Congenital hypotonia: clinical and developmental assessment

Review

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Identifying the underlying cause of congenital hypotonia remains difficult, despite advances in diagnostic laboratory and imaging techniques. Clinical evaluation strategies and standardized developmental tests can assist in differentiating hypotonia resulting from primary involvement of the upper motoneuron (central hypotonia) versus that involving the lower motoneuron and motor unit (peripheral hypotonia). This is especially important in infants with idiopathic hypotonia. This review outlines and describes the components of the clinical assessment: detailed infant and family history, clinical techniques and characteristics for differentiating hypotonia of central versus peripheral origin, and clinical evaluation (muscle tone, primitive reflexes, deep tendon reflexes, etc). Recent research that has contributed to the differential diagnosis of congenital hypotonia is reviewed and directions for future research are provided. Ideally, the assessment of infants with congenital hypotonia is best accomplished by an interdisciplinary team of developmental specialists including pediatricians, medical geneticists, child neurologists, and physical or occupational therapists.

Despite advances in diagnostic electrophysiological, neuroimaging, and molecular and genetic tests,[1,2] identifying the underlying cause of hypotonia in infants remains difficult,[3] except in more common and widely recognized conditions, such as Down syndrome. Differentiating the likely causes of hypotonia is important to spare some infants from needless, invasive diagnostic tests, such as muscle biopsy, if the underlying etiology is likely to be from upper motoneuron involvement (central) rather than lower motoneuron or motor unit involvement (peripheral). Similarly, in disorders of central hypotonia in which the etiology is genetic, e.g. Joubert syndrome, it is important to make a confirmed diagnosis to assist the family with genetic counseling for future pregnancy.[4] There are still several underlying causes of congenital hypotonia for which there is no definitive laboratory or imaging test, namely idiopathic hypotonia,[5] so the role of clinical and developmental assessments remains important, as suggested many years ago by Dubowitz.[6]

The underlying pathology of infantile hypotonia can be divided into four broad categories: the central nervous system (CNS), the peripheral nerves (motor and sensory), the neuromuscular junction, and the muscle.[7] Based on clinical estimates,[8] as well as data-based studies,[1,9] hypotonia of central origin accounts for about 66 to 88% of cases, with peripheral origins or unknown causes accounting for the balance. Consequently, clinicians should be cognizant of the much greater prevalence of hypotonia of central origin when assessing an infant for whom the underlying etiology of the hypotonia is not known.

In addition, several congenital disorders that are characterized by hypotonia have both central and peripheral origins. Examples include congenital muscular dystrophy (in which infants have abnormalities of brain formation and central white matter abnormalities on magnetic resonance images)[10] and congenital disorders of glycosylation, which can include cerebellar abnormalities as well as peripheral neuropathy.[11,12] It is also worth noting that some infants may demonstrate 'transient' hypotonia, e.g. those born preterm,[13]

those with prenatal drug exposure,[14] or those with acute infectious diseases.[8]

To aid in the early diagnosis of congenital hypotonia, especially for disorders in which definitive laboratory or imaging tests are not available, clinicians should include a detailed history of the infant, as well as the family's history, and clinical and developmental assessments.

Infant and family history

A detailed family, pregnancy, and birth history should be conducted first.[2,8] Family history should include any other family members with hypotonia, muscle diseases, or genetic disorders; parental consanguinity, and developmental milestones for parents and siblings, e.g. age of walking.[15] In fact, in their retrospective review of 89 'floppy' infants born from 1990 to 2000, Birdi et al.[16] reported that there was a family history of neurological or neuromuscular conditions in 46%. Parental consanguinity increases the possibility of autosomal recessive disorders,[15] such as Werdnig–Hoffman disease or spinal muscular atrophy type I.

