Neurological gait disorders in childhood

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Abstract

There are an enormous number of neurological illnesses that can manifest with gait disturbance in childhood. Whilst experience and clinical acumen are helpful in diagnosing these disorders, some basic principles in assessment and diagnosis are helpful in determining the phenomenology, time course, and neuro-anatomical localisation. In this review we focus on some of the more common movement disorders resulting in inserted postures (including spasticity and dystonia), inserted movements (including chorea and myoclonus), and impairment of motor control (including ataxia and neuro-muscular disorders). A number of case studies are included to illustrate the factual descriptions.

Keywords ataxia; chorea; dystonia; gait disorders in childhood; myoclonus; spasticity

Case study: a 14-year-old female is referred with a gait disorder. She was born prematurely, at 28 weeks gestation, but attained her motor milestones within the normal range. She has high functioning autistic spectrum disorder and anxiety. There is no relevant family history.

Examination reveals unequivocal upper motor neuron signs, predominantly in the lower limbs. MRI scan reveals white matter abnormalities adjacent to the lateral ventricles, consistent with white matter injury of prematurity.

Genetic testing revealed a mutation in the *KIF5A* gene, associated with Hereditary Spastic Paraparesis type 10. The history of prematurity and PVL was incidental to her gait disorder.

Introduction

Although many other neurological impairments can be a far greater barrier to independence, gait disorders remain an important group of presentations in child neurology. It is useful to be able to recognise the key features in presentation, to guide strategies for diagnosis and therapy.

The neurological building blocks of successful ambulation include strength, balance and planning of complex movement. Sensory input including vision, vestibular and proprioceptive feedback are also integral. It follows that ambulation can be threatened by weakness, poor balance, poor motor planning and control, and sensory impairments. These difficulties can be continually present, or episodic.

In this article, we focus primarily on some of the more common movement disorders resulting in inserted postures (including spasticity and dystonia), inserted movements (including chorea and myoclonus), and impairment of motor control (including ataxia and neuro-muscular disorders), which can overlap in many individuals. A number of case studies are included to illustrate the factual descriptions.

Spasticity

Spasticity is defined as a velocity-dependent increase in muscle tone. It typically results in co-contraction of antagonist muscle pairs, with a bias towards greater involvement of the upper limb flexors and lower limb extensor muscle groups. Spasticity of the lower limbs tends to lead to hip extensor tightness, reduced knee flexion during swing through, and equinus posture due to excessive contraction of gastrocnemius. This results in forefoot contact, and the so-called waddling gait as circumduction of the hip compensates to allow swing through. Spasticity may occur following lesions to the brain or spinal cord (pyramidal tract lesions), but can also occur in non-lesional disorders such as hereditary spastic paraparesis.

Investigations should always include imaging of the brain and spinal cord, and if normal may require further investigations e.g. metabolic investigations, and genetic screen for hereditary spastic paraparesis.

There are many therapeutic options to reduce spasticity in specific or wider muscle groups. These include drugs (e.g. oral Baclofen), localised neuromuscular blockade (Botulinum neuro-toxin), and neurosurgical procedures (e.g. selective dorsal rhizotomy and intra-thecal Baclofen delivery). Physiotherapy is at least as important as all these options, and the absence of physiotherapy renders the medical interventions nearly futile.

Whenever these treatments are employed it is important to have clear functional goals, and always remember that spasticity is one part of the upper motor neuron syndrome, along with weakness and poor motor planning. Spasticity reduction in itself may not always lead to improved function, and may even worsen function, particularly in the context of underlying weakness/instability.

Dystonia

Dystonia has similarities to spasticity, in leading to co-contraction of antagonistic muscle groups. However, the velocity-dependent element is absent, the disorder is more fluctuant with variability in tone, can be task specific, and more likely to lead to twisting postures.

Gait disorders in dystonia may appear at times frankly bizarre, due to the predominance of extensor activity and twisting postures. As a general rule, the ankles will demonstrate equinovarus posture, but there is a greater range of abnormalities than seen in spasticity. Moreover, the task specific element can be a source of confusion in distinguishing between dystonia

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and functional gait disorders. For example, it is entirely possible for an individual with dystonia to be unable to walk forward without assistance, but able to walk backwards unaided, or even ride a bicycle.

Dystonia is typically associated with lesions of the thalami and basal ganglia (extra-pyramidal tracts) but can also occur in non-lesional, usually genetic, disorders e.g. DYT1 and DYT5 (dopa-responsive dystonia).

