Dopa-responsive dystonia and its diagnostic challenges: A case report

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Introduction

Dopa-responsive dystonia (DRD), also known as Segawa syndrome, is an inherited disorder characterised by diurnal fluctuations of dystonia and a highly favourable response to levodopa. The commonest type of DRD is DYT5 dystonia which has a dominant inheritance and is due to mutations in the GTP-CH1 gene located on 14q22.1-q22.2[1-3]. The recessively inherited DRD frequently affects cognitive function[1]. A difference in ratio of mutant/wild-type GCH-I mRNA can explain phenotypical variations[4]. DRD is often inadequately recognised, and often erroneously diagnosed as dystonic cerebral palsy or familial spastic paraparesis. We report a child with DRD.

Case report

A 7 year old girl presented with progressive difficulty in walking and frequent falls for 4 years. Her symptoms aggravated towards evening and she felt better in the morning. During occasional afternoons she was completely unable to walk without support. These fluctuations were not related to illness or medications. She did not complain of generalized body weakness, difficulty in speech or swallowing. Her antenatal, intrapartum, and neonatal periods were uneventful. There was no developmental delay, regression or arrest noted. There was no family history of similar illness.

Her higher functions (learning ability, memory, orientation, attention span, insight etc.) were not altered. Her speech was hypophonic. She had an abnormal gait characterized by stiff legs and a tendency to walk in a tip toe gait, resulting in difficulty in maintaining balance. The muscle tone was increased only slightly in the upper limbs in comparison to significant increase in the lower limbs. Power in upper limbs was normal but 4/5 in the lower limbs. Postural tremor and dystonia were noticed on attempted movements of the upper limbs. Deep tendon reflexes were normal in upper limbs but increased in lower limbs with positive Babinski reflexes. Ankle clonus was present. The sensory system and cranial nerve examination were normal. Intention tremor was noted in both hands but other cerebellar signs were absent.

The peripheral blood smear revealed normal cell morphology. Liver functions and serum caeruloplasmin were within normal ranges. Slit lamp evaluation for Kayser Fleischer ring was negative. Anti-nuclear antibodies were negative and inflammatory markers were within the normal range. Magnetic resonance imaging (MRI) of brain and spine was normal.

In view of the typical diurnal variation of dystonia and the clinical picture, a therapeutic challenge with levodopa (syndopa & carbidopa) was tried and there was a dramatic reduction in dystonia within two days and the child's gait improved. Based on supportive clinical features and excellent response to levodopa, a diagnosis of DRD was made. This was clinically confirmed by observing recurrence of her symptoms when the treatment was withheld. During follow-up, the child showed persistent clinical improvement while on treatment with levodopa.

Discussion

The initial description of DRD was by Segawa in 1971 in a group of children who had progressive dystonia which showed diurnal fluctuation and marked clinical response to levodopa[5]. DRD can manifest throughout childhood (range 9 months to 16 years). However, adults with the disease have also been reported. Females are affected more commonly than males. It is likely to be misdiagnosed as cerebral palsy due to similarities in clinical presentation[6].

The presenting feature is always a gait disturbance manifesting as dystonic legs. This dystonia is progressive and more pronounced in lower than upper limbs. Dystonia can also affect the neck and axial musculature as well. DRD should be considered a possibility in any child presenting with a dystonic gait. Around 30–50% of patients with DRD have no family history[7].

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A diagnosis of Segawa syndrome in the past was made based upon a thorough clinical evaluation and documenting a response to therapy with low doses of levodopa as a diagnostic test. The majority responds promptly to 50 to 100 mg of levodopa, with dramatic relief from the dystonia and thus improvement in the gait[8].

An oral phenylalanine loading test may detect only about 80% of cases of DRD. Investigations characteristically experienced in DRD include low levels of pteridine metabolites in the cerebrospinal fluid, normal neuroimaging, and increased blood phenylalanine levels after the phenylalanine loading test[9]. Polysomnography shows a reduction of approximately 20% of normal twitch movements during REM sleep[10]. The general trend in settings with resources is to confirm the diagnosis by testing for the DRD genetic panel. A therapeutic trial with L-dopa should be done in all patients suspected of having DRD. Fluctuations in response, increased dose requirements, or long-term adverse effects have not been noted[11].

As these patients have selective striatonigral dopamine deficiency the natural history of the illness is gradual progression of the symptoms if left untreated[12,13]. There are reported cases where, if left untreated, they may develop severe contractures and motor disability due to severe dystonia[12,13]. However, no data are available on mortality related to DRD. Patients with good responses to levodopa typically continue to have a stable course without long-term adverse effects[14].

Authors intend to highlight that DRD should be thought of in any child presenting with paroxysmal or progressive hypertonia where the aetiology is not known. We also emphasize the importance of a trial of levodopa in all such patients. Detecting the specific mutation is of importance in confirming the diagnosis and facilitating genetic counselling.

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