

Atypical Presentation of Wilson Disease without Kayser-Fleischer Ring in Geriatric Age

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Abstract: It is a rare event for Wilson Disease to have onset in geriatric age with neurological symptoms. And it is even rarer for such a condition to occur in the absence of Kayser-Fleischer Ring. We present a case of 63 year male who present with neurological symptoms of Wilson Disease without Kayser-Fleischer Ring which was confirmed by raised urine copper levels and Magnetic Resonance Imaging features classical of Wilson Disease.

Introduction

Wilson disease is caused by an inherited defect in the enzyme pathway of excretion of excess copper from liver into bile duct. The patients usually present first time as adolescents or young adults. The onset of the disease in the geriatric age is rare. Neurological manifestations commonly appear in adolescence or early adulthood. Kayser-Fleischer ring is the brown or golden brown ring seen in outer cornea due to deposition of copper. It is described in 99% of patients with neurological manifestations of Wilson's disease [1]. Overall, it is rare for the disease to have its onset in the geriatric age and have neurological symptoms as the initial symptoms and it is even rarer to see such a patient without eye involvement. We present one such case of Wilson disease with late onset neurological disease without Kayser-Fleischer Ring.

Case History

A 63 years male presented with complaints of swaying to right side while walking since 4 months. The symptom did not worsen during night. There was no history of difficulty while walking through narrow and dark corridors. He had difficulty in writing and holding objects due to intentional tremors in the right hand. He had no history of truncal ataxia, diplopia or slurring of speech. No history suggestive of cranial nerve involvement, motor or sensory deficits, meningeal involvement. Patient is a known type 2 Diabetic on regular treatment. He was diagnosed to have chronic liver disease with portal hypertension 3 months back and had undergone sclerotherapy and hemo-clipping for variceal bleed. His family and personal history was unremarkable. On examination, he was afebrile with pulse 80 beats/min, regular and blood pressure measuring 130/70 mmHg. The patient had pallor and bilateral pitting edema extending up to the knees. He was not icteric. Central nervous system examination showed normal higher mental functions; increased tone, brisk deep tendon reflexes and flexor plantar reflexes bilaterally. Dysdiadochokinesia, intentional tremors, spastic ataxic gait were present right more than left. Sensory and posterior column examination was normal. Other systemic examination was normal.

A baseline investigation showed picture of pancytopenia (Hb -9.3gm/dL, Total Leucocyte Count -3000/mm³ and platelet count-1.2 lakh/mm³) and deranged coagulation profile (prolonged prothrombin and Activated Partial Thromboplastin Time). Liver function test revealed hypoalbuminemia (Serum Albumin- 2.3) with normal liver enzymes. Serum ammonia level was not elevated. Kidney function test was normal. Diabetes was under control (Random Blood sugar-144mg% and HbA1c-4.2). The serology for Human Immuno-deficiency virus and hepatic viral markers including Hepatitis B were negative. Ultrasonography of abdomen revealed features suggestive of chronic liver disease and splenomegaly. CT Brain showed bilateral centrum semiovale hypodensities. In view of chronic liver disease with neurological symptoms, a differential diagnosis of Wilson disease was considered and the patient was worked up. MRI Brain showed multiple chronic ischemic foci in bilateral periventricular and adjacent fronto-parietal subcortical matter. Bilateral basal ganglia showed diffuse T1 hyperintensities suggesting hepato-cerebral degeneration. 24-Hour Urine Copper was 114µg/day (normal-32 to 64µg/day). The values were rechecked. Slit Lamp examination showed no Kayser-Fleischer ring. Liver biopsy was not done in view of deranged coagulation profile. Patient was diagnosed to have Wilson Disease with late-onset of neurological manifestations. The anemia and splenomegaly were explained as complications of the disease and portal hypertension. The patient and his relatives were counseled about the condition and the treatment options. Unfortunately they denied the treatment and were discharged against medical advice.

Discussion

Wilson disease is an autosomal recessive disorder of copper transport with a gene frequency of 1 in 180 and an approximate homozygote prevalence of 1 in 30,000 [1]. The gene encodes for a homologous cation transporting P-type adenosine triphosphatase protein, most likely involved in copper transport and predominantly found in liver, kidneys, and placenta. Copper accumulation appears to be caused by decreased transport of copper into bile [2]. The damage of liver begins as early as 3 years as a result of accumulation of excess copper. The usual age of presentation is in the twenties with hepatic, neurological, psychiatric manifestations or a combination of these. Rarely hematologic, renal, or endocrine presentation of the disease has been reported [3]. The onset of Wilson disease after 40 years of age is rare, although cases have been described of patients presenting in the fifth and sixth decades [4-5]. Neurological manifestations commonly appear in adolescence or early adulthood and include dysarthria, movement disorders, ataxia, and micrographia. An adolescent may have deteriorating performance in school or athletics. Psychiatric symptoms have been under-emphasized, and Wilson disease should be considered in any young patient with newly occurring psychiatric illness, including an inability to cope, labile moods, depression, and outright psychosis [2]. Onset of neurological symptoms in the elderly has been reported in a few cases [6-7] Kayser-Fleischer rings, located at the periphery of the cornea, consist of dense granules of copper and sulfur and are green-yellow or brown. These rings are a valuable diagnostic sign in patients exhibiting neurological and psychiatric disease because they are almost

always present in these patients if they have Wilson disease. It is considered as one of the essential criteria for the diagnosis of Wilson disease [1]. When Wilson disease is considered a possible diagnosis, one of the best early tests is to measure 24-hour urine copper concentration, which is always elevated in symptomatic patients. The normal 24-hour concentration is 32-64 $\mu\text{g/d}$ and symptomatic patients will always have $> 100 \mu\text{g/d}$. The urine should be collected into trace element-free containers and the laboratory should have the capability to assay copper in the appropriate range. Rarely, a false-positive urine copper value may result because of obstructive liver disease [1] Liver biopsy though considered as gold standard for the diagnosis of Wilson disease is not essential for diagnosis [8]. We present a rare case of Wilson disease with onset of neurological symptoms in the sixth decade without Kayser-Fleischer ring. Ross et al reported a patient with Wilson disease with onset of neurological symptoms at 58 years with precedent severe hepatic dysfunction and laboratory investigations [7] Campanella and Lamberti have documented case of Wilson disease with atypical clinical course without Kayser-Fleischer ring in an adolescent male [9] Willet and Keichl reported a 23 year male with typical Wilson disease but no Kayser-Fleischer ring [10]. Demirkiran et al have reported a case of Wilson disease with neurological manifestation without Kayser-Fleischer ring in a 41 year old woman [11]. Penicillamine was considered as primary treatment in Wilson disease. Recently Zinc and tetrathiomolybdate is considered as the treatment of choice for hepatic and neurologic manifestation of the disease respectively. With treatment, liver function usually recovers with improvement in neurologic and psychiatric symptoms although the treatment has to be continued lifelong. In conclusion, diagnosis of Wilson disease should be considered in the presence of hepatic and neurological symptoms even in the absence of Kayser-Fleischer ring irrespective of the age of onset.

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