2 years she had been diagnosed as having Charcot-Marie-Tooth disease by the neurology department, where she was being followed up. She had an uncomplicated term delivery and was up-to-date with her immunisations. She had a positive maternal history of CMT. Genetic testing confirmed the diagnosis of CMT1A.

She did not have any other contributory chronic metabolic illnesses. She had had a previous ophthalmology consultation at age 7 years for a suspected ocular problem. At that stage, she had visual acuities of 6/6 in each eye, normal pupil reactions, full ocular motility and normal fundi.

Examination findings
The right eye was completely normal, with a visual acuity of 6/6 (Figure 1). She was orthotropically with full extraocular motility. Visual acuity in the left eye was measured at 6/9, with no improvement on pinhole. Her anterior segments were normal, as were her intraocular pressures (14 mmHg right, 13 mmHg left). Pupil responses were normal, with no relative afferent pupillary defect. On dilated fundoscopy,
Management
After consultation with a medical retinal specialist, oral acetazolamide 250 mg daily was commenced. At one-month follow-up, there was no improvement in her visual acuity, and the fundoscopic findings were unchanged. The macular cysts and retinal thickness were also unchanged on repeat OCT (Figures 5 and 6). Fundus fluorescein angiography (FFA) showed increasing macular hyperfluorescence in the early phases, consistent with macular oedema (Figure 7). The child reported no deterioration in symptoms and because there was no noticeable improvement in clinical findings, acetazolamide was then stopped. Routine monitoring was scheduled and the family counselled regarding the current stability of her vision, albeit in the context of an uncertain prognosis.

Discussion
This case of confirmed CMT1A is the first reported to present with macular oedema, which was unilateral and did not resolve after a one-month trial of oral acetazolamide. Electrophysiological features of CMT are known to mirror those of Refsum disease and retinitis pigmentosa. Both of these retinal degenerative diseases can be associated with macular oedema. We did not perform an electroretinogram (ERG) in this case, as only crude, mass response electrophysiological testing is available at our institution, which is unable to differentiate cone and rod photoreceptor dysfunction. Bakhavatchalam et al., in their systematic review of the English literature, showed that oral carbonic anhydrase inhibitors were effective first-line treatments in retinitis-pigmentosa-associated macular oedema. Improvement can occur within two weeks of starting treatment. However, the mechanism of macular oedema in CMT1A is yet unknown. The rationale for treatment in this case was that the electrophysiological features of CMT are similar to that of retinitis pigmentosa. As no subjective or objective improvement was observed after one month of treatment, the decision was made to stop acetazolamide because of its potential systemic side-effects. Topical ketorolac was not considered as a treatment option in this case, on the basis that the macular oedema was unlikely to be inflammatory in origin. Due to the absence of good evidence on the possible effectiveness and safety of anti-vascular endothelial

macular oedema and perifoveal exudates were present in the left eye. There were no associated haemorrhages, or cotton wool spots, and the retinal vasculature was normal (Figure 2). Her cup:disc ratios were 0.2. Ocular coherency tomography (OCT) showed cystic macular lesions and retinal thickening consistent with macular oedema (Figures 3 and 4). Special investigations, which included urea and electrolytes, a full blood count, blood glucose and lipogram, were all normal. The Treponema pallidum hemagglutination assay (TPHA) was negative.

Figure 1. Normal right fundus

Figure 2. Left fundus photograph showing macular oedema with perifoveal exudates

Figure 3. Left fundus photograph showing macular oedema and perifoveal exudates

Figure 4. OCT showing cystic macular lesions and retinal thickening consistent with macular oedema

Figure 5. OCT showing macular oedema

Figure 6. OCT showing macular oedema

Figure 7. FFA showing macular hyperfluorescence
growth factor (anti-VEGF) injections in paediatric macular oedema, it was decided not to pursue this therapeutic option.

**Conclusion**

This case describes the novel finding of macular oedema in a child with Charcot-Marie-Tooth disease. The underlying mechanisms for the macular oedema in this setting, and the fact that it did not respond to a one-month course of oral acetazolamide, remain unclear.

**References**


**Figure 3. Left macular OCT showing cystoid changes plus hard exudates**

**Figure 4. Left OCT showing increased macular thickness**

**Figure 5. OCT of left macula at one month, showing persistent cystoid changes**

**Figure 6. OCT at one-month follow-up, showing persistent macular thickening**

**Figure 7. Fluorescein angiography at one month, showing macular hyperfluorescence in the early phase**