Case Reports

Dopa-Responsive Dystonia (Segawa Syndrome)

Neel Kamal
Deepti Pagare Bhat
Emma Carrick

A 12-year-old boy with gradually worsening global developmental delay was diagnosed and managed as quadriplegic cerebral palsy since childhood. Subsequent evaluation revealed marked dystonia over spasticity leading to suspicion of Segawa syndrome. Dramatic improvement in clinical condition followed after therapy with low dose L-Dopa.

Key words: *Cerebral palsy, Dystonia, Segawa syndrome.*

Dopa-responsive dystonia (DRD) is a genetic disorder involving GTP cyclonydroiase 1, one of the rate-limiting enzymes in dopamine synthesis(1). Since the initial description by Dr. Segawa, in 1971, many authors have reported cases of DRD. Early diagnosis is difficult due to variable expressions(2,3) and this may result in considerable delay in starting treatment with L-dopa, which potentially achieves near complete resolution of symptoms.

Following is a description of a child who was initially diagnosed and managed as cerebral palsy. However, on subsequent clinical evaluation, marked dystonic features were noted which following treatment with L-dopa, radically altered the course of his illness and quality of life.

From the Children's Center, Hull & East Riding Community Health NHS Trust, Hull, United Kingdom.

Correspondence to: Dr. Neel Kamal (Consultant Pediatrician), The Children's Center, 70, Walker Street, Hull, UK HU3 2HE. E-mail: neel.kamal@humber.nhs.uk

Manuscript received: March 1, 2005;
Initial review completed: April 12, 2005;
Revision accepted: January 18, 2006.

Case Report

The patient is a twelve year old boy who was evaluated for development delay at Specialist Community Children's Service in Hull, United Kingdom, at the age of fifteen months. He was born following a full term normal delivery, weighing 4.1 kg. The mother's antenatal course was unremarkable. There was positive history of learning and physical disabilities in mother's twin brother and her maternal courins.

The patient's perinatal and neonatal course was normal. His developmental progress showed that he sat unsupported at 6 months, transferred objects from hand to hand but was not mobile or rolling at the age of fifteen months. Examination at that stage showed him to be generally hypertonic with his head held in extension and his fist clenched at rest. When seated, he flopped forwards with his head extended. Head circumference was carefully monitored as his fore-head was sloping, however, the head circumference remained within normal range. Routine investigations to exclude chromosomal, endocrine, myopathic and metabolic causes for developmental delay were found to be negative at this stage. However, MRI scan of the brain showed a non-specific increased signal till the inferior basal ganglia initially and also when repeated at the age of 8 years. The finding was thought to be of unclear clinical significance at this stage.

At about two years of age, patient began to

show some atypical features like head retraction towards left side, with limb stiffness that worsened as the day progressed and reflexes that did not suggest true spasticity. He demonstrated global developmental delay on the Griffith's scale indicating learning disability. Following detailed assessment; the child was assigned a diagnosis of quadriplegic cerebral palsy.

In the following years, the patient received multi-agency support in terms of regular medical care, physiotherapy, occupational therapy, educational therapy and social services. He subsequently underwent orchidopexy, and tendon lengthening procedure on his calf muscles. During this period, he continued to be wheel chair bound with gradually diminishing speech.

During a routine medical review at the special school clinic at ten years of age, the examining consultant pediatrician noted that the child had truncal hypotonia with rigidity in limbs, normal deep tendon reflexes and soft hands. The rigidity was attributed to dystonia. There was head retraction and excessive drooling of saliva. Prominent diurnal fluctuation was noted in patient's abilities of talking, swallowing, feeding and weight bearing all showing significant decline towards evening when he appeared fatigued. In view of these atypical features, the clinical impression of cerebral palsy was reviewed and he was referred to the Pediatric Neurology department at Leeds for further assessment. The finding of dystonia rather than spasticity was reconfirmed and the possibility of Dopa-Responsive Dystonia was suspected.

A test dose of L-Dopa (with initial dose of 2 mg/kg in three divided doses) was given to the child. Assessment after two weeks revealed considerable improvement in his speech and motor abilities of hands with improved truncal support. Some jerky choreiform hand movements had developed as a possible side effect of the treatment. The child, however, was continued on the medication.

The child was reviewed at the special school clinic after about three months, when he demonstrated improved ability to use hands, reduced drooling and improved speech with near normal muscle tone. The choreiform movements noted earlier had almost ceased. The physiotherapists and occupational therapist confirmed the same (*Table I*). About a month later, at the multi-agency meeting in the Community Pediatrics department of Children's center, patient's mother reported considerable improvement in fine motor, gross motor and speech abilities, which matched the observations made by the medical team, physiotherapist, and occupational therapist.

This boy is currently on L-dopa treatment and continues to show rapid improvement. He is an active, cheerful young lad and now likes to sit cross-legged. He occasionally sings during the clinic. His ability to ambulate has consistently been increased, so much so that he prefers to climb up and down the stairs by himself, holding on to the banisters rather than using the lift, which was fitted into his house earlier as a part of adaptation. The family has now requested for the lift at his house to be removed. The revision of diagnosis and implementation of medication has profoundly enhanced the quality of life as is evident from the above.