The investigation of dystonia should be targeted to the clinical context. An MRI brain scan is invariably required, and further investigations may include:

- Copper and caeruloplasmin (Wilson's disease)
- Blood film (for acanthocytes)
- TSH, T3 and T4 (Allan-Hernon Dudley syndrome)
- Urate (Lesch-Nyhan syndrome)
- Paired blood and CSF glucose (GLUT1 deficiency)
- CSF neurotransmitters (disorders of dopamine/serotonin synthesis, metabolism or transport) and lactate (mitochondrial disorders)
- Other metabolic tests — plasma lactate, manganese, biotinidase, very long chain fatty acids, lysosomal screen, vacuolated lymphocytes, acylcarnitine profile, transferrin isoelectric focussing
- Urine organic acids, creatine to creatinine ratio
- CGH microarray (for copy number variants, deletions and duplications encompassing disease-causing genes) and multigene panels for monogenic dystonia (e.g. DYT1, DYT11, *PANK2*/*PLA2G6* and other disorders of neurodegeneration with brain iron accumulation, *KMT2B* and other genes causing complex dystonia phenotypes)
- Neurophysiology should not be required to diagnose pure dystonia, but some disorders demonstrate a mixed pattern of dystonia and lower motor neuron signs

Therapeutic options to manage dystonia include medication (e.g. Trihexyphenidyl, Gabapentin, Clonidine), Botulinum toxin, ITB and deep brain stimulation. The latter is particularly effective in primary dystonia with normal imaging, but also offers some degree of benefit in secondary dystonia, notably Pantothenate Kinase Associated Neurodegeneration. The ketogenic diet may be considered in individuals with GLUT1 deficiency. A trial of Levodopa can significantly ameliorate or even abolish motor symptoms in patients with Segawa's disease (DYT5-dystonia) and other dopa-responsive disorders, and should be considered first line in patients with dystonia of undetermined aetiology.

Some forms of dystonia may be intermittent, and can be characterised as either movement related (kinesogenic), not-related to movement (non-kinesogenic), or specifically related to sustained exercise (Lance type). Paroxysmal kinesogenic dystonia is triggered by sudden movement, and episodes are short lasting on average, approx. 1 minute. They are associated with mutations in the *PRRT2* gene, and typically respond very well to low dose Carbamazepine. Non-kinesogenic dystonic episodes tend to last much longer (up to several hours), and may be triggered by caffeine or alcohol. They respond less well to Carbamazepine, but may respond to benzodiazepines. Exercise induced dystonia show mixed responses to these medications.

Case study: a 6-year-old girl is referred for advice on the management of cerebral palsy. On closer questioning she was born at term following an uneventful pregnancy, in good condition, and did not display any feature of neonatal encephalopathy. She had never walked unaided, but had been able to walk with the help of one from 3 years of age. MRI brain and spine were normal. Examination findings were suggestive of bilateral lower limb spasticity, although plantar responses were flexor (downgoing).
The specific question parents asked is "why doesn't she have cerebral palsy in the morning, doctor?".
The history of fluctuation, together with the unremarkable neonatal history and normal imaging, suggested the diagnosis of dopa-responsive dystonia (Segawa disease or DYT5). She was given an empirical trial of low dose L-Dopa (2 mg/kg/day), and was walking normally within one week. Subsequent genetic testing revealed a mutation in the *GCH1* gene. Neurotransmitters were not measured, but would be expected to show low neopterin, low BH4, low HVA, low/normal 5-HIAA, although for some patients, the CSF profile can be (near) normal.
She remained with near normal mobility until transition to adult services. The only residual abnormality was very mild ankle varus. However, she was susceptible to anxiety and depression (which is reported in this condition, and possibly related to cerebral serotonin deficiency) which was not corrected by L-Dopa replacement.

Case study: a 9-year-old girl is referred with in-turning of the left ankle. Over the following 12 months this progresses, with involvement of all four limbs. She becomes non-ambulant. Her facial muscles are spared. MRI scan and baseline metabolic investigations are normal. Genetic testing reveals the heterozygous common mutation (GAG deletion) in the *TOR1A* (DYT1) gene.
She proceeds to implantation of a deep brain stimulator, with bilateral electrodes positioned in the globus pallidus interna. Initial improvement is modest, but over 6 months she regains entirely normal function, which is maintained at last follow up over a decade later.

Case study: a 15-year-old male is referred with walking difficulties. For 6 months previously he had had some personality change attributed to teenage moodiness. Examination revealed generalised dystonia. MRI scan revealed high signal with the basal ganglia. There was no obvious Kayser-Fleisher ring to routine inspection. However, he was found to have low values of serum copper and caeruloplasmin, and a mutation in the *ATP7B* gene, confirming the diagnosis of Wilson's disease.
He was treated with chelation therapy with Trientene and Zinc, with satisfactory gradual reduction in urinary copper values. However, his dystonia continued to progress and he became non-ambulant.
Comment: Early diagnosis is crucial in Wilson's disease, although chelation therapy is not always effective in preventing further deterioration of physical signs.

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