

Spastic diplegia with nonperinatal asphyxia in pediatric population

Abstract

Spastic diplegia is a condition where patients have spasticity mainly in the lower extremities and highly associated with cerebral palsy. However, there exist other entities causing spastic diplegia in a pediatric population some of which are treatable and preventable. In this review, we describe disorders causing spastic diplegia which occur due to non-perinatal asphyxia.

Keywords: spastic diplegia, diagnosis, children

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Abbreviations: CP, cerebral palsy; HSP, hereditary spastic paraplegia; IEM, inborn errors of metabolism; DRD, dopa-responsive dystonia

Introduction

Spastic diplegia is characterized by spasticity in the upper or lower extremities whereby the lower extremities usually are more affected. Cerebral palsy (CP) with prematurity is highly associated with spastic diplegia.¹ In the European Cerebral Palsy Study, spastic diplegia was the most common subtype of CP.² Perinatal asphyxia events lead to bilateral periventricular white matter injury and disruption of corticospinal tracts controlling predominantly the lower extremities. A retrospective review study showed 44.4% of the children with CP spastic diplegia had periventricular leukomalacia.³ On the other hand, 46.3% of the children with CP spastic diplegia did not have identifiable etiologies for spastic diplegia.⁴ Since we frequently encounter spastic diplegia with unknown etiology in a clinical setting, it is important to keep in mind other etiologies causing this entity. There are numerous etiologies causing spastic diplegia except for cerebral palsy. We searched potential differential diagnoses on the internet with search terms "spastic diplegia" and reviewed the differential diagnoses that seem to be relevant to be considered in a clinical setting. This review deals with spastic diplegia with nonperinatal asphyxia.

Discussion

Myelopathies

Any spinal cord lesion can potentially cause spasticity in the extremities. Most importantly, hereditary spastic paraplegia (HSP) should be considered in pediatric spastic diplegia patients. HSP is a clinically and genetically heterogeneous neurologic disorder group. The typical features of HSP consist of progressive spasticity and weakness in the lower extremities without bulbar and upper extremity involvement, as well as occasional sensory disturbances or bladder dysfunction.⁵ The maintenance of axons in the spinal cord is impaired, affecting the corticospinal tract and the posterior columns.⁶ Mutations in SPG3A gene encoding for atalastin protein are the most common cause of early childhood-onset autosomal dominant HSP, which is relatively non progressive and presents with spastic diplegia.^{7,8} Treatment for HSP is exclusively symptomatic with physical therapy.⁶

Leukodystrophies

The leukodystrophies are genetic disorders affecting the white matter of the brain, potentially leading to motor impairments such as hypotonia in early life and spasticity over time. Several leukodystrophies including Canavan disease,⁹ Krabbe disease,¹⁰ Pelizaeus-Merzbacher disease,¹¹ metachromatic leukodystrophy,¹² adrenoleukodystrophy¹¹ and Alexander disease¹³ have been reported to cause spastic diplegia. Depending on the lesions, the patients have various symptoms from mild spastic diplegia to severe spastic quadriplegia, as well as other motor dysfunction in swallowing, chewing, and respiration.¹⁴ Behavioral problems and cognitive decline can differentiate the leukodystrophies from CP.¹⁵ MRI of the brain shows T2-weighted hyper intensity in the white matter in leukodystrophies. The pattern of brain MRI abnormalities can be useful in identifying the type of leukodystrophies.¹⁴

Metabolic disorders

Inborn errors of metabolism (IEM) develop spastic diplegia. Amino and organic acid disorders such as non-ketotic hyperglycinemia and branched chain amino acid disorders such as maple syrup urine disease and 2-methyl-3-hydroxybutyryl-CoA dehydrogenase deficiency can cause slowly progressive spasticity in the lower extremities.^{4,16} Other metabolic disorders exhibiting spastic diplegia are disorders of purine and pyrimidine metabolism such as deficiency of hypoxanthine phosphoribosyl transferase, which is essential in the purine salvage pathway¹⁷ and urea cycle disorders such as argininemia.¹⁸ Sjogren-Larsson syndrome, one of the IEMs due to mutations in the ALDH3A2 gene coding fatty aldehyde dehydrogenase, causes ichthyosis, developmental delay and spastic diplegia.¹⁹ Furthermore, cretinism due to maternal iodine deficiency has been reported to cause spastic diplegia in children.²⁰ To make a diagnosis of metabolic disorders, good history taking is essential because patients with metabolic disorders usually have no symptoms but develop encephalopathy under stressful conditions provoked by illness or high protein intake.¹⁶ Some of these diseases are treatable and preventable; therefore, it is important to recognize the diseases and initiate treatment as soon as possible.

Ataxia with spastic diplegia

Patients with ataxia with spastic diplegia, an X-linked recessive

inheritance, manifest with nystagmus, ataxia and pyramidal signs in infancy, then gradually develop spastic diplegia and mild mental retardation.²¹ In this group, Friedreich ataxia can also cause ataxia with spastic diplegia.

Idiopathic toe-walking

Children with toe-walking have bilaterally toe gait with an absence of normal heel strike. It can be seen in both only normal children under the age of 2 years, as well as patients with spastic diplegia due to Achilles tendon contracture or neurodevelopmental abnormalities such as autism.²² Idiopathic toe-walking is a diagnosis of exclusion. In such instance neurological examination is usually benign and the patient is able to walk and run at normal velocities.²² Most children with idiopathic toe-walking are able to walk normally with physical therapy²² Strong family history is suggested.²³

Dystonia

Dystonia is a syndrome of sustained muscle contractions, frequently resulting in twisting and repetitive movements or abnormal postures in affected body parts. When both agonistic and antagonistic muscles in the legs contracted simultaneously, it can cause spastic diplegia-like symptoms. Dopa-responsive dystonia (DRD) is an autosomal dominant inherited progressive dystonia with considerable diurnal fluctuation, caused by abnormalities in the gene GTP cyclohydrolase I.²⁴ Most children with DRD develop rigidity in the lower extremities and equinovarus foot posturing with brisk deep tendon reflexes. The symptoms improve dramatically with low-dose levodopa/carbidopa (4–5 mg/kg/day of levodopa).²⁴

To make a correct diagnosis, it is important to take a good history including prenatal and birth history. If there is any history of asphyxia at birth, it suggests asphyxia-related spastic diplegia. If there are any dysmorphic features, genetic disorders need to be considered. Images such as an MRI of the brain is useful to evaluate periventricular leukomalacia or leukodystrophies. An MRI of the spine can be helpful to evaluate myelopathies. Metabolic evaluations such as serum amino acids, urine organic acids, lactate, ammonia or others are helping to make a diagnosis of metabolic disorder.⁴

Conclusion

Beyond cerebral palsy, there are a wide variety of diseases associated with spastic diplegia. Some of these are treatable and preventable. Therefore, it is important for clinicians to understand the differential diagnoses and offer appropriate care to the affected patients.

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Conflict of interest

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