Discussion

Dopa Responsive Dystonia is characterized by variable penetrance and phenotypic variability as noted by various authors, sometimes leading to misdiagnosis of these cases as cerebral palsy(2-4). The present case report is an example of the same. Some workers have reported a delay of upto 30 years in diagnosis, with some patients requiring

TABLE I–*Results of Assessment of Physiotherapist Before and After Commencing Treatment with L-Dopa*

Functional ability	Pre-treatment	Post-treatment
On the floor		
Ability to lay straight	No (wind sweep to right)	Yes
Isolating movement in all limbs	No	Yes
Bridging at knees	Maximal assistance	Minimal assistance
Prone lying	No	Yes
Sitting		
Cross legged sitting	No	Yes (independently)
Sitting holding ladder	No	Yes
Dynamic sitting	No active trunk extension	Yes, good trunk control
Standing		
Holding furniture	No, (stands in prone standing frame)	Yes (independently)
Holding hand	No	Yes (with good pelvic and trunk control)
Mobility		
Rolling	Not independently	Yes (independently)
Creeping	No	Yes (with some assitance)
Commando crawling	No	Yes
Walking		
Manual assisted walking	Walks in Rifton gait trainer: approx 10 M: Quickly fatigued	Yes (with an adult on either side for approx. 20 m)
Wheel chair		
Manual self-propelling	Slumps, if not supported with butterfuly harness	Requires supportive system to maintain symmetric posture
Sequencing		
Rolling		
supine to prone	No	Yes (independently)
supine to sitting	No	Yes (with minimal assitance)
sitting to standing	Uses hand and neck extension	Yes (with minimal assistance)
Respiratory function & speech		
Lip control	Vocalize few words at a time: fatigued in the evening	Able to hold conversation in full sentence
Saliva control	Poor	Improved
Upper limb function	Left side neglect	No neglect of left side
Hands to midline		Yes
Grasp and release		Yes (good with right hand)
Ability to bend and straighten		Yes
Ability to open & close hands		Yes (both hands)
Tone		
Central	Hypotonia	Slight low tone, improved trunk extension
Limbs	Generalized hypertonicity (More on the left)	No longer extension pattern

TABLE I (contd...)–*Results of Assessment of Physiotherapist Before and After Commencing Treatment with L-Dopa*

Functional ability	Pre-treatment	Post-treatment
Posture		
Pelvic and shoulder girdle Stability	Poor	Improved
Head control	Poor	Improved

several surgical interventions in the interval(2). Our patient also underwent tendon-lengthening surgery over calf muscles during the preceding 12 years. Another report presents some cases of DRD who were initially misdiagnosed as spastic cerebral palsy and were wheel chair bound for several years but later responded dramatically to low dose L-dopa(3,4) similar to our patient. Many patients of DRD show prominent diurnal fluctuation in symptoms(5), Our case illustrates the importance and diagnostic utility of this symptom during evaluation in the community settings. It further emphasizes the need to carefully elicit clinical signs on each occasion, even in long standing cases.

Segawa syndrome is known to respond to very low doses of Dopamine, which can be subsequently increased based on clinical response. Our patient was commenced on initial dose of 2 mg/kg in three divided doses, which has been gradually doubled following response. Sustained improvement with medication thus has a significant implication over quality of life and cost-effectiveness of the treatment in terms of care and resource provision.

Variable and evolving clinical presentation of movement disorders in children can sometimes lead to a misdiagnosis of cerebral palsy. Future neurological re-evaluation, therefore, must be open minded in cases where a definite identifiable cause is not found. Achieving a precise diagnosis may lead to accurate therapeutic interventions, as it happened in this case. Significant therapeutic response may be obtained influencing the clinical outcome in terms of quality of life

Contributors: NK conceptualized the idea for reporting the unusual case for publication, reviewed the data collected and critically approved the final version of the report. DPB designed the concept of the paper, collected and analyzed data, drafted the final version of the paper. EC helped in acquisition of and interpretation of data.

Funding: None.

Competing interests: None stated.

REFERENCES

1. Maita N, Hatakeyama K, Okada K, Hakoshima T. Structural basis of biopterin-induced inhibition of GTP cyclohydrolase I by GFRP, its feedback regulatory proteins. J Biol Chem 2004; 279: 51534-51540.
2. Slawek J, Friedman A, Bogucki A, Budrewicz S, Banach M. Dopa-responsive dystonia (Segawa variant): clinical analysis of 7 cases with delayed diagnosis. Neurol Neurochir Pol 2003; 37 Suppl 5: 117-126.
3. Jan MM. Misdiagnoses in children with dopa-responsive dystonia. Pediatr Neurol 2004; 31: 298-303.
4. Patel K, Roskrow T, Davis JS, Heckmatt JZ. Dopa responsive dystonia. Arch Dis Child 1995; 73: 256-257.
5. Costeff H, Gadoth N, Mendelson L, Harel S, Lavie P. Fluctuating dystonia responsive to levodopa. Arch Dis 1987; 62: 801-804.