Research Paper

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Dopa Responsive Dystona: a Study and Literature Review

Medical Science

KEYWORDS : Dystonia, Dopa Responsive, Levodopa, Parkinsonism, Cerebral palsy

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ABSTRACT

Dystona is a disorder characterised by sustained or repetitive involuntary muscle contractions frequently associated with twist or repetitive movements and abnormal postures. Dystonia may range from minor contractions in an individual muscle group to severe involuntary movements.

Amongst the dystonias which appear at an early age, Dopa Responsive Dystonia (DRD) is of particular importance. Its importance lies in the fact that even a small dose of levodopa can abolish the dystonia, even it is present for a very long time, and the patient can lead a normal life. We present a case series of Dopa responsive dystonia and review the literature.

INTRODUCTION:

Dystonia is an unnatural spasmodic movement of posture that puts the limb in a twisted posture. It is often patterned, repetitive or tremulous and can be initiated or worsened by movements. Dystonia may vary considerably in severity and may show striking fluctuation in individual patients. It involves the proximal limb muscles more than the distal limb muscles.

Dystonia can be classified in to generalized and focal; according to the age of onset; or into primary and secondary (Drugs or other neurological disorders)

The pathophysiological basis of dystonia is still primitive. The phenomenon is characterised by co-contracting synchronised bursts of agonist and antagonistic muscle groups. This is associated with a loss of inhibition at multiple levels of the nervous system as well as increased cortical excitability and reorganisation.

Amongst the dystonias which present at an early age, Dopa responsive dystonia(DRD) is of particular importance. DRD must be considered in any child or young adults with dystonia or unexplained paraparesis or gait disorder. Its importance lies in the fact that very low doses of levodopa can abolish the dystonia helping the patient lead a normal life.

MATERIALS AND METHODS:

The study was done in the Medicine department of Jawahar Lal Nehru Medical College, Bhagalpur. We examined 6 patients of dystonia,5 were females and 1 male. All of them were in age group of 10 to 18 years. They presented with stiffness of lower limbs for last 2 to 4 years. They had complaints of freezing of gait occasionally for the same duration. Their attendants stated that they had bouts of peculiar postures and falls. A striking feature in their history was that their stiffness increased as the day progressed and they were better after rest or on waking up from sleep.

We asked about their birth history & their birth history were uneventful and cried immediately after birth. They were vaccinated properly and all developmental milestones were within normal limits and there was no significant illness in the family.

On General examination no abnormality was detected.

On examination of CNS, Higher mental function, cranial nerves, cranium and spine and, sensory system were within normal limits. There were no signs of cerebellar abnormality. On examination of motor system, there was increased tone in the lower limbs. Jerks were brisk in the lower limbs and few had an unsustained clonus. Gait was spastic/dystonic.

Other systems like CVS, GIT, Respiratoy AND Locomotor were within normal limits.

The routine blood investigations like CBC, Blood sugar, kidney function tests , liver function tests & ASO titres were normal. Serum ceruloplasmin in the patients were normal. CSF examination and MRI brain also came out to be normal.

We diagnosed the cases as dystonia probably Dopa Responsive Dystonia (DRD). They were started on SYNDOPA(LEVODOPA/CARBIDOPA) 110 mg twice a day. On administration of SYNDOPA their symptoms subsided completely. Thus the final diagnosis was established as DOPA RESPONSIVE DYSTONIA (DRD).

We followed the cases for 2 years, the patients currently has no dystonia and no dyskinetic features.

