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DOPA RESPONSIVE DYSTONIA: A CASE REPORT

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ABSTRACT

Dopa responsive dystonia (DRD) is a dystonic syndrome of childhood, usually affecting gait and subsequently developing into parkinsonism with a dramatic therapeutic response to levodopa.

At the best of our recollection this is the first case in Iranian medical literature of a 13 year old boy, affected by this interesting, rare and treatable disease which can be easily diagnosed if clinicians have a high index of suspicion.

We also have a brief discussion on the pathophysiology of DRD.

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INTRODUCTION

Dopa Responsive Dystonia (DRD) or Segawa disease is a rare form of autosomal dominant extrapyramidal disease in the pediatric age group.[6] It is also known as "hereditary progressive dystonia with marked diurnal variation" and "hereditary dystonic parkinsonism syndrome of juvenile onset" in the medical literature.[2]

The dystonic and parkinson-like symptoms are the main clinical features of the disease, and a dramatic relief of symptoms is observed with small doses of L-dopa.

We report a 13 year old boy with this disease in hope to draw the attention of our colleagues to this entity which is arousing considerable interest; since it appears to be treatable and its diagnosis is often delayed or even totally missed.[7]

A high index of suspicion along with a trial of levodopa still remains the basis for diagnosis.[8]

CASE REPORT

A 13 year old boy was referred to our neuro-pediatric clinic with complaints of difficulty in walking, writing, clothing and in short, performing any activity of daily living. Mentation remained intact but he left school because of restriction of physical ability. Symptoms began, as parents claimed, 3 years ago after being exposed to cold weather (journey to a cold climate), after which the patient's condition steadily deteriorated. He was better in the morning but symptoms worsened throughout the day or after physical exertion.

The parents were cousins. Past history was unremarkable, with no family history of neurologic disease.

Upon neurologic examination, he was normal. He had a mask-like, unblinking facies with dysarthric speech. Cranial nerves were intact. Bradykinesia was noted on beginning of any motor activity. Cogwheel rigidity with slightly exaggerated deep tendon reflexes and flexor plantar reflexes were observed. Dystonic posturing of the leg was present which caused toe walking and a wide base gait with a tendency to fall. Lumbar lordosis was noticed upon walking. No tremor was detected.

Routine hematologic and biochemical investigations were normal. CSF analysis was normal for protein and cells, no oligoclonal band was found in CSF electrophoresis, and CSF IgG level was normal.

To rule out Wilson's disease, serum copper, ceruloplasmin and 24 hour urinary copper excretion were measured which were all reported to be within normal ranges.

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Brain CT scan and MRI revealed no abnormality.

Trihexiphenidyl, haloperidol, imipramine and citicoline were tried in appropriate dosage with no benefit. Madopar 125 mg (L-dopa 100 mg + benserazide 25 mg) was started at a dosage of 1/2 tab./bid, and gradually increased to one tab./bid. A dramatic response was observed two days after starting L-dopa with gradual attainment of normal motor activity in two weeks.

Electrodiagnostic studies (EMG and NCV) performed two days after treatment with L-dopa, were within normal limits.

At three month follow-up, he was doing well on two tablets of Madopar 125 mg/daily, but parents report that in the winter time with exposure to cold weather his symptoms recur.

DISCUSSION

Dopa responsive dystonia (DRD) which was probably first described in 1969 by Coleman[2] is a disorder characterized by childhood onset dystonia usually affecting gait with concurrent or later development of signs of parkinsonism and a dramatic response to L-dopa.

The age of onset is usually between four to eight years (range 9 months to 16 years).[3] The initial feature is nearly always a gait disturbance caused by leg dystonia. Dystonia is progressive and more pronounced in the leg than in the arms, but also affects the neck and axial musculature.[2] Elements of Parkinsonian features such as cogwheel rigidity, mask-like facies and bradykinesia appear sooner or later.[1]

Diurnal fluctuation of symptoms has been emphasized as a distinguishing characteristic of DRD, but it appears to vary between individuals. Symptoms are considerably improved on awakening and become worse later in the day or after prolonged exertion.[1]

Nothing unusual can be detected in the previous history of children with DRD. There are no prenatal or perinatal problems, no precipitating event such as drug exposure, no evidence of visual, sensory, cerebellar or intellectual disturbance, and no clues for etiology. Cranial MRI and/or CT scan are normal.[2]

Dopa responsive dystonia is inherited as an autosomal dominant trait with a 31% penetrance rate.[1] The abnormal gene (GTP cyclohydrolase I gene) is located in the short arm of chromosome 14. GTP cyclohydrolase I is the rate limiting enzyme for the biosynthesis of tetrahydrobiopterin, which is the co-factor for tyrosine hydroxylase, the rate limiting enzyme for dopamine biosynthesis. DRD is caused by the mutation of GTP cyclohydrolase I gene with resultant decrease in the striatal dopamine level to less than 20% of normal values.[4]

The estimated frequency of DRD is low (1 in 2 million) based on reported cases.

There has often been a prolonged delay from symptom onset to treatment with L-dopa. In a series of 66 patients reviewed by Nygaard et al.,[5] this delay averaged 14.5 years and ranged from less than one year to 61 years. This fact illustrates that it is never too late for L-dopa therapy in patients with DRD. However, ideally the correct diagnosis should be made as early as possible in childhood and appropriate therapy given at the very beginning of the clinical manifestations.[2]

DRD must be considered in the differential diagnosis of the child or adolescent presenting with a dystonic gait disorder, diplegic cerebral palsy, sporadic spastic paraplegia, ataxic syndrome and juvenile parkinsonism. The response to L-dopa is so dramatic and occurs so quickly that a diagnostic therapeutic trial should be undertaken in all patients presenting with these syndromes.[3]

The point of interest in our patient which was not mentioned in previous reports, was exacerbation of symptoms with cold weather.

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