

Case Report

Multifocal myoclonus as a heralding manifestation of Wilson disease

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ABSTRACT

Wilson disease (WD) is one of the few curable movement disorders that manifests with varied presentations so that WD needs to be considered in any patient with a movement disorder under the age of 50 years. Although WD is one of the causes of myoclonus, it is rarely seen in WD and usually as an associated finding. We report a case of an adolescent female patient of WD who presented with cortical multifocal myoclonus of 6-month duration with later development of generalized dystonia, extrapyramidal syndrome, and cognitive decline. Kayser–Fleischer ring was present on slit lamp examination. Serum copper, urine copper, serum ceruloplasmin, and magnetic resonance imaging brain were consistent with the diagnosis of WD. Copper chelation was started along with other symptomatic treatments and diet modifications. Myoclonus had resolved by 3-month follow-up with the improvement of other symptoms. This case report emphasizes that myoclonus can be the main and presenting feature of WD.

Key words: Dystonia, epilepsy, myoclonus, Wilson disease

Introduction

Wilson disease (WD) is a hereditary degenerative disorder of copper metabolism due to autosomal recessive ATP7B mutation manifesting with liver symptoms, neurological symptoms, psychiatric symptoms, or a combination of these. Neurological presentations include parkinsonism, tremor, dystonia, dysarthria, ataxia, seizures, behavioral and cognitive impairments. Myoclonus is rarely reported and is seen during the course of illness. We present a case of WD who presented to us with the predominant symptom of myoclonus at onset.

Case Report

A 9-year-old female with no significant past medical or family history presented with a complaint of intermittent irregular

sudden jerky movements in all the four limbs and head of 6-month duration. This abnormal movement started in the right lower limb which over the next 1 month progressed to the right upper limb, head, left lower limb, and then left upper limb. The movements used to occur asynchronously in the limbs and head lasting less than a second with no loss of consciousness, diurnal variation, clustering, and never in sleep. Because of the movements, the patient used to have occasional falls, slippage of objects from hand, and occasional spillage of food while eating. The frequency of jerks also progressed over 6 months [Video 1]. For the first 3 months, these were the only symptoms. Then, 3 months from the onset, the patient started having drooling of saliva with progressive swallowing difficulty and speech problems. The symptoms progressed that at presentation the patient could eat only semisolid food

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with severe dysarthria and able to utter only few words. There was also inappropriate laughter. Simultaneously to the onset of bulbar symptoms, the patient also developed abnormal posturing of limbs which started in the right half of the body followed by the left with difficulty in walking and performing daily activities with hand. The posturing was associated with stiffness which used to get resolved completely in sleep. There was also poor attention with worsening performance in school. There was no history of convulsions, fever, headache, vomiting, visual complaints, motor weakness, sensory impairment, or bowel and bladder abnormalities. There was no history of jaundice, gastric complaints, bleeding tendency, or measles in the past. The patient was fully vaccinated according to the national vaccination program.

On examination, the patient was alert, conscious, inappropriately smiling with drooling of saliva, and persistently open mouth. Cognitive function was severely impaired. There was no auditory or visual abnormality with normal fundus examination, extraocular movement, and pupillary reflex. Kayser–Fleischer (KF) ring was evident in both eyes. There was repeated dystonic, synchronous, uprolling of both eyes without impairment in sensorium and other associated movements. Severe dysarthria and dysphagia were noted with tongue dystonia but with normal gag reflex and symmetrical palatal movement on vocalization. Motor system examination revealed generalized rigidity with normal power, normal deep tendon reflexes, and flexor plantar response. There was multifocal myoclonus involving head and all the four limbs predominately in the right half of the body. In addition, there was dystonic posturing involving all the four limbs. Sensory and cerebellar system examination was normal. On gait examination, the patient showed short shuffling gait with festination. Other system examinations were normal.

Routine investigation comprising complete blood count, renal function test, and liver function test was normal. Serum copper increased, serum ceruloplasmin reduced, and 24 h urine copper increased. Slit lamp examination confirmed KF ring in both eyes. Magnetic resonance imaging (MRI) of the brain revealed bilateral basal ganglia, thalamic, midbrain, and pontine hyperintensity consistent with WD [Figure 1]. Electroencephalogram (EEG) was normal despite multifocal myoclonus suggesting cortical origin. Ultrasonography of the abdomen did not reveal any liver abnormality.

