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Practice Pearls

Practice Pearls: Spinal Myxopapillary Ependymoma Masquerading as Charcot-Marie Tooth (CMT) Disease

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Practice Pearls

- **Heel-walking vs. toe-walking**: In Charcot-Marie-Tooth disease (CMT), ankle dorsiflexion is most commonly weaker than plantar flexion. The ability to walk on the heels but not the toes (weaker plantar flexion) should prompt a search for alternative diagnoses, such as an intraspinal lesion.
- **Pes cavus as a sign of other neurological diseases**: Although pes cavus is often seen in hereditary neuropathies, it can also signal other neurological diseases.
- **Caution with genetic testing results:** Genetic testing must be interpreted in light of the patient's clinical findings, especially when managing variants of uncertain significance or low-penetrance mutations.
- **Bladder involvement**: progressive lower limb weakness with bladder issues should prompt evaluation for spinal pathology, unless another cause for urinary symptoms is clearly established.

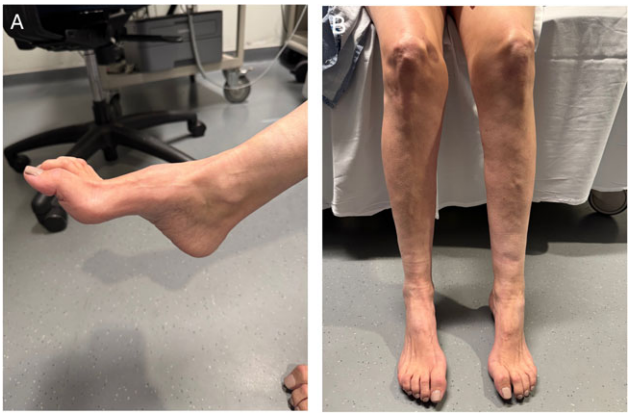

Figure 1. (A, B) The appearance of this patient's feet and distal legs, demonstrating pes cavus and distal leg atrophy.

Case Report

A 62-year-old woman developed progressive gait difficulty over a period of 5 years. She had previously seen a urologist for a 10-year history of mixed stress and urge urinary incontinence and had an implanted bladder neurostimulator, but was otherwise well. She had an insidious onset of bilateral foot deformities and distal lower limb atrophy. She recalled having high-arched feet and delayed walking as a child, but no gait difficulties until her late 50s. There was no back pain or sensory loss. Examination revealed bilateral pes cavus with hammer toes, slightly asymmetrical distal lower limb atrophy (Figure 1A and B) and 2+ reflexes in the upper limbs and knees, with absent ankle reflexes and flexor plantar responses. Tone was normal. There was mild weakness of hip and knee flexion, as well as mild ankle dorsiflexion weakness, with moderate ankle plantar flexion weakness. She was able to walk on her heels, but not on her toes. Sensory testing was normal. CMT was initially suspected, and genetic testing identified a heterozygous variant in the NEFL gene (c.54c >G, p.Tyr18*), labelled as likely pathogenic.

A year later, prior to her appointment at our centre for a second opinion, worsening gait difficulties and urinary incontinence, despite bladder neurostimulation, prompted an MRI of her spine, which revealed a T12-L1 enhancing intradural extramedullary lesion (Figure 2A–D). Urgent resection confirmed a spinal myxopapillary ependymoma (SME). Post-surgery, her weakness improved, and 2 months later at our centre, she had isolated residual 4+/5 plantar flexion weakness bilaterally, with no dorsiflexion weakness. Nerve conduction studies did not show evidence of a demyelinating peripheral neuropathy, but there were features of a chronic left S1 radiculopathy.

Discussion

The diagnostic clue to an intraspinal lesion in this case was the pattern of weakness: the patient could heel-walk but not toe-walk, opposite to the usual presentation in CMT, where dorsiflexion is weaker than plantar flexion. Bourke and Dyck[1] first reported this pearl in 1990, describing four patients with distal weakness and hyporeflexia, presumed to have peripheral neuropathy, who were

