Mimics of cerebral palsy

Lucinda J Carr
Joanna Coghill

Abstract

Cerebral palsy (CP) is the commonest cause of movement disorder in childhood, with an incidence of around 1 in 400 live births. Many other conditions can masquerade as CP in their clinical presentation, particularly in the early stages. Neuroimaging is often a helpful tool in discriminating CP from other conditions, where characteristic patterns of damage and/or developmental changes are described. However, epidemiological reports consistently report that imaging is normal in up to 15% of children with established CP. Such cases need to be carefully distinguished from other metabolic and genetic conditions, which may also show normal imaging or only slowly evolving change. This article highlights features that may point to an underlying genetic or metabolic disease rather than the static insult that defines causation in CP and suggests an approach to examination and investigation.

Keywords cerebral palsy; genetic conditions; metabolic disorders; neuroimaging; 'red flags'

Introduction

In developed countries the incidence of cerebral palsy (CP) is estimated at 1 in 400 live births. CP remains the most common cause of movement disorders in childhood.

CP is an umbrella term describing a permanent disorder of movement and posture caused by an insult to the developing brain, either through damage or developmental anomaly. Although, by definition, we are primarily dealing with a motor disorder in CP, other associated factors are often present and this is captured in the revised definition from 2006: namely that 'The motor disorders of CP are often accompanied by disturbances of sensation, cognition, communication, perception, and/or behaviour and/or a seizure disorder'.

The aetiology of CP can be best defined as prenatal, perinatal and postnatal (Table 1). It is then classified by the predominant motor type and distribution. The incidence of predominant motor type in CP is reported as 70% spasticity, 15% extrapyramidal or dyskinetic (which includes both dystonia and choreoathetosis), 10% mixed and 5% ataxic. In clinical practice it is very rare to see absolutely pure spasticity or dystonia and indeed if present, may raise the possibility of an alternative diagnosis. Standardised assessment measures such as the Gross Motor Function Classification System (GMFCS) and Manual Ability Scale (MACs) can be helpful in defining a child's functional ability.

Lucinda J Carr *MD FRCPCH is a Consultant Paediatric Neurologist based at Neuroscience Department, Great Ormond Street Hospital, London, UK. Conflicts of interest: none declared.*

Joanna Coghill *MRCPCH MSc PgCert Med Ed. is Locum Consultant in Paediatric Neurodisability, Great Ormond Street Hospital, London, UK. Conflicts of interest: none declared.*

When to question a diagnosis of CP

The pathology of CP is not progressive but the clinical manifestations will evolve as the child matures. As a child grows, muscles often become 'tighter' (or lose length) and this can lead to the development of contractures and impact on function. Most clinicians will have seen children with CP who 'go off their feet' in adolescence. Also subtle sensory or cognitive difficulties may not be immediately apparent. Such features may lead to the question whether this is part of the natural history of CP or if the condition itself is progressive. GMFCS levels are helpful in enabling longitudinal prediction of how motor development is likely to progress in a child with CP.

Confirming the diagnosis of CP

In the absence of a clear aetiology further questions and investigations need to be considered. Red flags in history and examination will confirm the need for further investigation (Table 2). Establishing an accurate diagnosis of CP is imperative for the child as it enables doctors and families to:

- understand the child's health status and predict natural history;
- offer early intervention and treatment;
- remove the doubt and fear of 'not knowing';
- offer accurate genetic counselling to child and family;
- prevent further (unnecessary) investigation;
- identify and secure benefits and support in raising a child with CP;
- inform registers/epidemiological studies of prevalence.

Neuroimaging

An MRI brain scan is the investigation of choice to confirm the diagnosis of CP. Scans are most likely to show abnormality once myelination is advanced so ideally once over 18 months of age, but this is not a reason to defer if there is any uncertainty about the diagnosis.

- Normal scan:

Systematic reviews of neuroimaging in CP (which include CT and MRI scans) find that up to 17% of children with a clinical diagnosis of CP do not show any abnormality on scan. The yield is higher with MRI but still over 10% of scans are normal in children who clinically present as CP. If the MRI brain scan is normal then further metabolic and genetic tests should be performed, guided by the phenotype of the child. Imaging should also be extended to the spine if appropriate. *Scan changes may evolve over time so imaging should be repeated if there is a history of progression of symptoms or signs*.

