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Unmasking Juvenile Parkinsonism – A KF Ring Negative Case Report

Dr Prapti Reddy, Dr Vivek Srivastava, Dr Adithi K.

[1]Dr Prapti Reddy, Department of Internal Medicine, K S Hegde Medical Academy, Mangalore, Karnataka, India.

[2]Dr Vivek Srivastava, Department of Internal Medicine, K S Hegde Medical Academy, Mangalore, Karnataka, India.

[3]Dr Adithi K., Department of Internal Medicine, K S Hegde Medical Academy, Mangalore, Karnataka, India.

Corresponding Author: Dr Prapti Reddy, Department of Internal Medicine, K S Hegde Medical Academy, Mangalore, Karnataka, India.

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Abstract

Our case is one of the very rare atypical presentations of Juvenile Parkinsonism on which a detailed work up was undertaken and diagnosed as Wilson's disease. It is an enigmatic case of Wilson's disease reported in the world with no family history, severe neurological impairment in absence of KF ring, normal liver function and only basal ganglia degeneration on MRI brain. The diagnosis was arrived upon by using Leipzig's score for Wilson's disease. A high index of suspicion is required to diagnose such cases as an excellent recovery of function can be seen in such patients who initially present with Parkinsonism features.

Keywords: wilson's disease, KF ring, Juvenile Parkinsonism

Introduction

Wilson's disease is a rare metabolic disease showing the failure of natural pathway of copper handling and metabolism leading to gradual deposition of copper in various tissues of the body namely, brain, liver and eyes. It is caused by mutation in the ATP7B, a copper transporting beta polypeptide ATPase, located on chromosome 13, with autosomal recessive inheritance. Patient's usually present as two sets: one with hepatic features and other with neurological features, with or withouthepatic involvement, psychiatric features and Kayser-Fleischer's ring (KF ring) in eye. The KF rings occur in up to 98% cases with neurological manifestations and up to 60% cases with hepatic manifestations.

Case Report

A 22 years old Hindu female patient, youngest child born of a non-consanguineous marriage, presented with history of progressive slowness with difficulty in performing daily activities and repeated falls since 2 years and swelling of her left shoulder following a fall 5 days back. Patient was leading an apparently normal life till 15 years of age, when she started having mood disturbances and emotional liability which was diagnosed as a case of Bipolar Affective Disorder. She was started on Risperidone and Lithium for the same. There was no significant improvement except a slight reduction in emotional labiality. After continued medication for two years Valproate was added to her medications.

After 3 years of treatment with waxing and waning of her mood symptoms, patient's mother observed her to be progressively lazy and complained of slowness in most of her daily activity. Her symptoms gradually progressed over the next two years and started interfering with daily

chores. She gradually became dependant on her family members with a later confinement to bed and inability to move. She was unable to maintain sitting position without support. She also reported change in the quality of speech which became progressively less fluent and her facial expressions became forced and unnatural.

During the two years of progressive deterioration she consulted multiple psychiatrists. A diagnosis of Drug induced Parkinson's was made and Risperidone and Lithium were withdrawn. However even with the withdrawal of antipsychotics she did not have significant relief in her symptoms. She presented to us with difficulty in moving left upper limb and painful swelling of left Supraclavicular region, following an episode of fall, five days prior to admission.

Detailed history did not reveal any trauma or head injury,meningitis or similar complaints in any family members. X-ray chest revealed fracture left clavicle for which her arm was immobilised and bandaged. Detailed neurological examination revealed dysarthria with normal mentation(MMSE score of 26/30), severe bradykinesia, cogwheel rigidityand axial rigidity with exaggerated reflexes without pill rolling tremors. Abdominal examination revealed no organomegaly. USG abdomen was also normal. Lab investigations revealed a normal hemogram and liver function tests. Slit lamp examination did not show any KF rings. Levodopa, Carbidopa combination along with Amantadine was started with a provisional diagnosis of Juvenile Parkinson's, but patient responded poorly with only slight reduction in rigidity and bradykinesia. She further developed severe orofacial dyskinesia and bladder incontinence so the dose of Levodopa and carbidopa combination was significantly reduced.In the absence of clinical improvement an MRI Brain was ordered which showed degeneration of basal ganglia with mineral deposits. Then 24-hours urine copper estimation was done which showed high values at 188 mcg/24 hours (Ref range: 0- 70 mcg/24 hours). Blood ceruloplasmin was 22.20 mg/dL (Ref range: 20-60 mg/dL).Due to financial constraints liver biopsy and mutation analysis was not done.

