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Review Article

Initial Approach Hypotonic Syndrome "Floppy Infant"

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Abstract

Hypotonic syndrome is a real challenge for the clinician in the pursuit of its etiology. Relating to the broad spectrum of entities that are associated with this. As initial approach entities systemic as hypothyroidism, hypoglycemia, hypocalcemia, sepsis, effect of relaxing and sedative drugs among others must be ruled out. Hypotonia must try to classify according to its topographical origin, in central (upper motor neuron) or peripheral (lower motor neuron) not leaving aside the option of mixed hypotonia. Central origin is the most frequent and of them the commonest cause hypoxic-ischemic encephalopathy. Evidence available for diseases such as spinal muscular atrophy, hereditary Neuropathies and Prader-Willi syndrome, myotonic dystrophy. Although in most of entities handling is not healing is important to the etiologic diagnosis for the management and forecast, the child with hypotonic syndrome require a multidisciplinary management.

Keywords: *Muscle Hypotonia; Pediatric; Hypotonic Infant; Syndrome; Hypotonia*

Introduction

Two types of muscle tone can clinically be evaluated: posture and physical fitness. Postural tone (antigravity) is a muscular contraction sustained and low intensity in response to gravity. It is mediated by systems of gamma and Alpha motor neurons in the spinal cord and is clinically evaluated by the passive manipulation of limbs. Tone phase is a brief contraction in response to a stretch of high intensity. It is only mediated by the system of Alpha motor neurons and examined clinically to cause the muscle stretch reflexes. The maintenance of muscle tone depends on the integrity and proper function of the nervous system is either at the level of the motor cortex, ascending and descending tracts, peripheral nerves, the motor endplate and muscle. A change in any of these areas can be manifested in a box of hypotonic syndrome. Hypotonia is defined as the reduction in postural tone, with or without a change in the physical tone. When he is depressed the postural tone the trunk and limbs cannot overcome gravity and the child it seems hipotonico [1].

Discussion

Points 1: Terminology

The "floppy infant" is an informal term for generalized hypotonia and is a feature presentation for a wide range of systemic and neurological disease. It represents a diagnostic challenge. Patients may hypotonia due to multiple abnormalities of the central or peripheral nervous system, myopathies, genetic disorders, endocrinopathies, metabolic diseases and diseases acute or chronic disease. A systematic approach to a child with hypotonia, paying attention to history and clinical examination are essential to locate the problem to a specific region of the nervous system level [2].

The list of disorders with presentation features including hypotonia has expanded rapidly in the genomic era and continues to grow. Although currently most conditions have few disease-modifying treatments, diagnosis is essential, as it provides both families and physicians with prognostic information and screening strategies associated pathologies. You can also expose certain risks associated with diagnosis known; for example, people with RYR1 mutations may be at increased risk for malignant hyperthermia. In addition, many diagnoses are genetic and have implications for family members who live or future planning familiar [3].

Severe hypotonia usually occurs in the neonatal period but mild or slowly progressive disease cannot get detected until the child fails to neurodevelopmental milestones in the mid-late first or second year. In the neonatal period, the differential diagnosis should include events related to parturition, hypoxic encephalopathy, intraventricular hemorrhage and systemic disease such as hypoglycemia, sepsis and heart failure among others [3,4].

The ratings are variables from the clinical point of view, we must consider the existence of hypotonic syndromes of central and peripheral origin, although some diseases such as disease Fukuyama and Prader Willi syndrome involving both levels, based on this you can consider mixed hypotonic syndrome [5].

Points 2: The patient's history

The first step in evaluating a patient with hypotonia is the compilation of a complete story, investigate and family medical history (prenatal, perinatal and neonatal evaluation) background. Prenatal history should include information about fetal movement in utero, fetal presentation and the amount of amniotic fluid. Occasionally obstetric history can identify a cause and the time of onset of associated symptoms. A history of preterm birth; toxoplasmosis, other infections, rubella, cytomegalovirus and herpes simplex; neonatal seizures or other pre or postnatal involvement increases the likelihood of dysfunction of the central nervous system (CNS) as underlying etiology for this condition. maternal exposure to toxins or infection suggests a central cause [2,3].