The patient was diagnosed as a case of WD and started on pencillamine, zinc, and diet modification. Clonazepam was also added for myoclonus. The patient was discharged after initial observation. At 3-month follow-up, the patient had no myoclonus with improvement in extrapyramidal symptoms and static cognitive impairment.

Discussion

WD commonly presents with hepatic symptoms (40%), neurological symptoms (40%), or psychiatric symptoms (15%).^[1]

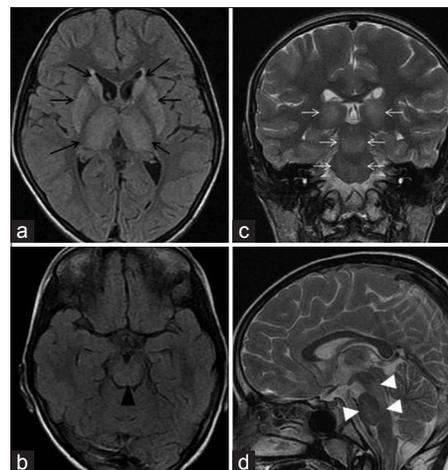


Figure 1: Magnetic resonance imaging brain of the patient showing hyperintensities of bilateral caudate, putamen, thalamus ([a] black arrows), and midbrain ([b] black arrowhead) in axial fluid-attenuated inversion recovery section, T2-coronal section showing hyperintensities in bilateral thalamus, midbrain, and pons ([c] white arrows), and T2-midsagittal section showing hyperintensities in midbrain and pons ([d] white arrowhead)

Hepatic symptoms present early in the first decade compared to neurological symptoms that present in the second or third decade and have better prognosis on treatment. Those with neurologic symptoms usually present as (1) an akinetic–rigid syndrome resembling parkinsonism, (2) a generalized dystonic syndrome, or (3) postural and intention tremor with ataxia, titubation, and dysarthria.^[1] Epilepsy is not so uncommon in WD occurring in around 10% of patients.^[2] Of this, myoclonus is very rare, and according to a study, it is seen in only 3% of patients although the type of myoclonus is not mentioned in this study.^[3] Other case series of WD does not mention myoclonus in their patient cohort.^[4–7] In a retrospective study of epilepsy spectrum in WD comprising 41 patients done by Prashant *et al.*, only one case of periodic generalized myoclonus that occurred during the disease process is described.^[2] In a review of epilepsy in WD done by Dening *et al.*, involving 44 literatures, four cases of myoclonus have been described, of which only one was the presenting symptom.^[8] Two case reports describe myoclonus in their patients of WD, both of which are generalized myoclonus.^[9,10] Our patient presented with myoclonus which was multifocal and cortical onset that was the only symptom for the initial 3 months before the onset of other typical symptoms of WD. Such multifocal cortical myoclonus as the initial and presenting symptom has been rarely described in literature. Such presentation may delay the diagnosis of WD as usually the workup may be focused on progressive myoclonic epilepsy or subacute sclerosing panencephalitis in measles-endemic region such as India. The presence of other extrapyramidal symptoms with KF ring on routine examination helped us suspecting WD in this case. Furthermore, this case emphasizes that WD should be kept in the differential diagnosis of myoclonus, and slit lamp examination should be done at least as up to 99% of patients with neurological WD have KF ring and this can be a useful investigation. EEG is usually positive with multifocal spikes in cortical myoclonus but it is not essential for labeling myoclonus as of cortical origin.^[11]

High serum-free copper with increased 24 h urine copper excretion and low ceruloplasmin seen in our patients confirmed the diagnosis further. The well-recognized sign in MRI brain is of panda sign and panda cub sign, but it is not seen in all cases and is not necessary in all patients. The MRI findings seen in our patient were consistent with the diagnosis of WD [Figure 1].

To conclude, myoclonus can be seen in a case of WD in either cortical multifocal form or as generalised synchronous myoclonus. Although myoclonus usually develops during the course of illness, it can be a predominant and presenting symptom, and WD needs to be considered as an etiology of myoclonus even if rare.

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Conflicts of interest

There are no conflicts of interest.

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