Case report

Dopa-responsive dystonia – diagnosed 50 years after onset of symptoms

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Introduction

Dopa-responsive dystonia (DRD) is a rare hereditary hyperkinetic movement disorder usually seen in childhood which responds dramatically to treatment with levodopa. Its features may mimic other neurological illnesses and is thus under-diagnosed. I report a patient with DRD, whose illness evaded diagnosis for over 50 years. Its treatment has brought excellent results even at this late stage of the disease. This case also gives an idea of the natural course of the illness, if untreated.

Case report

A 58-year old female presented with progressive gait difficulty since childhood. She was born to non-consanguineous parents, after a normal vaginal delivery. Her perinatal history was uneventful. At around 6 years of age, her gait was noticed to be slightly abnormal at times. While schooling, she recalls having difficulty walking even short distances, as her legs felt stiff and heavy. This would clear up after a good night sleep. Mornings were better and sometimes she felt almost normal. Symptoms progressed during the course of the day. Gradually the stiffness involved her hands. She found difficulty playing the piano and was reported to be clumsy by her teachers. She was seen by many doctors over the years but of no avail, and had then accepted to live with her disability.

In her late twenties, she had to walk holding onto furniture and walls. She could only stand with support towards the evenings. She had several falls due to loss of balance. She could not leave the house alone and preferred to stay at home. Her disability continued to progress even after 50 years of age. She could not get up from bed unassisted. She needed two persons to lift her up from a chair. Her hands had also further slowed down. Speech and swallowing, and higher functions were not affected. She had an elder brother who was well. There was no family history of any similar illness. Her situation had become desperate and she once again decided to seek medical advice.

She was brought in a wheelchair and needed two people to help her get onto the examination bed. She had marked increase in tone in both lower limbs with dystonic posturing of her feet. Power, deep tendon reflexes and plantar reflexes were normal. There was bradykinesia of the hands but no tremor. No sensory deficits were detected. General examination did not reveal any Kayser-Fleischer rings.

Investigations showed normal blood counts, liver and renal function tests. Serum caeruloplasmin level was normal. MRI brain did not reveal any abnormality.

She was diagnosed to have a childhood onset progressive dystonia with diurnal variation. A trial with levodopa 125 mg twice per day was commenced. The next morning, she was able to get out of bed without help and walk without any assistance. Over the next few days, all her disabilities with which she lived for over 50 years disappeared. She now goes for daily 4 km walks and is catching up with things she never could do previously. Three years since the diagnosis, she is on levodopa 125 mg three times a day. She is now totally independent in all activities of daily living and her neurological examination is normal.

Discussion

DRD was described by Segawa as a new entity in the 1971 and is also known as Segawa disease[1]. It is a genetically inherited disorder, and accounts for about 10% of the childhood onset dystonias. It typically presents around 6-16 years of age and is about 3 times more common in girls.

The classical presentation is an abnormal gait due to a foot dystonia. There is plantar flexion and inversion (equinovarus posture) of the foot causing the child to walk on toes. Patients have as a result undergone unnecessary corrective surgery for equinovarus deformity. The dystonia can slowly extend to the arms and trunk. Some have Parkinsonism features in addition like tremor and bradykinesia, and may be mistaken for Juvenile Parkinsonism. The presence of a “striatal toe” (dystonic extension of the big toe) may mimic Babinski sign and along with hyperreflexia, DRD may be mistaken for cerebral palsy or hereditary spastic paraparesis[2]. Patients with DRD do not demonstrate intellectual, cerebellar or sensory disturbances.

Another classical feature of DRD is diurnal fluctuation, where patients are relatively symptom free

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in the morning and become progressively disabled as the day progresses. Patients also show improvement after sleep.

DRD is commonly due to an autosomal dominantly inherited mutations of the gene Guanosine triphosphate (GTP) cyclohydrolase 1[3]. The gene regulates the production of an enzyme involved in activation of tyrosine hydroxylase involved in the production of dopamine. However, only 30-40% genetically affected persons manifest symptoms due to reduced penetrance and variable expressivity. Therefore a family history is important, though may not be found as in this patient. About 40% of patients with DRD do not carry this mutation and DRD results from other recessively inherited metabolic disorders.

A diagnostic feature in DRD is the dramatic improvement seen with low doses of levodopa resulting in a near complete resolution of symptoms[4]. All suspected patients need to be given an adequate trial with levodopa for at least 3 weeks. Motor benefit often begins almost immediately on starting levodopa and full benefit may be seen within days to a few months. The response to the therapy is sustained throughout their lives, without any of the long term complications like dyskinesia and wearing off as seen in Parkinson disease. A therapeutic trial with levodopa remains the most practical way in making the diagnosis. In the majority, a restoration of complete physical function can be achieved even after many years without treatment, like in this case.

Clinicians should be alert in suspecting DRD in all children with dystonia and those labeled cerebral palsy with an unclear history. This case highlights the need to maintain such alertness even in adults whose diagnosis may have been unfortunately missed for many years. Diagnosing DRD is one of the most rewarding experiences in the practice of neurology as the response to treatment is often dramatic and miraculous.

References

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