Case Reports

Charcot-Marie-Tooth disease with co-occurrence of syringo-hydromyelia

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Introduction

Charcot-Marie-Tooth disease (CMT) is the commonest inherited neuromuscular disorder affecting about 1 in 2,500[1]. We describe a child with CMT with co-occurrence of syringo-hydromyelia.

Case report

A 10-year-old boy, presenting with poorly healing ulcers for 3 years in both feet, but more predominantly over the plantar surface of the left foot, was admitted to the paediatric surgical ward for further management. He had taken treatment several times from a general practitioner without improvement. From the very beginning, his illness was complicated with pain and numbness over both lower limbs interfering with his activities and the symptoms have steadily progressed over the last 3 weeks. There were no similar symptoms in the upper limbs. He was an average performer at school with no recent deterioration. The mother denies any behaviour changes over the last few years. He is non-vegetarian and not on long-term medication and has had no exposure to toxins.

There was no urinary or faecal incontinence. Moreover, he was born to non-consanguineous parents as the 2nd child in the family and there was no family history of a similar condition. He was developmentally normal and his academic performances were average.

On examination, he was pink and afebrile with no photosensitive rash. His neurological examination revealed normal higher functions. All motor cranial nerves were normal but optic nerve examination revealed reduced visual acuity (6/24) together with red / green colour blindness. Motor system examination revealed normal gait and tone.

Examination of the feet revealed high-arched feet, hammer toes, atrophy and weakness of the intrinsic muscles of the feet (score 4/5 on Medical Research Council scale), impaired dorsiflexion of the feet (score 4/5), equivocal plantar response and a few trophic ulcers over the heads of the first metatarsal bones (Figures 1 and 2).

Figure 1: ***showing trophic ulcer over left sole***

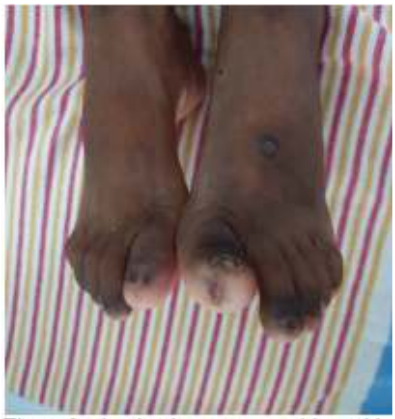

Figure 2: ***showing hammer toes with trophic ulcer on left toe***

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Cerebellar signs were negative. However, there was marked sensory impairment in both big toes on the dorsal aspect. In addition, slit lamp examination revealed pale optic discs. There was no papilloedema. Rest of the central nervous system (CNS) examination was normal. In addition, slit lamp examination revealed pale optic discs without papilloedema. Abdominal examination revealed no organomegaly and the respiratory and cardiovascular system examinations, including blood pressure, were normal.

He was extensively evaluated for peripheral neuropathy. A summary of the investigations is shown in Table 1. Figure 3 shows the magnetic resonance imaging (MRI) of the entire spine and Figure 4 shows the MRI of brain and orbit.

Table 1: ***Summary of investigations carried out in the child***

Investigation	Result
Full Blood Count	
Total white blood cell count	12.3 x 10^9/L
Neutrophil/ Lymphocyte	54/42%
Haemoglobin level	10.4g/dl
Mean corpuscular volume	86fl
Mean corpuscular haemoglobin	29pg
Mean corpuscular haemoglobin concentration	32%
Platelet count	210 x 10^9/L
Vitamin B 12 level	214pg/ml (normal range 140-650pg/ml)
Erythrocyte sedimentation rate	65mm/hour
Monteux test	Negative
Antinuclear antibody	Negative (1:40)
Fasting blood sugar	4.1mmol/L
Thyroid stimulating hormone / free thyroxine	1.58/13.1pmol/L
Optical coherence tomography (OCT)	Bilateral temporal side increased thickness
Nerve conduction study	Findings are suggestive of sensory-motor polyneuropathy
Whole exome sequence	GNB4 (c.136C>G(p.Arg46Gly), Heterozygous variant identified

Figure 3: *Magnetic resonance imaging of whole spine Arrow shows high signal intensity in spinal cord at D5 to D9 level suggesting syringohydromyelia*

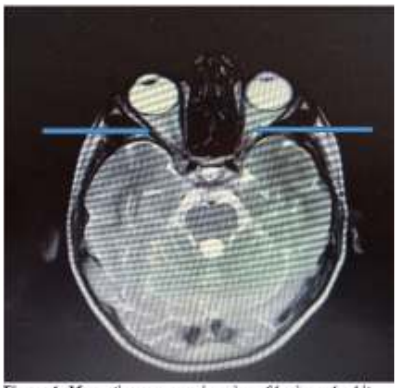

Figure 4: *Magnetic resonance imaging of brain and orbit Arrows show that both optic nerves and optic chiasma are probably atrophic. No abnormal enhancement of optic nerves*

Meantime, he was given a trial of IM vitamin B12 1000mcg every other day (6 doses) followed by weekly doses for 2 months for which he did not respond. Subsequently, child was referred to a rehabilitation physician, an orthopaedic surgeon and an ophthalmologist and was prescribed customized weight off-loading shoes. Family screening was done after making the genetic diagnosis of CMT. Parents were counselled regarding the prognosis of the condition and follow up was arranged. The elder sibling and younger one were clinically screened and there was no sensory-motor impairment.

