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A RARE PRESENTATION OF WILSON DISEASE: A CASE REPORT

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ABSTRACT

Wilson Disease results from autosomal recessive mutation in ATP7B gene which leads to reduced formation of ceruloplasmin protein in the body that acts as a copper transporter. Due to its deficiency, there is the build-up of copper in the liver and brain among other organ systems and it leads to the development of various clinical abnormalities but commonly presents either as hepatic dysfunction and/or cirrhosis in young patients with movement disorder. Here we present a case that presented with hypoglycemia and hypothermia in absence of any infection, drug abuse or metabolic abnormality. He was later diagnosed as Wilson disease. Wilson Disease is mostly thought of hepatic /neurological disease. Contrary to this Wilson's disease is a multisystem disease affecting multiple organ system including, kidneys, endocrine system and musculoskeletal system and can present with manifestations of above-mentioned systems.

Key words: Wilson disease, Endocrinologic manifestations, Copper toxicity.

INTRODUCTION

Wilson disease, also known as hepato-lenticular degeneration, is due to disordered copper metabolism having an autosomal recessive pattern of inheritance and characterized by deposition of copper in the brain, liver, and other tissues secondary to the mutation in ATP7B gene leading to impaired biliary excretion of copper. It has a wide range of clinical manifestations from an asymptomatic state to hepatic failure, chronic liver disease, and neurologic and psychiatric manifestations, and can be fatal if left untreated.[1] Half of the patients with Wilson disease have neurologic or psychiatric symptoms.[2] Joint disease is present in 20-50%, hemolytic anemia in 15%, and Fanconi anemia in up to 16%, along with cardiac, ophthalmological, skeletal, and hepatic manifestations.[3, 4] Presentation is partially dependent on the age of disease onset, however rare presentations like endocrine disorders, kidney dysfunction, and hematological disorders are also reported.

Here we report a case of a young male with Wilson disease who initially presented with symptoms suggestive of an underlying endocrine disorder. We present diagnostic and treatment dilemmas associated with Wilson disease in this patient.

CASE PRESENTATION

An unaccompanied young boy was brought into the Emergency Department of Pakistan Institute of Medical Sciences by the police and paramedics in an unconscious state with no identity available. Police stated that they found him in an unconscious state at the roadside. At the time of presentation, his blood pressure was 100/60 mm Hg, Pulse 64 beats/min, respiratory rate 18 breaths/min, random blood sugar level 48 mg/dl, and temperature of 35 degrees Celsius. His Glasgow coma scale (GCS) was 7/17 (E1V1M5). He had superficial wounds on his forehead, nasal bridge, and cheeks with decreased skin turgor, no pupillary abnormalities, and no signs of meningeal irritation with bilateral down going planters. He had cogwheel rigidity in all four limbs. Cardiovascular, respiratory and abdominal examinations were unremarkable. No injection marks were noted.

Prompt correction of low blood sugar level was done with 25% Dextrose water along with thiamine. He gained consciousness after the correction of hypoglycemia, but he remained disoriented and confused. Gastric lavage was done because of suspected poisoning. But after a few hours, he had abnormal limb movements inconsistent with fits. He had dysarthria when he spoke and did not obey commands.

Preliminary investigations including arterial blood gases, blood complete picture, Serum chemistry, hepatic and renal, and coagulation profiles were normal. Chest radiography and electrocardiography were normal. Plain computed tomography brain was unremarkable. Urine routine examination was normal.

Workup for causes of sudden onset abnormal body movement initiated. The peripheral blood smear was normal. Anti-nuclear antibody (ANA) HIV screening was negative. A slit lamp examination of an eye revealed Kaiser-Fleischer (KF) rings bilaterally (Figure 1). The thyroid hormone profile was normal. Ultrasonography of the abdomen and pelvis was unremarkable. Serum ceruloplasmin level 4.7 mg/dl (15-30 mg/dl). Table 1 shows the lab workup.

