

Challenging diagnosis of Wilson's disease: A case report

Valeed Bin Mansoor, Saad Yunus Khan, Muhammad Arsalan Khan, Shafat Khatoon, Muhammad Arqam Miraj, Fibhaa Syed, Mohammad Ali Arif

Abstract

Wilson's disease is a rare inherited disorder of copper metabolism. If left untreated, it can turn into a multi systemic disease with copper deposition in the liver, brain, and other tissues. Diagnosis of Wilson's is delayed in Pakistan by many years on average due to variable presentations. In adolescents, the initial signs are more likely to be neuropsychiatric. Here we present a case of Wilson's disease that presented initially with hepatic symptoms and did not have signs specific to the disease such as Kayser-Fleischer rings. Our case was diagnosed to be Wilson's Disease only on further investigations and subsequently the patient was treated with chelation therapy using D-Penicillamine. Wilson's Disease should be kept in mind as a differential diagnosis in adolescent patients that present with unexplained acute liver failure and cytopenias without any neurological symptoms, as a missed diagnosis can prove to be fatal.

Keywords: Wilson's Disease, copper toxicity; Kayser-Fleischer rings, diagnosis, family screening, clinical variability, anticopper therapy.

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Introduction

Wilson's disease is a rare inherited autosomal recessive disorder of copper metabolism which results in deposition of copper in the liver, brain, and other tissues, with a global prevalence of approximately 0.5 cases per 100,000 inhabitants.¹

The disease results from a deficiency or absence of the transporter protein, causing decreased biliary excretion of copper, and copper accumulation initially in the liver.²

In children, initial signs are most likely to be hepatic, while in adolescents, they tend to be neuropsychiatric. Although the mean age of onset of symptoms is between 20-30 years, however initial signs can occur at any age.^{3,4}

Department of General Medicine, Pakistan Institute of Medical Sciences, Islamabad, Pakistan.

Correspondence: Muhammad Arqam Miraj. e-mail: arqam234@gmail.com
ORCID ID. 0000-0003-0528-9694

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Many cases of Wilson's Disease go un-diagnosed for years due to its varied presentation and the consequences of a late or missed diagnosis can be fatal.

The hepatic presentation of Wilson's disease is seen more frequently in women worldwide, comprising 55%–60% of all cases.⁵ A study in Karachi suggests a higher prevalence of Wilson's disease in males in Pakistan.⁶

The typical sign of Kayser-Fleischer rings are only present in up to 50 % of the cases however they are highly specific for the disease.⁷ Even Serum Ceruloplasmin levels can appear normal in patients with Wilson's Disease.⁸

Therefore it is important to recognize Wilson's Disease early so that timely treatment can be provided, especially in patients presenting with liver disease of unknown origin.

We present a case with initial hepatic signs, thought to be having liver disease, but on further investigation, revealed to be a form of Wilson's Disease.

Case Report

First Admission: A 33 year old male patient with no previous comorbidities, presented to the A&E of Pakistan Institute of Medical Sciences, Islamabad, Pakistan with a low grade fever, diarrhoea persisting for 40 days and bleeding per rectum for 3 days, along with significant weight loss.

Professionally, he worked as a chef, and no significant family history was revealed at that time.

On presentation in the ER, the patient was vitally stable. Physical examination revealed a pale complexion with mild upper abdominal tenderness. Hepatospleno-megaly was present and gut sounds were audible. Digital rectal examination showed streaks of blood without any haemorrhoids or anal fissure. Rest of the systemic examination was unremarkable. Investigations revealed pancytopenia with macrocytosis, anisocytosis and poikilocytosis with minimally deranged LFTs; Bilirubin 1.7 mg/dl (Normal: 0.3-1.2mg/dl) and ALT 45 U/L (Normal: 4-42U/L). Albumin 2.7 g/dl (Normal: 3.5-5.5 g/dl) PT was 80 Seconds (Normal: 11 seconds) and aPTT was 50 seconds (Normal: 32 seconds).

Serum Vitamin B12 was low along with slightly raised LDH. HBsAg and Hep C antibody tests along with blood cultures were also negative.

An ultrasound of the abdomen was performed which showed borderline hepatomegaly and coarse texture with splenomegaly of 15 cm.

A CT Scan of the Abdomen and Pelvis showed splenomegaly with acalculous cholecystitis and mild free fluid in mesentery along with Caecal wall thickness.

The patient was managed conservatively. During his 6 day hospital stay, cytopenias improved, fever subsided while per rectal bleeding stopped. Colonoscopy and Bone Marrow Biopsy was planned but patient refused and left the ward against medical advice.