Floppy Strong	Floppy Weak
Tendon reflexes normal	Decreased tendon reflexes
Abnormalities other brain functions	Total failure in voluntary movements
Dysmorphologic	Total failure of postural reflexes
Entrapment of thumb	Muscular atrophy
Malformations in other organs	Failure to thrive
Movements through postural reflexes	Decreased tendon reflexes
Hyperreflexia or normorreflexia	Total failure in voluntary movements
Scissor legs	Total failure of postural reflexes

Low Apgar scores may suggest hypotonia from birth and a newborn hypotonic should be considered septic until proved otherwise. A full-term baby born healthy but develops floppiness after 12 to 24 hours may have an inborn error of metabolism. Trauma of the cervical spinal cord is a complication of a breech presentation or cervical. Delayed motor part to social development and normal language reduces the likelihood of brain pathology. Conversely, loss of milestones increases the index of suspicion of neurodegenerative disorders. A food dietary history may indicate diseases of the neuromuscular junction, which can occur with suction and swallowing difficulties "tired" or "worse" with repetition. Various genetic disorders can present with hypotonia, including Prader-Willi syndrome, which in future shows childhood hypotonia, obesity, mental retardation and hypogonadism, but is characterized in children by feeding [2,5,6].

Points 3: The physical examination

The motor exam includes assessment of posture, muscle tone, mobility, muscle strength and muscle stretch reflexes. Most hypotonic children show a classic position "frog like" type: Full abduction and external rotation of legs, and a flaccid extension or flexion of the arms. You can see a congenital dislocation of the hips because poor muscle tone in the uterus failed to hold the femoral head in the acetabulum. Antigravity spontaneous limb movements may be absent or reduced. Muscle tone can be evaluated further performing traction response, vertical suspension and horizontal maneuvers suspension. In children with cerebral hypotonia or central, nearly two thirds of cases, perinatal or prenatal history may suggest an insult to the CNS. There may also be delayed global development associated (rather than a thick insulated motor), occasionally convulsions, microcephaly, dysmorphic features and brain malformation or other organs [2,3,6].

The central hypotonia can associated with rapid and persistent primitive reflexes and brisk reflexes normal muscle stretching. The degree of weakness observed in children with central hypotonia is usually less than the degree of hypotonia (nonparalytic hypotonia) [2].

In hypotonic lower motor unit or peripheral hypotonia, developmental delay is mainly gross motor and is associated with muscle stretch reflexes absent or depressed and muscle atrophy and fasciculations of the tongue. In general, the movements of the lower limbs antigravity and cannot be lead through postural reflexes. In infants with this condition, the degree of weakness is proportional or greater than the degree of hypotonia. Trauma to the upper cervical cord traction due to breech presentation or cervical may also initially manifested as flaccid paralysis, which can be asymmetrical, and no muscle stretch reflexes; Later, however, upper motor neuron signs develop [2,3,7].

Practice Pearls **Important diagnostic clues on examination**
* Skin pallor, bruising, petechiae, or evidence of trauma and traumatic myelopathy.
* Abnormalities of respiratory rate, pattern, or diaphragmatic movement and congenital myopathies.
* Cardiomyopathy and carnitine deficiency Consider, fatty acid oxidation disorders, acid maltase deficiency, Pompe's disease.
* Hepatosplenomegaly and storage disorders or congenital infections.
* Renal cysts, liver dysfunctions, high forehead and wide fontanelles e Zellweger's spectrum disorder.
* Congenital cataracts, glaucoma and oculocerebrorenal (Lowe) syndrome.
* Abnormal urine odor and metabolic disorders.
* Hypopigmentation, undescended testes and Prader Willi syndrome.
***** Abnormal fad pad and nipples and congenital disorders of glycosylation (CDG) inverted.

Because the tone muscle is also determined by the viscoelastic properties of muscles and joints, connective tissue disorders such as Marfan and Ehlers-Danlos, osteogenesis imperfecta and benign ligament laxity may manifest as hypotonia. In addition, a combined cerebral hypotonia and unity is observed lower motor in infants and children with congenital myotonic dystrophy, some congenital muscular dystrophies, peroxisomal disorders, mitochondrial encephalomyopathies, neuroaxonal dystrophy, leukodystrophies (p. Ex., globoid cell leukodystrophy), familial dysautonomia and secondary choking motor unit disease also hypotonia without significant weakness may be a feature of systemic diseases such as sepsis, congenital heart disease, hypothyroidism, renal tubular acidosis and rickets [3,6].