- Abnormal scan:

This often provides the confirmation of typical and expected features of CP with damage or brain maldevelopment. *If scan features are NOT concordant with the clinical history this may suggest another underlying condition*.

It is easier to refine further tests by first defining the neurological nature of a child's motor disorder. They can usually be placed into one of three groups on the basis of clinical examination and history: spastic motor disorders, dyskinetic (extrapyramidal) motor disorders or ataxic disorders (see Table 3).

Classification of aetiology of CP

Prenatal	Perinatal	Postnatal
• Maternal TORCH infections or medical illness • Antepartum haemorrhage, Pregnancy-related hypertension • Chorioamnionitis • Drugs and toxins • Intrauterine growth restriction	• Prematurity; around 43% of children with CP • Intrapartum catastrophes such as asphyxia, cord prolapse or uterine rupture, (less than 10%). • Infection (HIV, Group B Strep) • Metabolic disturbances — (jaundice, hypoglycaemia	• Traumatic brain injury • Hypoxia • CNS infections • Metabolic disturbance • Cerebrovascular accident

Table 1

'Red Flags' where another diagnosis should be considered

History	Examination
No risk factors for CP	Dysmorphic
Regression of skills	Optic atrophy/retinopathy
Fluctuation in motor function	Pes cavus
Pure neurological signs	Evolving sensory signs
Positive family history	

Table 2

Spastic motor disorders

Spasticity is defined as dynamic hypertonus (i.e. elicited as a muscle 'catch' or clonus with rapid movement of the limb). In CP, spasticity is usually seen along with other features of an upper motor neuron syndrome, namely co-existing distal weakness, loss of selective muscle control and hyperreflexia. Spasticity may be unilateral, as with perinatal stroke and on rare occasions progressive signs are seen, such as in Rasmussen's encephalitis. However with an underlying genetic or metabolic cause, signs are usually bilateral and symmetrical. There are a number of other conditions which may result in bilateral spasticity:

Spinal dysraphism

This describes a spectrum of disorders where closure of the neural tube is defective in early foetal life, leading to anomalous development of the spinal cord. Open spina bifida is part of this spectrum but more often the skin is closed. The cord may become 'tethered' to the vertebral column or subcutaneous tissues by a thickened filum terminale, fibrous band, dermal sinus tract, diastematomyelia, or a lipoma and so cause traction to the neural elements. Brain MRI scan is normal but the spine characteristically shows a low lying conus medullaris below L2 level or the presence of a lipoma or dermal tract.

In childhood, spinal dysraphism can cause progressive gait abnormalities, particularly during periods of rapid growth (5–15

Alternative diagnoses and investigations in suspected CP by motor type

Spasticity	Dyskinetic	Ataxia
• Spinal Dysraphism • HSP • Leukodystrophy • Arginase deficiency • Sjorgen Larsson syndrome • Biotinidase/Folate deficiency	• DOPA responsive dystonia • Mitochondrial disease • Lesch Nyhan • Wilson's disease • Glutaric aciduria • GLUT 1A • Neurodegeneration with brain iron accumulation	• Anglemans • Jouberts • Friedreich's ataxia • Ataxia telangiectasia • Cockayne syndrome • Pelizaeus-Merzbacher disease • Non-ketotoc hyperglycinaemia • Maple syrup urine disease
Spasticity	**Dyskinetic**	**Ataxia**
• HSP Genetics • Nerve conduction/EMG • White cell enzymes • Very long chain fatty acids • Plasma ammonia • Plasma amino acids • ALDH3A2 gene • CSF lactate, folate & neurotransmitters • Serum biotinidase and folate	• CSF neurotransmitters • Genetics • MECP2 (Retts) • Plasma/CSF lactate and glucose • Respiratory chain enzymes in muscle • Serum urate • Serum/urine Copper Caeruloplasmin • Urine organic acids	• Genetics • Nerve conduction • DNA fragility • AFP • Plasma amino acids

Table 3