Second Admission: The patient presented 30 days later to the A&E in critical condition with severe icterus since the last one week, altered sensorium for 2 days and haematochezia. Examination revealed high grade fever with flapping tremors suggesting hepatic encephalopathy. The patient was admitted for further evaluation and management.

Investigations revealed pancytopenia with markedly deranged LFTs. The patient had a Child Pugh Score 13 (Class C).

On further investigation of family history, which was previously not provided, it was revealed that the patient's father and younger brother had died of liver cirrhosis. This fact had been concealed by the patient during the initial visit.

Due to suspicion of Wilson's Disease, relevant investigations were initiated. Slit lamp examination showed dilated pupils which were reactive to light. No Kayser Fleischer ring were observed.

Serum Ceruloplasmin	19	Normal range: 20-60 mg/dL
24-hr urinary copper excretion	153	Normal range: 10-30µg

The patient was finally diagnosed as a case of Wilson's Disease according to Leipzig Criteria with a score of 4; Serum ceruloplasmin <0.1 g/L and >2x upper limit of normal 24-hr urinary copper excretion.⁹ Unfortunately Genetic testing could not be performed as it is not widely available in Pakistan.

The case was managed on lines of Decompensated Liver Disease (DCLD) with supportive transfusions and correction of coagulopathy. Chelation therapy with D-Penicillamine was started. During the stay, the patient's condition improved noticeably and showed a rise in haemoglobin level to an optimal range.

The Department of Gastroenterology was taken on board to evaluate the patient for liver transplantation and he was discharged with a referral to the Gambat Institute of Medical Sciences for liver transplant. The siblings of the patient were counselled to get screened for Wilson's Disease.

Informed consent was taken from the patient to publish his experiences in a case series. He was admitted and provided care in the Medicine Department of Pakistan Institute of Medical Sciences, Islamabad, Pakistan, from September 2022 – October 2022.

Discussion

Neurologic signs are thought to be the most common initial presentation in patients with Wilson's disease. This is supported by a case series from the Philippines, and neighbouring India.^{3,10}

However, our patient presented initially with hepatic symptoms including hepatomegaly, jaundice and abdominal pain, without any neurologic symptoms.

In a study done at a tertiary care hospital in Pakistan, it was reported that the most common presenting symptoms of Wilson's disease were hepatic (46.8%), followed by neurological (36.2%) and neuropsychiatric (17%) symptoms.^{6,11}

In European countries, more than 85% of patients have raised 24-hr urinary copper excretion. According to a study in a tertiary care hospital in Pakistan, this is found in less than 50% of patients. Our patient had raised 24 Hr Urinary copper excretion and reduced serum ceruloplasmin. This has been reported normal in up to 15% patients with Wilson's Disease by a tertiary care hospital in Pakistan.⁶

Our patient displayed elevated 24-hour urinary copper excretion. Simultaneously, our patient demonstrated reduced serum ceruloplasmin levels. Nonetheless, it is noteworthy that serum ceruloplasmin has been documented to be within the normal range in up to 15% of patients with Wilson's Disease who present at tertiary care hospitals in Pakistan.⁶

The diagnosis of Wilson's Disease is further complicated by the fact that in Pakistan, Kayser Fleischer (KF) rings are absent in over 70% of patients who initially present with hepatic symptoms, while they are present in nearly all patients who initially present with neurological symptoms.⁶ In our case the patient did not have KF rings.

Sometimes, the criteria prescribed are not enough to detect the disease which can lead to delayed diagnosis and treatment, that can prove to be fatal.

Acute Liver Failure can be a possible initial presentation of Wilson's Disease. It occurs initially in 5% of cases and is more frequent in women and thus should be considered in any patient with unexplained Acute Liver Failure.^{8,9}

The main reasons Wilson's Disease had been overlooked initially in our case were lack of classic history of liver disease, along with concealing of family history by the patient, per rectal bleeding and encephalopathy, which indicated a differential diagnosis in another direction.

Conclusion

In Pakistan, Wilson's Disease remain undiagnosed for years. A societal stigma is attached to the condition which leads many patients to conceal family history, creating further difficulty in the diagnosis.

A high percentage of Wilson's Disease patients in Pakistan present initially with hepatic symptoms.

Primary care level screening must be ensured with cheap screening tests to enable diagnosis at earlier stage and prevent fatal outcomes.

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Author Contribution:

UA: Literature search, data collection and drafting.

NC: Supervision, study design and concept, drafting