Case Report

Dopa-Responsive Dystonia in a Ten-Year-Old Girl

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Abstract

Children with recent onset dystonia and gait abnormalities may pose a diagnostic challenge. A ten-year-old, developmentally normal girl, presented with a six-month history of gait abnormality and dystonia. Her complaint worsened as the day progressed. In view of typical diurnal variation of dystonia, a therapeutic challenge with levodopa/carbidopa was given and there was a dramatic response. Hence, a diagnosis of dopa-responsive dystonia (DRD) was made. DRD is an inherited disorder characterized by dystonia with diurnal variation and favorable response to levodopa/carbidopa. The inheritance is usually autosomal dominant, however, in some cases, autosomal-recessive inheritance is also seen.

Keywords: Autosomal dominant dystonia with diurnal variation, dopa-responsive dystonia, Segawa's disease

Introduction

Dopa-responsive dystonia (DRD) is characterized by childhood-onset dystonia and a dramatic and sustained response to administration of low-doses of oral levodopa. The average age of onset is approximately six years.[1] This disorder typically presents with gait disturbance, caused by lower limb dystonia with diurnal variation, a positive family history, and gradual progression to generalized dystonia. Higher mental functions are usually normal with normal sensory and cerebellar functions. We report a ten-year-old girl with features of DRD.

Case Report

A ten-year-old girl was brought with complaints of difficulty in walking and stiffness of both lower limbs, for the past six months. She also had a history of frequent falls while walking and was unable to stand for prolonged periods. Her antenatal, birth, and neonatal periods were uneventful and developmental milestones were appropriate for her age. There was no family history of similar illness. On examination, her higher mental functions were normal, speech was hypophonic; she had a gait disturbance characterized by leg stiffness, and a tendency to walk in an equinus posture, resulting in difficulty in balancing. Her tone was slightly increased in all the four limbs, with cog-wheel rigidity. Power in both upper limbs was normal and 4/5 in the lower limbs. Postural tremor and dystonia were noticed on attempted movements of the limbs. Deep tendon reflexes in all the four limbs were exaggerated with extension of both great toes (striatal toes). Clonus was absent. The sensory system and cranial nerve examination were normal. There were no cerebellar signs. In the hospital, it was found that the symptoms and signs were relatively mild in the morning during rounds, whereas, they gradually worsened as the day progressed, rendering the child almost unable to walk by evening. The peripheral blood smear study was normal. Serum electrolytes and serum Ceruloplasmin were in normal range. Slit lamp evaluation for Kayser Fleischer ring was negative. Magnetic resonance imaging (MRI brain and spine were normal. In view of the typical diurnal variation of dystonia, a therapeutic challenge with levodopa/carbidopa was tried and there was a dramatic decrease in dystonia within two days and the child's gait improved. Hence, a diagnosis of DRD was made. The child was treated with a combination of Levodopa, Carbidopa, and Trihexyphenidyl. On follow-up the child showed persistent improvement in the clinical condition. Genetic studies were planned, but could not be done due to lack of resources.

Discussion

DRD is an inherited disorder characterized by dystonia with diurnal variation and favorable response to levodopa/carbidopa. The inheritance is usually autosomal dominant; however, autosomal recessive inheritance is also seen in some cases. The enzyme deficiency responsible for the manifestations is GTP

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cyclohydrolase 1 (GCH), which is a rate-limiting enzyme in the synthesis of dopamine.[2] This disorder had been referred to as hereditary progressive basal ganglia disease, hereditary progressive dystonia with marked diurnal variation, Segawa disease, and DRD in the past. At present, Segawa disease specifically denotes an autosomal dominantly inherited mutation in the *GCH 1* gene located on chromosome 14q22.1 to q22.2.[3] The disease usually manifests in school age children, however, adults with the disease have also been reported.[3] Females are affected more commonly than males.[4] It is likely to be misdiagnosed as cerebral palsy.[5] Initial manifestations of this disease include postural dystonia of the lower limbs with characteristic equino varus deformity of both feet. Segmental dystonia and tremors are also seen, particularly in the upper limbs. The dystonia gets worse as the day progresses, becomes maximal by evening, and decreases after sleep by morning. The diurnal variation of symptoms is seen in three-fourths of all cases.[6] Investigations characteristically reveal low levels of pteridine metabolites in the cerebrospinal fluid, normal neuroimaging, and increased blood phenylalanine levels after phenylalanine loading tests.[7] Assessing the therapeutic response to Levodopa is a useful and recommended method of diagnosing DRD, when the diagnosis is in doubt and when dystonia is not attributable to hypoxic ischemic encephalopathy.[8] In one reported series, administration of low-dose levodopa had resulted in complete to near-complete recovery of symptoms in a cohort of Chinese patients, with no significant long-term side effects.[9] In our case, the child presented with gait disorder characterized by dystonic movements of the lower limbs of gradual onset, which disappeared during sleep, and reappeared after getting up from bed and progressively worsened throughout the day with symptoms, for the past six months. With the above-mentioned clinical findings and a dramatic response to the levodopa/carbidopa combination, a diagnosis of DRD was made. The child continues to be symptom-free to date.

Conclusion

Children with recent onset dystonia and gait abnormalities may pose a diagnostic challenge. A careful history and focused neurological examination, looking for diurnal variation in symptoms, holds the key in arriving at the diagnosis. In such children a therapeutic response to levodopa might be a safe and appropriate way of confirming DRD. Children presenting to primary care physicians with similar symptoms require referral and neurological evaluation.

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