VOLUME - 11, ISSUE - 10, OCTOBER - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

General Medicine

LIVING WITH THE COPPERS - A RARE CASE OF WILSON'S DISEASE

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ABSTRACT Wilson's disease is a rare metabolic disorder characterized by accumulation of copper in various organs. A wide range of clinical manifestations are known to occur involving mainly the hepatobiliary and central nervous system. We encountered this rare case in a 23 year old female patient who presented with cirrhosis of liver. After extensive workup, she was diagnosed with Wilson's disease. Often, a high index of suspicion is required to make a diagnosis of this disease in suspected cases presenting with cirrhosis of liver with unknown aetiology. In this case report we aim to review the clinical presentation of Wilson's disease with special emphasis on its diagnosis and prognosis.

KEYWORDS : Wilson's disease, Liver cirrhosis, Liver transplantation

INTRODUCTION

Wilson's disease, also known as hepatolenticular degeneration, is a disorder of copper metabolism with autosomal recessive inheritance. It is characterized by deficient incorporation of copper into ceruloplasmin and decreased biliary copper excretion, leading to over accumulation of copper in the body, especially in the brain, liver, kidney and cornea. This excessive deposition of copper in the body results in a range of clinical presentations, such as liver dysfunction, neurological disturbance and/or other derangements. [1][2]It is due to mutations in the gene ATP7B. The disease was named after a British neurologist, Samuel Alexander Kinnier Wilson (1878–1937). He described the condition first in 1912. In most populations the frequency of Wilson's disease is about 1 in 30,000-40,000. [3]

Case Report

A 23 year old woman born out of a non-consanguineous marriage presented with history of yellowish discoloration of sclera & skin since 6 months, swelling of lower limbs since 2 months and passing high coloured urine and stools since 1 month. These symptoms were progressive in nature. Patient also gave a history of vomiting since 5 days, which was non-projectile and non-bilious.

No history of jaundice noted in the past or history suggestive of chronic liver disease such as hematemesis, pruritus, abdominal distention. There was no history of similar complaints in the family.

On examination, she was moderately built and nourished, conscious and cooperative for examination. Her vitals were within the normal range and stable. Although the patient had icterus and bilateral pitting pedal oedema, she had no other stigmata of chronic liver disease. Abdominal examination did not reveal any evidence of free fluid or splenomegaly. Liver was not palpable. Examination of other systems appeared normal. On slit lamp examination, Kayser-Fleischer rings were noted bilaterally (Figure 1). She did not have dysarthria, rigidity, exaggerated DTR'S or involuntary movements.

Her blood investigations revealed haemoglobin of 6.9 g/dL and platelet count of 1 L/cumm. LFT showed serum bilirubin (T) of 23.6 mg/dL; (D) 18 mg/dL; AST- 109 U/L; ALT- 55U/L; ALP-230 U/L and albumin was 1.5 mg%. Her Thyroid function tests and chest X-ray were normal.

Abdominal ultrasonography revealed features of chronic liver parenchymal disease & splenomegaly. Upper GI endoscopy showed grade 1 small oesophageal varix and mild portal hypertensive gastropathy (Figure 2,3). Her serum ceruloplasmin level was 0.17 g/L (normal 0.2 to 0.6 g/L) and 24 hr urinary copper excretion was 93μg (normal, 15 to 60 μg/day) Diagnosis of Wilson's disease was made in this young lady using Leipzig criteria[4] with a score of 4, with the presence of Kayser-Fleisher rings, low serum ceruloplasmin & increased 24 hr urinary copper excretion. She was treated with chelating agents such as D-Pencillamine and Zinc. In view of Nazer prognostic index being 9, she was referred for liver transplantation.

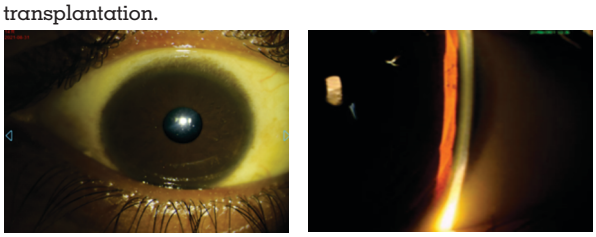

Figure 1: On slit lamp examination - Kayser-Fleisher ring present

Endoscopy findings

Figure 2 : Grade 1 esophageal varices

Figure 3 : Mild Portal Hypertensive Gastropathy

Table 1: Leipzig diagnostic criteria for Wilson disease

Leipzig diagnostic criteria for Wilson disease		
Clinical/laboratory findings		Points
Kayser-Fleisher ring	Present	2
	Absent	0
Neurological symptoms /MRI findings	Severe	2
	Mild	1
	Absent	0
Serum Ceruloplasmin (g/L)	<0.1	
	0.1-0.2	
	Normal >0.2	
24 hour urinary copper (normal, 15 to 60 μg/day)	Normal	0
	1-2x ULN	1
	>2x ULN	2
	Normal but >5x ULN after D-pencillamine	2
Coombs-negative haemolytic anaemia	Present	1
	Absent	0
Total liver copper (μmol/g)	>5x ULN (>4 μmol/g)	2
	0.8-4 μmol/g	1
	<0.8 μmol/g	-1
	Rhodamine positive granules	1
Mutation analysis	Present on both chromosomes	4
	Present on one chromosome	1
	Absent	0
Total score	Diagnosis established	4 or more
	Diagnosis possible	3
	Diagnosis unlikely	2 or less

DISCUSSION

Patients with Wilson's disease usually present with either Hepatic or Neuropsychiatric manifestations. Usually symptoms appear between the ages of 6 and 20 years. Hepatic manifestations include chronic active hepatitis, fulminant hepatic failure, cirrhosis, portal hypertension, ascites, and hepatocellular carcinoma. Neuropsychiatric manifestations include Parkinson features, ataxia, dystonia, seizures, migraine, frontal, memory loss, depression, anxiety and psychosis. Renal, Cardiac, Endocrinal abnormalities are also reported. [5]

Once diagnosis is established with low serum ceruloplasmin & increased 24 hr urinary copper excretion, the patient needs to be educated regarding compliance, long-term medications & follow-up. [6]

However, for patients presenting with hepatic decompensation, the initial step in evaluation is to establish the disease severity, which is calculated using Nazer prognostic index. Immediate liver transplantation should be considered for patients with scores >9. Clinical judgment is required for patients with scores between 7 and 9, in deciding whether to recommend medical therapy or transplantation. Patients can usually be managed with medical therapy if the scores are<7. [7]

Table 2 : Prognostic Index of Nazer

Measurements	Normal	Score in points				
		0	1	2	3	4
Serum Bilirubin	0.2-1.2 mg/dl	<5.8	5.8-8.8	8.8-11.7	11.7-17.5	>17.5
Serum AST	10-35 U/L	<100	101-150	151-200	201-300	>300
Prolongation of PT(s)		<4	4-8	9-12	13-20	>20

CONCLUSION

Wilson's disease is an extremely rare metabolic disorder. As the diagnosis can often be missed, a high index of suspicion is required in cases presenting with cirrhosis of liver with unknown aetiology and/or with neurologic, hematologic and ophthalmic manifestations. Early diagnosis and prognostication of the disease is of utmost importance as it helps to decide whether the patient requires medical therapy or liver transplantation. An overview of the diagnostic criteria and prognostic index used in this patient has been discussed here.

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