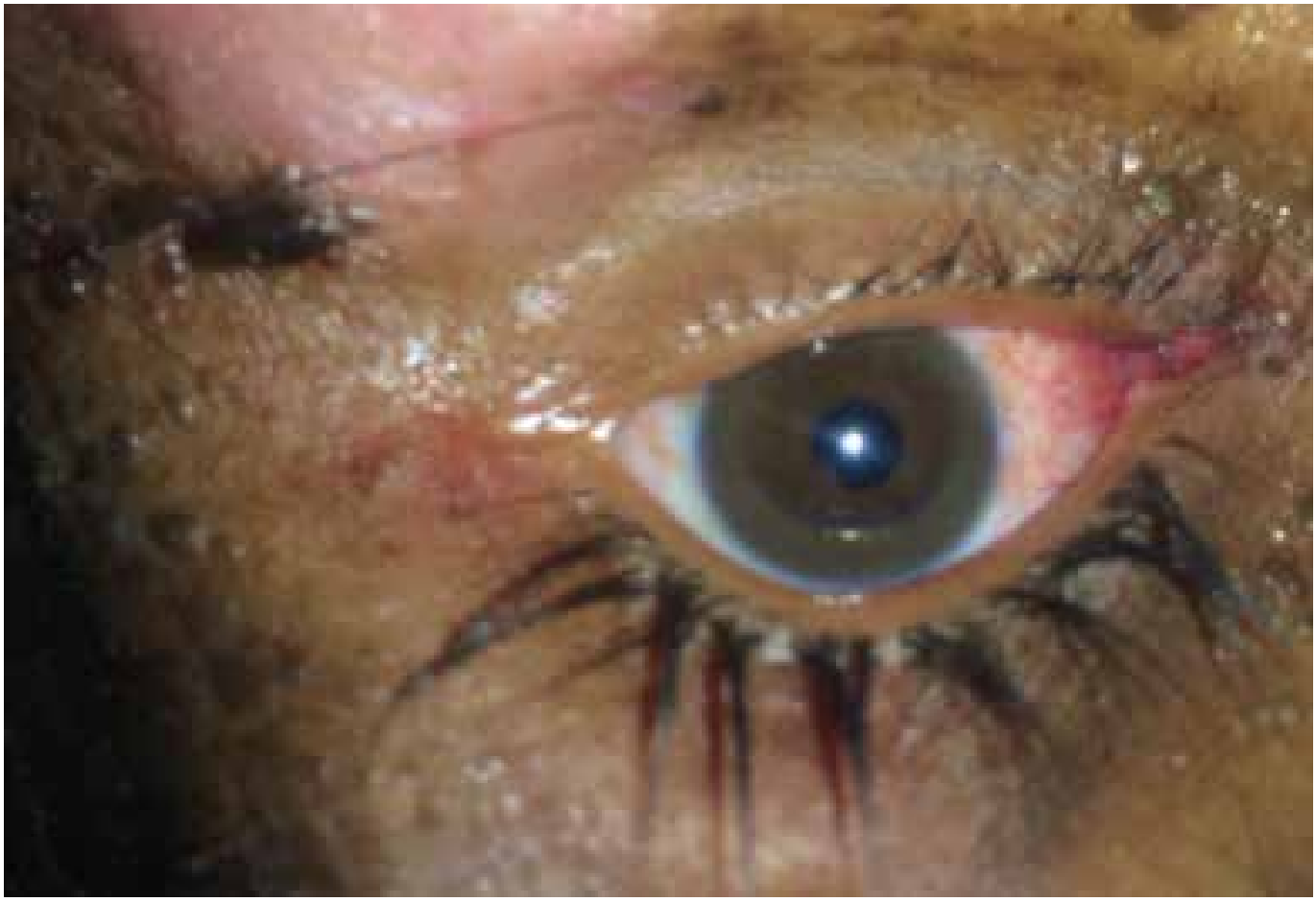

Figure 1: Kayser-Fleischer ring

Table 1: Workup and laboratory investigations

Laboratory Investigations		
	Patient Value	Normal Reference range
TLC	7000 / microliter	4000-11000 / microliter
Hemoglobin	14.1 g/dl	13.2-16.6 g/dl
Platelets	220000	150000-400000 / microliter
Serum Urea	9 mg/dl	5 – 20 mg/dl
Serum Creatinine	0.7 mg/dl	0.5-1.1 mg/dl
Serum Sodium	136 meq/l	135-145 meq/l
Serum Potassium	4.1 meq/l	3.5-4.5 meq/l
ALT	35 mg/dl	35 – 45 mg/dl
Serum Bilirubin	0.8 mg/dl	0.2 – 1.2 mg/dl
Covid-19 PCR	Negative	Negative
ESR	5 mm/Hour	< 15 mm/Hour
Anti-nuclear antibody	Negative	Negative
HIV screening	Negative	Negative
TSH	2.1 mIU/L	0.5 to 5.0 mIU/L
T3	1.5 nmol/L	0.92 to 2.76 nmol/L
T4	89 nmol/L	77–155 nmol/l
Serum ceruloplasmin	4.7 mg/dl	15-30 mg/dl
Urine analysis		
Color	Yellow	Yellow
Turbidity	Nil	Nil
pH	5.2	4.5-8

Specific Gravity	1.010	1.005-1.025
Nitrite	Absent	Absent
Leukocyte esterase	Absent	Absent
Bilirubin	Absent	Absent
RBC	0 /hpf	< 3 /hpf
WBC	3 / hpf	≤2-5 /hpf
Protein	20 mg/dl	≤150 mg/dl

(Abbreviations: TLC –Total leukocyte count, ALT- alanine amino transferase, ESR- erythrocyte sedimentation rate, HIV- human immunodeficiency virus, TSH-thyroid stimulating hormone, RBC-Red blood cells, WBC- white blood cells, HPF- high power field)

Magnetic resonance imaging (MRI) of the brain showed that in the midbrain the red nucleus was surrounded by a high T2 signal in the tegmentum, known as the face of the Giant Panda sign in radiology (Figure 2). There was hypointensity in the superior colliculus which is a classical radiological sign of Wilson disease. Electroencephalography (EEG) showed diffuse non-specific slowing. The rest of the diagnostic testing was not done due to the non-availability of facilities in the hospital and affordability issues.