Discussion

CMT is a common inherited neuromuscular disorder and it could manifest as autosomal dominant, recessive or X linked pattern depending on the type of CMT[1]. The cardinal features of CMT are a constellation of lower motor type neuron deficiencies manifesting as sensory-motor neuropathy[2]. The chronic nature of the motor neuropathy may result in pes cavus, hammertoes and high-arched feet[2]. Involvement of the hands may follow as the disease progresses[1]. Sensory symptoms are less frequent than in acquired chronic neuropathies[2] like diabetic peripheral neuropathy. Electromyography (EMG) and nerve conduction studies (NCS) are extremely helpful in the clinical classification of hereditary peripheral neuropathies and in guiding genetic testing[1]. Electrophysiological

studies distinguish two major types, the demyelinating form, which is characterized by symmetrically slowed nerve conduction velocity (NCV) and the axonal form, which is associated with normal or subnormal NCV and reduced compound muscle action potential[2].

Treatment of CMT is largely supportive. As CMT is a slow continuous neurodegenerative disease, regular assessment is vital for the management of complications. To maintain the integrity and functional capacity of the patient, physiotherapy and occupational therapy play an important role[3]. For some patients, surgical approaches like tenotomy and contracture release for the hands and feet may be warranted[4,5]. Symptomatic supportive treatment with nonsteroidal anti-inflammatory drugs may help to relieve backache or lower limb pain due to radiculopathy. Neuropathic pain could be alleviated with medications like topiramate or tricyclic antidepressants like amitriptyline[2,6].

GNB4 gene is associated with autosomal dominant intermediate CMT[7]. This gene was identified in our patient. To our knowledge, there is only one previous report in the literature of the co-occurrence of CMT with syringomyelia or syringo-hydromyelia[8]. So, this could be the second such case.

Management of syringomyelia depends on the aetiology. Most of the cases are secondary to Chiari malformations and are subjected to surgical interventions like arachnolysis, CSF shunting and duraplasty. Other strategies are conservative treatment and symptomatic treatment with regular follow up depending on the aetiology[9].

References

1. Szigeti K, Lupski JR. Charcot-Marie-Tooth disease. *European Journal of Human Genetics* 2009; **17**(6): 703-10. https://doi.org/10.1038/ejhg.2009.31 PMid: 19277060 PMCid: PMC2947101

2. Reilly MM, Murphy SM, Laura M. Charcot-Marie-Tooth disease. *Journal of the Peripheral Nervous System* 2011; **16**(1): 1-14. https://doi.org/10.1111/j.15298027.2011.00324.x PMid: 21504497

3. Njegovan ME, Leonard EI, Joseph FB. Rehabilitation medicine approach to Charcot–Marie–Tooth disease. *Clinics in Podiatric Medicine and Surgery* 1997; **14**: 99–116.

4. Mann DC, Hsu JD: Triple arthrodesis in the treatment of fixed cavovarus deformity in adolescent patients with Charcot–Marie–Tooth disease. *Foot Ankle* 1992; **13**: 1–6. https://doi.org/10.1177/107110079201300101 PMid: 1577335

5. Guyton GP, Mann RA: The pathogenesis and surgical management of foot deformity in Charcot–Marie–Tooth disease. *Foot and Ankle Clinics* 2000; **5**(2): 317–26.

6. Backonja MM: Use of anticonvulsants for treatment of neuropathic pain. *Neurology* 2002; **59**: S14–S17. https://doi.org/10.1212/WNL.59.5_suppl_2.S14 PMid: 12221151

7. Soong BW, Huang YH, Tsai PC, Huang CC, Pan HC, Lu YC, *et al.* Exome sequencing identifies GNB4 mutations as a cause of dominant intermediate Charcot-Marie-Tooth disease. *American Journal of Human Genetics* 2013; **92**(3): 422-30. https://doi.org/10.1016/j.ajhg.2013.01.014 PMid: 23434117 PMCid: PMC3591844

8. Lassalle A, Durufle A, Le Tallec H, Laboute E, Kerdoncuff V, Plassat R, *et al.* Charcot-Marie-Tooth disease associated with syringomyelia revealed by urinary disorders. *Annales de Readaptation et de Medecine Physique* 2005; **48**(3): 146-9. https://doi.org/10.1016/j.annrmp.2004.09.007 PMid: 15833262

9. Giner J, López CP, Hernández B, de la Riva ÁG, Isla A, Roda JM. Update on the pathophysiology and management of syringomyelia unrelated to Chiari malformation. *Neurologia (English Edition)* 2019; **34**(5): 318-25. https://doi.org/10.1016/j.nrleng.2018.10.004