Prenatal history should include the mother's description of fetal movements, polyhydramnios or olygohydramnios,[2] any maternal illness, maternal exposure to infectious agents,[15] and maternal drug or alcohol use.[17] Perinatal history should include abnormal fetal presentation, e.g. breech, requiring Cesarean section,[15] Apgar scores, need for respiratory support, feeding difficulties, abnormal postures, and seizures.[2,17] The presence of dysmorphic features and malformations in other organ systems should be documented.[17] Developmental history in infants older than a few months should include ages at attainment of major motor milestones, such as rolling over, independent sitting, and ambulation.

Differential diagnosis of hypotonia of central versus peripheral origin

According to Aydinli and colleagues, the first goal in assessing an infant with hypotonia is to determine if the underlying cause is central or peripheral.[18] Several clinical evaluation techniques, as well as standardized developmental assessments, can assist in differentiating the two overall underlying causes.

Although there can be considerable overlap of clinical signs between infants with hypotonia of central versus peripheral origin, Table I outlines some common differences or distinctions based on information from review articles,[15,19] as well as original research[2] or case reports.[7] Furthermore, Vasta et al.[2] examined the sensitivity and specificity of various clinical parameters in the 39 infants in their sample with neuromuscular disorders (hypotonia of peripheral origin). The highest sensitivity and specificity (0.97 and 0.75) were found for absent or markedly reduced antigravity movements during infant assessment. Secondly, history of reduced fetal movements and polyhydramnios had sensitivity of 0.75 and specificity of 0.88. The third highest pairing of sensitivity and specificity for neuromuscular disorders was presence of contractures (0.69 and 0.63).

Specific characteristics that are associated with certain diseases of peripheral origin are listed in Table II. In their 11-year retrospective study of the outcomes of 50 infants with neonatal hypotonia, Richer and colleagues[1] identified the proportions of various perinatal or neonatal risk factors, facial dysmorphology, deep tendon reflexes, or need for ventilation among those ultimately diagnosed with hypotonia of central or peripheral origin (Table III). The most noteworthy differences reported were the need for assisted ventilation during the neonatal period (36% of infants with central origin vs 100% of infants with peripheral origin), decreased

Table I: Differentiating congenital hypotonia of central versus peripheral origin[2,7,19]

Characteristic	*Central*	*Peripheral*
Weakness	Mild to moderate	Significant ('paralytic')
Deep tendon reflexes	Decreased or increased	Absent
Placing reactions	Sluggish or slow	Absent
Motor delays	Yes	Yes
Antigravity movements in prone and supine	Some (but less than a typical infant)	Often absent
Pull-to-sit	Some head lag (more so than typical infant)	Marked head lag
Cognition/affect	Delayed	Typical
Ability to 'build up' tone, e.g. tapping under knees with infant in supine to assist them in holding hips in adduction[a]	Yes	No

[a]Bennett FC, personal communication 1980.

Table II: Specific characteristics of peripheral hypotonia by disease or disorder

Specific characteristic	*Disease/disorder*
Tongue fasciculations; sparing of weakness in muscles of face, diaphragm, and pelvic sphincters[7,15]	Werdnig–Hoffmann disease (spinal muscular atrophy type 1)
High arched palate[7]	Congenital myopathies
External ophthalmoplegia, ptosis[15,17]	Myasthenic syndromes
Wasting of temporalis muscles, inability to open the hand after maximum grip (as found in the infant's mother)[15]	Myotonic dystrophy

Table III: Percentage of infants with different risk characteristics (from Richer et al.[1])

Characteristic	*Central (%)*	*Peripheral (%)*
Neonatal seizures	18	12
Cesarean section	39	53
Facial dysmorphism	42	29
Decreased antigravity movement	39	88
Intubation needed	33	71
Assisted ventilation for intubated infants	36	100
Decreased or absent deep tendon reflexes	39	88

or absent antigravity movement (39% vs 88% respectively), and decreased or absent deep tendon reflexes (39% vs 88%).