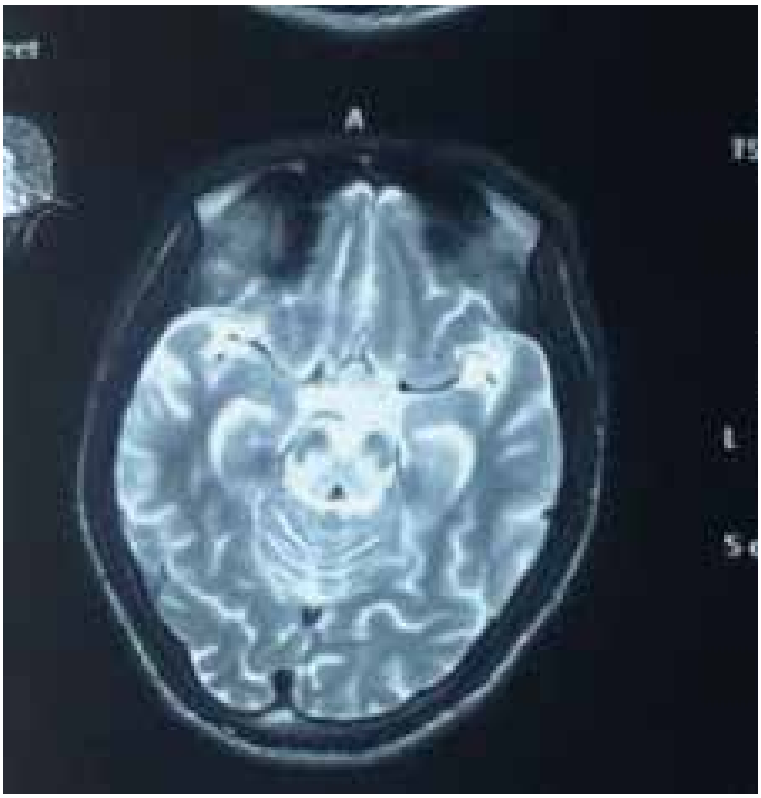

Figure 2: Face of Giant Panda sign on T2-weighted MRI Brain

Treatment started with chelating agent D-penicillamine along with zinc supplementation. Clonazepam in low dose was started to control the choreoathetoid movement. Marked improvement was observed in the patient's condition. He remained hospitalized for one week to monitor any worsening of symptoms when chelation started. During hospitalization, no episode of hypoglycemia was documented. He was looked after by the paramedical staff. He was then referred to a non-government welfare organization for further care. His prescription included all details regarding adverse effects commonly associated with penicillamine use and avoiding foods with high copper content. He was also advised regarding screening the siblings for the possibility of Wilson disease. Consultation with gastroenterologists was also advised for future surveillance. He was also particularly advised endocrinologist consultation to identify a possible underlying endocrine disorder that resulted in hypoglycemia leading to the manifestation and diagnosis of Wilson disease.

DISCUSSION

The young man's instance mentioned above suggests that Wilson disease may have its first manifestation as an endocrine problem. Wilson disease has been shown to produce hypoglycemia, however this only showed up in the latter stages of the illness, when overt hepatolenticular degeneration was also present in the clinical picture.[5] Notably, the absence of a typical clinical presentation of Wilson disease, together with a normal morphological image of the liver on ultrasound (USG), suggests that the symptoms reported in our patient manifested during the early stages of the disease. However, the presence of Kayser-Fleischer corneal ring and low plasma levels of ceruloplasmin indicate that it is indeed feasible to accurately diagnose the condition even in its early stages. The simultaneous occurrence of hypoglycemic regression and improvement in the patient's clinical state strongly indicates a connection between the patient's clinical condition and Wilson's illness. Furthermore, it rules out the possibility that the symptoms were caused by other concurrent disorders. The effectiveness of zinc preparations, which promote copper binding through metallothionein and hence decrease copper absorption in enterocytes, also suggests that endocrine symptoms may be reversible if medication is initiated early.[6]

The diversity of the clinical manifestation of Wilson disease makes it a differential diagnosis in various pathologies. Rare manifestations like hypoglycemia, galactorrhea, and menstrual abnormalities may lead to the diagnosis of underlying endocrine disorders like insulinoma and prolactinoma due to overt hepatolenticular degeneration, ultimately leading to the diagnosis of Wilson's disease.[7] Hypopituitarism was presented as a rare endocrine complication of Wilson disease who presented with nausea, fatigue and writer's cramp and treatment with chelation therapy resulting in symptoms improvement.[8]

In our case, we observed Whipple's triad, but the only differences compared to the clinical picture of insulinoma were the age of the patient and lack of weight gain. Thus, the case report presented herein indicates that this triad is not pathognomic for insulinoma. Due to limitations in the diagnostic workup, either on the part of the available testing facility or the non-affordability of the patient, a specific endocrine disorder was not identified.

CONCLUSION

Wilson disease is a commonly encountered disease in medical clinics. It is mostly considered a hepatic /neurological disease. Contrary to this Wilson’s disease is a multisystem disease effecting multiple organ system including, kidneys, endocrine system and musculoskeletal system. Awareness of these manifestations of Wilson’s disease can lead to improved diagnosis and improve patient management.

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Soban Khan; concept, case management, manuscript writing
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Ahmed Farhan; case management, manuscript revision
Shajee Siddique; case management, manuscript revision
All the authors have approved the final version of the article and agree to be accountable for all aspects of the work.