Case Report

Wilson's disease: a rare presentation

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Abstract

Introduction: Wilson's disease is a rare disease, exact prevalence in Indian subcontinent is not known. Here we present a rare case of Wilson disease which directly presented with neurological manifestations without history of any hepatic manifestation.
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INTRODUCTION

Wilson disease is a rare autosomal recessive inherited disorder of copper metabolism that is characterized by excessive deposition of copper in the liver, brain, and other tissues. Wilson disease is often fatal if not recognized and treated when symptomatic.

CASE REPORT

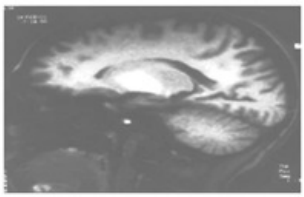
A previously apparently healthy, 20-year-old, single, right handed male, born by non consanguineous marriage

1. Joint pain involving bilateral knee, elbow, wrist joints (2 month ago)
2. Focal seizures involving right upper limb (2 month ago)

He was admitted in Dept. of Internal medicine G.M.C Nanded for further evaluation and management .During course of admission he developed prominent extra pyramidal features consisting of rigidity, tremors at rest and in action (typical batwing tremors) in all 4 limbs, shuffling gait, slurred speech and emotional lability. No sensory and motor deficit.[7] RA, CRP, ESR was normal, CT brain scan was normal Started on antiepileptic therapy T. Carbamazepine 200 mg TDS and T. Phenytoin 100 mg BD , T. propanolol 40 mg OD for tremors and T. baclofen 5mg bd for spasticity .Patient did not improve symptomatically; on the contrary there were worsening of clinical features.

MRI brain (plane) was performed for the same which suggested

Bilateral hyperintensity in putamen, thalami, tegmentum, sup. cerebellar peduncle[10]



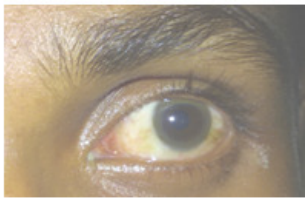


Figure 1 and 2: Kayser-Fleisher rings

Presumptive Diagnosis of Wilson disease was suspected considering MRI Brain findings. Patient was further investigated and was found to have Low ceruloplasmin (less than 8 mg/dl) and 24 hour urinary copper 132 miligram. Liver transaminases were within normal limits. Ophthalmologic examination confirmed Kayser-Fleisher rings. Considering these facts diagnosis of Wilson disease was confirmed as patient was having neurological manifestation he was started on T. zinc 50 mg BD. Patient was followed up at end of 1 month and 2 month. Patient was symptomatically improved rest tremors completely abolished, rigidity and action tremor reduced very much. He was able to do all his daily routine without much difficulty. A review MRI Brain Plain film showed some changes of regression than earlier scan.

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DISCUSSION

Wilson's disease is an autosomal recessive disorder caused by mutations in the *ATP7B* gene, a membrane-bound, copper-transporting AT Pase on chromosome 13.The frequency of Wilson's disease in most populations is about 1 in 30,000–40,000. Most cases have been reported in developed countries .Children with WD are usually normal at birth and may remain healthy for a variable period of time; most cases present in the second and third decade of life .[6,15] Wilson's disease may present as hepatitis, cirrhosis, or as hepatic decompensation, typically in the mid to late teenage years in western countries, although the age of presentation is quite broad and extends into the fifth decade of life. An episode of hepatitis may occur, with elevated blood transaminase enzymes, with or without jaundice, and then spontaneously regress. Hepatitis often reoccurs, and most of these patients eventually develop cirrhosis. Hepatic decompensation is associated with elevated serum bilirubin, reduced serum albumin and coagulation factors, ascites, peripheral edema, and hepatic encephalopathy. In severe hepatic failure, hemolytic anemia may occur because large amounts of copper derived from hepatocellular necrosis are released into the bloodstream. The association of hemolysis and liver disease makes Wilson's disease a likely diagnosis.The neurologic manifestation of Wilson's disease typically occur in patients in their early twenties, although the age of onset extends into the sixth decade of life. Most patients who present with neuropsychiatric manifestations have cirrhosis. MRI and CT scans reveal damage in the basal ganglia and occasionally in the pons, medulla, thalamus, cerebellum, and subcortical areas. The three main movement disorders include dystonia, in coordination, and tremor. In some patients, the clinical picture closely resembles that of Parkinson's disease. Autonomic disturbances and seizures may occur. Sensory abnormalities and muscular weakness are not features of the disease. The neurological features of WD are primarily due to the deposition of copper in the lenticular nuclei, although areas like the brainstem and cerebellum can be affected .[3,4] Patient had most of the neurologic features described in the literature: rigidity, dystonia, dysarthria, tremor at rest, festinant gait . He was also emotionally labile with abrupt mood changes[2,3,7]

Table 1: Useful Tests for Wilson's disease

Test	Usefulnessa	Normal Value	Heterozygous Carriers	Wilson's disease
Serum ceruloplasmin	+	180–350 mg/ L (18–35 mg/dL)	Low in 20%	Low in 90%
KF rings	++	Absent	Absent	Present in 99% + if neurologic or psychiatric symptoms presentPresent in 30–50% in hepatic presentation and presymptomatic state
24-h urine Cu	+++	0.3–0.8 mmol (20–50 mg)	Normal to 1.3 mmol (80 mg)	>1.6 mmol (>100 mg) in symptomatic patients0.9 to>1.6 mol (60 to >100 g) in presymptomatic patients
Liver Cu	++++	0.3–0.8 mmol/g (20–50 mg per g tissue)	Normal to 2.0 mmol (125 mg)	>3.1 mmol (>200 mg) (obstructive liver disease can cause false-positive results)
Haplotype analysis	++++ (Siblings only)	0 Matches	1 Match	2 Matches(2)(5)

The long-term treatment of symptomatic cases of WD entails the chronic use of copper chelators (Penicillamine and Trientine) and zinc, while liver transplantation provides a cure. For patients with hepatitis or cirrhosis, but without evidence of hepatic decompensation or neurologic/psychiatric symptoms, zinc is the therapy of choice. For initial medical therapy of patients with hepatic decompensation, a chelator (trientine is preferred) plus zinc is recommended For initial neurologic therapy, tetrathiomolybdate is emerging as the drug of choice because of its rapid control of free copper, preservation of neurologic function, and low toxicity. Penicillamine and trientine should be avoided because they each have a high risk of worsening the neurologic condition. As tetrathiomolybdate is commercially not available everywhere yet, zinc therapy is recommended.Newer modalities being investigated are use of gene replacement therapy, gene repair, Hepatocytes transplantation[11,12,13,14,17]

CONCLUSION

A diagnosis of Wilson disease should be entertained in the evaluation of a young patient presenting with liver dysfunction and/or extra pyramidal neurological features (in our case patient directly presented with neurological manifestation).

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