The diagnosis of Wilson's disease was established using Leipzig's Score and patient was started on Zinc 50 mg thrice daily, to which she responded with significant improvement over next 6 weeks and at discharge was able to walk and carry out all her daily activities with support.

Discussion

Wilson's disease is a rare metabolic disease showing the failure of natural pathway of copper handling and metabolism leading to gradual deposition of copper in various tissues of the body namely, brain, liver and eyes. It is caused by mutation in the ATP7B,a copper transporting beta polypeptide ATPase, located on chromosome 13, with autosomal recessive inheritance[1].

Patients usually present as two sets: one with hepatic features and the other with neurological features with or without hepatic involvement and psychiatric features. The near diagnostic sign of Wilson's disease is the KF ring, which is best visualized with the use of a slit lamp andare present in >99% of patients with neurologic/psychiatric forms of the disease and present in only~30–50% of patients diagnosed in the hepatic or presymptomatic state; thus, the absence of rings does not exclude the diagnosis[2].

The presentation of Wilson's disease as hepatic disease and neuropsychiatric disease is usually equal in proportions but they differ mainly in its age distribution. Hepatic formsusually present in late childhood or adolescence and neuropsychiatric forms present mostly

between 20-40 years and rarely ever before 15 years of age[1].

The clinical spectrum of hepatic manifestations vary considerably ranging from asymptomatic hepatosplenomegaly, asymptomatic modest elevation of transaminases or recurrent attacks of jaundice with acute hepatitis, to chronic active hepatitis, macronodular cirrhosis of liver with or without features of portal hypertension and fulminant hepatic failure.

In general the extent of hepatic involvement is inversely related to age of disease onset[1].The clinical manifestations of neuropsychiatric subset are equally varied and encompass the features related to affliction of extrapyramidal, cerebral and cerebellar systems. Unlike hepatic manifestation the neurological manifestation are usually subacute or chronic[1].The most common neurological manifestation is dysarthria, dysphagia and drooling of saliva usually as result of bulbar muscle dystonia or pseudobulbar palsy. This is commonly associated with difficulty in daily activities due to limb dystonia. Accompanying features of Parkinsonism like rigidity, bradykinesia, hypomimia, micrographia and tremors are all common. Tremor may be postural, action-induced, intentional, resting or rarerbut characteristic 'wing-beating' type tremor. Patients may have a ‘vacuous smile’ (a stiff face with a gaping mouth) as a result of facial muscle dystonia. Cerebellar involvement is associated with ocular movement abnormalities, limb incoordination, impaired tandem gait, and a wide-based gait[1].

Behavioural disturbances may affect patients before or after the clinical disease manifests itself and may present as obsessive behaviour,attention deficit hyperactivity disorder, impulsivity, paranoid psychosis, changes in work-related performance, emotional labiality and depression with suicidal tendencies[1].

Autonomic disturbances including postural hypotension, abnormal sweating, and sphincter and sexual dysfunction are frequently present. Others relatively rare conditions which may be associated with Wilson’s disease are chorea, acute onset of tremor of the head, neck and limbs, acute generalized severe dystonia, myoclonic or tonic–clonic seizure andpainful proximal myopathy[1].

Our case is one of the very rare atypical presentations of Wilson’s disease reported in the world with severe neurological impairment in absence of KF ring, normal liver function and only basal ganglia degeneration on MRI brain. The diagnosis was arrived upon by using Leipzig’s score for Wilson’s disease [3] of more than 4 (confirmed Wilson’s disease) with severe neurological impairment and with elevation of 24hrs urinary copper estimation to more than double the upper limit of normal.

Youn J et al [4] from Korea in their study have reported 12 such cases of Wilson’s Disease in whom neurological manifestations were present without any KF ring and found that Wilson's disease patients without KF ring demonstrated a higher ceruloplasmin concentration and serum copperlevel than those with KF ring. In addition, liver cirrhosis and typical signalchanges in brain magnetic resonance imaging were less common in neurologic Wilson'sdisease patients without KF ring, which is consistent with our case.

Ours is the first such reported case from India and it gives a new insight into this rare presentation of Wilson’s disease. It also suggests that Wilson’s disease should be ruled out with further workup in all cases presenting with neurological symptoms suggestive of disease even without KF ring.

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