OBSERVATIONS AND REVIEW OF LITERATURE:

Dopa responsive dystonia is a rare disorder probably accounting for 5-10 percent of all childhood onset dystonia with a population frequency of about 0.5 per million (Nygaard 1995). In clinical neurology, it is one of the most important diagnosis as it is effectively cured by small doses of levodopa, even after many years of neurological disability. Dopa responsive dystonia occurs commonly in females and also the severity is more than that in males. Patients often have a family history suggesting autosomal dominant inheritance. Penetrance of Dopa responsive dystonia gene is approx 45 percent in women and 15 percent in men. Typically the onset is in the first decade but some may have a congenital onset with a delayed motor milestone while others may present in adolescent and adult life. In children dystonia of legs and feet causes stiffness of the lower limbs, inturning of feet and toe walking. Gait may appear to be spastic or dystonic. Pyramidal signs including spasticity, ankle clonus and extensor plantar responses are often present along with mild parkinsonian cogwheel rigidity and bradykinesia of the upper limbs. Most patients gradually progress to generalised dystonia but other neurological features such as cognitive impairment or seizures do not occur. It is seen that patients with a childhood onset the dystonia is mild and remains confined to the feet and others have focal dystonias such as torticollis. In older patients there is often mild Parkinsonism, including rest tremor, showing an excellent and sustained response to small doses of levodopa. Diur-

nal fluctuation of symptoms with improvement in the morning or after sleep and increasing dystonia later in the day or after exercise is characteristic of Dopa responsive dystonia but may be absent. Atypical presentations include exercise related dystonia, muscular weakness, scoliosis, oromandibular dystonia and myoclonic dystonia.

Investigations are not much helpful in this condition. Cerebral imaging including CT scan and MRI scan are normal. CSF examination is also normal in this condition. With this we can say that correct diagnosis depends entirely on a high index of suspicion and readiness to deploy a therapeutic trial of levodopa in cases where Dopa responsive dystonia is even a remote clinical possibility. This means that Dopa responsive dystonia must be suspected in any child or young adult with dystonia or unexplained paraparesis or gait disorder.

The two differential diagnosis which needs to be excluded are athetoid or spastic cerebral palsy and early onset Parkinson's disease. In this case series, a normal developmental milestone excludes cerebral palsy. Moreover taking levodopa would not have dramatically resolved the dystonia if it would have been cerebral palsy. Early onset Parkinson's disease may also present with similar features of prominent lower limb dystonia and Parkinsonian features. In Dopa responsive dystonia, significant motor fluctuations and dyskinesias never develop whereas they appear at an early stage after starting levodopa in Parkinson's disease. It is quite true that this distinction cannot be made with confidence until the response to levodopa has been observed for a few years. We observed these cases for two years and still now no dyskinetic features have developed. This distinction between early onset Parkinson's disease and Dopa responsive dystonia could only be made by examination of the dopaminergic nigrostriatal system with positron emission tomography which is not an widely available investigation. The dopaminergic nigrostriatal system is normal in dystonia but abnormal in Parkinson's disease.

Biochemically Dopa responsive dystonia is characterised by a striking reduction in central nervous system dopamine metabolism with reduced CSF dopamine metabolites and tetrahydrobiopterin , BH4 is a cofactor for tyrosine hydroxylase tetrahydrobiopterin. Pathologically there are normal numbers of nigral neurons but these are hypopigmented ; striatal dopamine is reduced with normal levels of tyrosine hydroxylase immunoreactivity but reduced enzyme activity.

Treatment of Dopa responsive dystonia is with small doses of levodopa. The response of levodopa is dramatic. Dystonia is rapidly abolished even after decades without treatment. The dose of levodopa is variable though. Many patients require only 50-100 mg of levodopa per day, with a decarboxylase inhibitor. It is advisable to try at least 600 mg per day for three months before concluding that patient does not have Dopa responsive dystonia.

CONCLUSION:

In view of the above study and the literature reviewed we can conclude that Dopa Responsive Dystonia must be considered in any child or young adult with dystonia or unexplained paraparesis or gait disorder.

The response to levodopa is dramatic.Investigations are unhelpful and correct diagnosis depends entirely on a high index of suspicion & readiness to deploy a therapeutic trial of levodopa in cases where Dopa Responsive Dystonia is even a remote clinical possibility.

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