Neuromuscular diseases in childhood is mainly manifested by hypotonia and weakness; However, infants with severe weakness and hypotonia only marginal generally have a disorder of the lower motor unit (anterior horn cells, peripheral and cranial nerves, neuromuscular junctions and muscle). These babies may have genetic disorders, metabolic disorders or systemic disorders (Congenital heart disease, kidney failure). From the beginning, newborns with CNS pathology may present profound hypotonia, decreased reflexes and moderate to severe but transient weakness; however, they tend also to have seizures, obtundation, cranial nerve abnormalities and/or history of perinatal asphyxia. With the recovery gradually they develop better strength, increased muscle stretch reflexes, muscle tone and often distal to proximal. This image contrasts with children with disorders asphyxiated lower motor unit who persist weakness, hypotonia and hyporeflexia. Alternatively, the profound weakness and hypotonia without signs of CNS occur in infants with isolated neuromuscular disease and no history of perinatal asphyxia. The profound weakness and hypotonia without signs of CNS occur in infants with isolated neuromuscular disease and no history of perinatal asphyxia. The profound weakness and hypotonia without signs of CNS occur in infants with isolated neuromuscular disease and no history of perinatal asphyxia [3,4].

Muscle stretch reflexes vary depending on the anatomic level of pathology along the motor unit (prominent hyporeflexia or complete areflexia in disorders of the anterior horn cells and neuropathies, reduced in proportion reflexes to the degree of weakness in myopathies and often normal reflexes in the neuromuscular junction disorders). Approximately two thirds of patients with neonatal hypotonia with brain etiologies and one third have diseases of the motor unit inferiors [4,6].

Points 4: Investigations and Diagnostic

The first step is to determine the area condition, either brain, spinal or motor unit. More than one site may be affected. The brain and peripheral nerves are damaged in some diseases of lipid Hoarding, mitochondrial disorders and family dysautonomia. Brain and skeletal muscle are abnormal in acid maltase deficiency and neonatal myotonic dystrophy. Small with HIE hypoxic damage may have spinal cord. Disorders of the motor unit causes severe hypotonia at birth condition in breathing and cause perinatal asphyxia [2,4,7].

Investigations of peripheral hypotonia
Creatinine Kinase.
Lactate.
EMG/NCS/repetitive nerve stimulation test.
Muscle biopsy (histology, immunohistochemistry, electron microscopy, respiratory chain enzyme analysis).
Genetic testing (SMN gene deletion present in 95% of cases of spinal muscular atrophy type 1, myotonic dystrophy, congenital myasthenic syndromes).
Nerve biopsy (rarely).
Tensilon test.

Taken from Evaluation of the floppy Rakesh Kumar Jain Sandeep infant Jayawant.

Investigations in cases where the central cause for hypotonia is suspected
Serum electrolytes, calcium and phosphate Including, serum alkaline phosphatase, venous blood gas, thyroid function tests
Plasma copper/caeruloplasmin assay (as screening test for Menkes syndrome)
Chromosomal analysis (trisomy), testing for Prader and Willi syndrome (15q11and13)
Plasma amino acids and organic acids urine
Urine mucopolysaccharide screen (GAG)
Molecular/biochemical diagnosis of pro-collagen disorders
Very long chain fatty acids
Medical genetics review
Ophthalmology review
Brain imaging (CT/MRI)

Taken from Evaluation of the floppy Rakesh Kumar Jain Sandeep infant Jayawant

Points 5: Research

The history and physical examination should guide investigations. If there is good evidence of central nervous system dysfunction, brain imaging may be the first step. Metabolism suspected disease trigger appropriate tests; immediately seek disorders of energy metabolism, amino acid metabolism, metabolism of fatty acids and function of the urea cycle should be undertaken immediately if the child has a metabolic crisis Such disorders may be more easily detected during metabolic crisis once the child It has been stabilized the pres-

ence of dysmorphic features individual may request tests karyotype. Detection of hypothyroidism should be performed in all infants for whom etiology is unclear. If it is a disorder of the muscles, nerves or neuromuscular junctions seem likely a creatine phosphokinase (CPK) may be useful, considering that most Congenital myopathies are associated with normal CPK level while disease anterior horn cells may be associated with slight increases A significant increase in CPK suggests a form of congenital muscular dystrophy [3,8].

After initial screening tests and non-invasive investigations, electromyography (EMG), nerve conduction studies may be considered and muscle biopsy. If muscle biopsy or EMG are considered blood for a test CPK should be drawn before these procedures because the procedures can cause a short-term elevation of CPK levels [2,9].

Given the advances in genetic testing, muscle biopsies are not as frequently as in the past. Specific genetic tests are available for disorders such as Prader-Willi and spinal muscular atrophies (SMA). However, many muscle disorders presenting with hypotonia in the newborn or child period can only be diagnosed specifically using a muscle biopsy. Processing the biopsy should include sophisticated electron microscopy and special staining: biopsy "routine" may miss a pathology [3,10].