Clinical assessment

The continued value of clinical assessment of infants with hypotonia, despite the many technological diagnostic advances, cannot be overstated. In Birdi et al.'s retrospective analysis of 89 floppy infants, of the 60 for whom an ultimate diagnosis was identified, the diagnosis was based solely on clinical assessment in 40%.[16]

Clinical assessment should include evaluation of muscle tone, primitive reflexes, deep tendon reflexes, placing reactions, resting postures in prone and supine, head-righting-into-flexion (pull-to-sit), antigravity movements, and visual following/alertness.[2,17] Infants with hypotonia of peripheral origin also often have joint contractures, e.g. those with congenital muscular dystrophies,[10] spinal muscular atrophy type I,[20] or congenital myasthenic syndrome.[21]

Measurement and plotting of head circumference on growth charts[15] (in relation to height and weight centiles) can also provide clues because infants with central hypotonia, either from acute or chronic encephalopathy, would be more likely to have microcephaly than those with hypotonia of peripheral origin.

To aid in assessing the foregoing behaviors, there are several neurological or neurodevelopmental tests available. In Vasta et al.'s[2] retrospective study of 83 neonates presenting with hypotonia, the Neurological Assessment of the Preterm and Full-term Newborn Infant, a standardized, norm-referenced test, was used.[22] Other standardized tests that assess several of the above behaviors include the Test of Infant Motor Performance,[23] covering an age range from 34 weeks' gestation to 4 months postterm (corrected age), and the Harris Infant Neuromotor Test,[24] spanning 2.5 to 12.5 months of age, and including an item to measure head circumference, as suggested by Crawford.[15]

Developmental assessment

In addition to conducting a neurodevelopmental or neurological assessment, a standardized assessment of cognitive development is important. Although there is a higher prevalence of cognitive delay in infants with hypotonia of central origin, infants with congenital myopathies, congenital muscular dystrophy, and congenital myotonic dystrophy can also have significant cognitive impairment.[10] The Bayley Scales of Infant and Toddler Development (Bayley-III) are the likely ideal test because they include the domains of motor, cognitive, and social–emotional, as well as language and adaptive behavior, and cover an age range from 1 to 42 months.[25] In infants with profound weakness,[15] assessment using the Bayley-III or any other standardized developmental test may be difficult or impossible, particularly in infants with spinal muscular atrophy type I, for example.

Clinicians should also provide observational assessments of the infant's affective behavior. In the author's clinical experience, even young infants with profound trunk and extremity weakness of peripheral origin, such as spinal muscular atrophy type I, tend to have their facial muscles spared and are bright and interactive. This is in stark contrast to young infants with disorders of central hypotonia, e.g. Down syndrome or Prader–Willi syndrome, who tend to display little (or 'flat') affect and social interaction.

Suggestions for future research

Although several review articles,[10,12,15,17,19,26–32] texts,[6] and chapters[33,34] have been written over the past 20 years about evaluation of the infant with congenital hypotonia, there are few data-based studies to help clinicians in determining what assessment strategies are most reliable and valid in differentiating the underlying cause of the hypotonia. Although those few studies provide valuable information,[1–3,5,9,16–18] all but two[3,17] were retrospective. Prospective, longitudinal studies of infants born with congenital hypotonia, using clinical evaluation strategies, as well as norm-referenced, standardized tests, are needed to further our understanding of the signs and characteristics that differentiate hypotonia of central and peripheral origin. The predictive validity of various signs and characteristics during infancy to later diagnoses and developmental outcomes should be further studied.

Conclusion

Diagnosis of the underlying cause of congenital hypotonia remains elusive in many cases, despite the advent of sophisticated laboratory and neuroimaging tests. Pediatric clinicians have an important role to play in contributing to early diagnosis and in differentiating disorders of central versus peripheral origin by performing a careful history of the infant and family, and conducting non-invasive clinical and developmental assessments. Ideally, these assessment and diagnostic strategies are best accomplished by an interdisciplinary team of developmental specialists including pediatricians, medical geneticists, child neurologists, and physical or occupational therapists.

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