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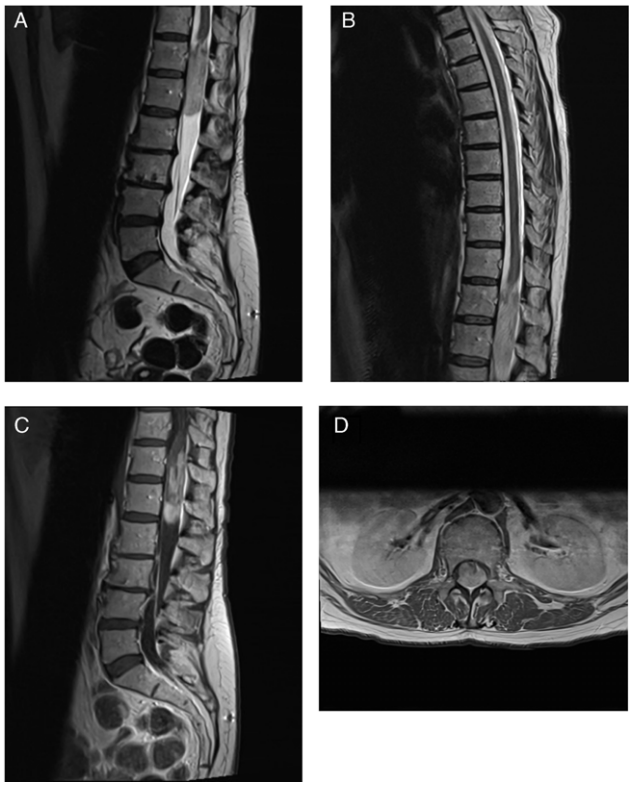

Figure 2. MRI of the lumbosacral spine, demonstrating an enhancing intradural extramedullary lesion centred at T12-L1 filling the thecal sac. (A, B) Sagittal T2-weighted imaging of the thoracic and lumbar spine. (C) Sagittal T1-weighted imaging of the lower thoracic spine with contrast. (D) Axial T2-weighted imaging at L1.

later found to have intraspinal lesions. Their unifying clinical feature was an ability to walk on their heels, but not on their toes (plantar flexion > dorsiflexion weakness). Further evaluation of 86 patients with HMSN-1 showed that without exception, ankle plantar flexion weakness never exceeded dorsiflexion weakness. Whilst any muscle compartments in the lower limb can be affected in CMT, it commonly first involves the intrinsic foot musculature and peroneal-innervated muscles, leading to anterolateral compartment weakness and pes cavus deformity.[2] A more recent description of CMT due to SORD mutations noted that 41% of patients had prominent involvement of foot plantar flexion (equal or weaker than foot dorsiflexion).[3]

Whilst pes cavus strongly suggests CMT – one study demonstrated a 78% probability of CMT in patients with bilateral cavovarus feet[4] – pes cavus can have causes beyond CMT. These include spinal cord lesions, acquired peripheral nerve injuries or other inherited neurological diseases such as spinocerebellar ataxia.[5] Careful clinical examination is necessary to decide if the deformity is due to a neuropathy or another neurological condition. In intraspinal lesions, tibialis anterior and foot intrinsics are usually preserved compared to tibialis posterior and gastrocnemius-soleus, and cavus deformities are commonly unilateral, although bilateral cases have been reported.[1,4,6] Recognizing this subtle difference in weakness should prompt spinal imaging.

SME is a slow-growing World Health Organization Grade I neoplasm, typically found in the lumbosacral spine, often affecting the conus medullaris and cauda equina. Symptoms vary depending on tumour location and size, with non-specific back pain being the most common initial symptom, then motor deficits, sensory and gait disturbances and possibly sphincter dysfunction.[7] Due to slow progression, SMEs often present with symptoms of several years' duration. In adults, pain is most common (60–70%), with motor and gait issues more prominent than sensory involvement. Unilateral limb weakness is more typical.[8,9] This patient's bilateral pes cavus and distal lower limb weakness, absent ankle reflexes and no back pain or sensory complaints made the diagnosis more challenging. The bladder neurostimulator was placed for mixed stress and urge incontinence, confirmed by urodynamics, before any motor symptoms appeared and without spinal imaging, and so was not an immediate clue to the final diagnosis.

The reported NEFL variant further complicated the presumptive diagnosis of a hereditary peripheral neuropathy. NEFL variants can cause both autosomal recessive (AR) and dominant CMT. The patient had one copy of a variant that has only been associated with the AR form of disease. Due to variable penetrance and expressivity, the presence of a genetic variant does not automatically imply causation. Pathogenic variants are often found incidentally in asymptomatic individuals, raising questions about their relevance and penetrance.[10] Genetics consultation was obtained, and they felt that this variant was unrelated to her clinical presentation.

Conclusion

This case underscores the importance of maintaining a broad differential diagnosis, even in the presence of seemingly classic signs. The patient's foot deformities and gait abnormalities were assumed to be due to CMT, but close attention to her clinical presentation, more specifically the finding of plantar flexion weakness greater than dorsiflexion weakness, raised the possibility of an intraspinal lesion. This case also highlights the necessity of ensuring that genetic findings align with clinical expectations.

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