Method of Diagnosis	Successfully %
History and Physical Examination (Step 1) Family history Pregnancy and delivery Clinical and neurologic examination	50%
Imaging Study (CT or MRI/MRS) (Step 2)	13%
Clinical Evaluation Genetic (Step 3)	9%
Genetic Testing (Step 4) Karyotype, FISH, CGH	6%
Biochemical Evaluation (Step 5) Amino acids, organic acids, peroxisomes, carnitine, CDG test	6%
Neuromuscular Testing (Step 6) CK, EMG, NCV, DNA for SMA and CMD, muscle biopsy	6%
Follow-up Testing Some tests Repeated/Further tests	7%

CK: Creatine Kinase; CMD: Congenital Muscular Dystrophy; CDG: Congenital Disorder of Glycosylation; CGH: Comparative Genomic Hybridization; CT: Computed Tomography Scan; EMG: Electromyography; FISH: Fluorescence In Situ Hybridization; MRI: Magnetic Resonance Imaging; MRS: Magnetic Resonance Spectrography; NCV: Nerve Conduction Velocity; SMA: Spinal Muscular Atrophy

Adapted from Paro-Panjan D, Neubauer D. Congenital hypotonia: is there an algorithm? J Child Neurol. 2004; 19: 439-442- 2. And awn E. Peredo, Mark C. Hannibal. Pediatrics in Review Sep 2009, 30 (9): e66-e76.

Points 6: Principles of Management

- Physiotherapy and Stretches Aimed at prevention of contractures
- Occupational therapy - appliances, improvement of posture and function, activities of daily living Facilitating
- Prevention and correction of scoliosis
- Evaluation and treatment of associated cardiac dysfunction

- Respiratory support - assessment of requirement for invasive or non-invasive ventilation and/or tracheostomy
- Feeding - nasogastric feeding, caloric supplementation, gastrostomy
- Management of gastro esophageal reflux - medical or fundoplication
- Orthopedic intervention in setting of established joint contractures or evolving
- Encouragement of overall development and stimulation of learning
- Prevention (influenza and pneumococcal vaccination) and prompt treatment of respiratory infections [3,8].

Management and Prognosis

The early onset of symptoms, close to birth or the first weeks of life, is related to a poor prognosis due to severe weakness of the intercostal muscles. Most of these patients die due to complications associated with respiratory diseases such as infections during the first year of life. Mechanical ventilation in these patients is common and complications related to this lead to infections. In milder presentations of spinal atrophy usually with onset of symptoms towards 6 months of life, being able to sit without support, but not bear weight in the legs for which respiratory complications are variable and to a large extent determines the prognosis for survival to long term [10,11].

The posture in these patients often produces scoliosis and can be rapidly progressive. In congenital muscular dystrophy in contrast, the condition tends to remain static and improve over time. The development or progression of contractures and associated deformities must be prevented [10,11].

There are pathologies such as congenital myotonic dystrophy can be fatal in the newborn due to respiratory dysfunction, once these babies survive in the newborn period, there is a tendency toward gradual resolution of the respiratory part and swallowing, hypotonia and motor function they also improve. Children with dystrophy usually manage to walk, although this may be very late is towards the preschool age. Physical Therapy with tools in the management of hypotonia, in patients with myotonic dystrophy, are sensitive to anesthetics, particularly relaxants and narcotics. Therefore, management with these medications must be approached with care and caution. Patients with severe form such as myotubular myopathies may be born dead or not survive the period of the newborn, if they overcome this period have a slow improvement, need support for feeding and handling secretions and may require tracheostomy [10,11].

Conclusion

Hypothyroid child syndrome is a frequent entity, an initial classification should be done to guide the etiology as there are many options depending on the degree of involvement, although treatment in most entities is not curative, it is important to treat interdisciplinary to guarantee the best quality of life.

Findings of a lazy baby with delayed development milestones should draw attention to the possibility of a glycogen storage disease (type II Pompe, disease or maltase deficiency). Depending on the pathology, specific studies are done, for example; The diagnosis of Pompe disease is established by the muscle biopsy, with a definite diagnosis demonstrated by deficient activity of acid maltase in fibroblasts or other tissues. It is likely that recent trials using tandem mass spectrometry will be useful for early diagnosis and institution of therapy.

The cause of hypotonia in most affected patients is central. The highest diagnostic performance begins with a detailed medical history and examination, including a neurological evaluation and the search for dysmorphic features.

The selective use of neuroimaging, genetic studies, and biochemical investigations can contribute to the diagnosis in an additional subset of patients. Invasive studies with EMG and muscle biopsy only contribute to a small fraction of diagnoses.

Conflict of Interest

None of the authors has any conflicts of interest to disclose and all authors support submission to this journal.

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