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Genetic Copper Overload Leading to Rapid Hepatic Decompensation: A Case Report on Wilson's Disease in a 21-Year-Old

Mrs. Subadradevi J[1]*, Mr. Shiv Sundar S[2], Mr. Vaikunda John J[3], Dr. Lydia James P[4]

[1] M Pharm, Assistant Professor, Department of Pharmacy Practice, PSG College of Pharmacy, Coimbatore, India.
[2]Pharm D, Department of Pharmacy Practice, PSG College of Pharmacy, Coimbatore, India.
[3]Pharm D, Department of Pharmacy Practice, PSG College of Pharmacy, Coimbatore, India.
[4] Clinical Pharmacist, Department of Gastroenterology, PSG Hospitals, Coimbatore, India.

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ABSTRACT:

Wilson Disease (WD) is an autosomal recessive disorder caused by mutations in the *ATP7B* gene, resulting in defective copper metabolism. Impaired copper excretion leads to accumulation in the liver, brain, and other organs, causing a wide range of clinical symptoms. This case report discusses a 21-year-old female who presented with signs of acute decompensated chronic liver disease, including jaundice, ascites, pedal edema, anorexia, and fatigue. She had no history of alcohol intake or hepatotoxic drug use. Laboratory evaluation showed anemia, thrombocytopenia, hypoalbuminemia, elevated bilirubin and transaminases, INR >2.0, low ceruloplasmin (6.29 mg/dL), and markedly elevated 24-hour urinary copper (2360 µg/day). Genetic testing confirmed *ATP7B* mutation. Kayser-Fleischer rings were noted on slit lamp examination. Imaging revealed chronic liver disease, ascites, and splenomegaly. Upper GI endoscopy showed grade I esophageal varices and portal hypertensive gastropathy. Her New Wilson's Index (15) and Nazer Index (8) indicated a poor prognosis requiring liver transplantation. She was managed with antibiotics, diuretics, albumin, zinc, N-acetylcysteine, nutritional support, and later started on trientine. On readmission a week later, she had worsening ascites and spontaneous bacterial peritonitis due to polymicrobial infection, requiring escalation of antibiotics. Despite therapy, liver function continued to decline. This case highlights the importance of early diagnosis, use of prognostic indices, and prompt initiation of chelation therapy in WD. Liver transplantation remains the definitive treatment in advanced disease.

Keywords: ATP7B Protein, Liver Transplantation, Kayser-Fleischer Ring, Copper Overload.

1. INTRODUCTION:

Wilson Disease (WD) is an autosomal recessive disorder caused by mutations in the ATP7B gene, leading to impaired copper metabolism and accumulation in various organs, primarily the liver and brain.[1] The ATP7B gene encodes a copper-transporting ATPase responsible for incorporating copper into ceruloplasmin and facilitating its excretion into bile. Mutations in ATP7B disrupt this process, resulting in copper accumulation and subsequent tissue damage.[2] The pathological accumulation of copper induces oxidative stress by generating reactive oxygen species, disrupting mitochondrial function, and altering gene expression, culminating in hepatocellular injury and neurotoxicity.[3] Clinically, WD presents with a spectrum of hepatic manifestations, ranging from asymptomatic hepatomegaly to fulminant hepatic failure, and neurological symptoms, including tremors, dysarthria, and movement disorders. Psychiatric symptoms, such as depression, personality changes, and cognitive decline, are also common and may precede hepatic or neurological signs. Ophthalmologic findings, notably Kayser-Fleischer rings, result from copper deposition in Descemet's membrane and are a key diagnostic feature. Renal involvement may manifest as tubular dysfunction, leading to aminoaciduria, hypercalciuria, and nephrolithiasis. Cardiac complications, including arrhythmias and cardiomyopathy, have been reported due to myocardial copper accumulation. Diagnosis of WD involves a combination of clinical assessment, biochemical tests (serum ceruloplasmin, 24-hour urinary copper excretion), ophthalmologic examination, and genetic testing for ATP7B mutations. Magnetic resonance imaging (MRI) of the brain often reveals characteristic findings, such as the 'face of the giant panda' sign in the midbrain.[8] Liver biopsy can provide a definitive diagnosis when copper quantification exceeds threshold levels.[9] Treatment strategies focus on reducing copper accumulation using chelating agents like penicillamine or trientine, and zinc therapy to inhibit copper absorption.[10] Emerging therapies, such as gene therapy with adeno-associated virus vectors delivering functional ATP7B, are under investigation and show promise in preclinical studies.[11] Long-term follow-up and adherence to therapy are essential for preventing irreversible organ damage.[12]

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2. CASE SUMMARY:

A 21-year-old female on first admission presented with signs of acute decompensation of chronic liver disease, including jaundice, abdominal distension, bilateral pedal edema, anorexia, and profound fatigue. With no history of alcohol use, hepatotoxic drug intake, or previously diagnosed liver disease and her workup revealed advanced hepatic dysfunction (**Table1).**

Laboratory investigations demonstrated normocytic normochromic anemia, thrombocytopenia, hypoalbuminemia, low ceruloplasmin (6.29 mg/dL) and Serum copper (58µg/dL) (**Figure 1)**, elevated bilirubin and transaminases, ATP7B mutation and INR >2.0 and markedly elevated 24-hour urinary copper (2360 µg/day) (**Figure 2)**. Slit lamp examination showed Kayser-Fleischer ring positive (**Figure 3)**. The Upper GI Endoscopy reveals grade I esophageal varices, lax lower esophageal sphincter, Hill grade III changes, and mild portal hypertensive gastropathy. The CT Whole Abdomen shows chronic liver parenchymal disease, moderate splenomegaly and ascites. Her New Wilson's Index (15) and Nazer Index (8) indicated a poor prognosis necessitating liver transplantation. She was managed with IV antibiotics, diuretics, albumin, zinc, N-acetylcysteine, nutritional support, and later started on trientine HCl after confirmation of WD. Her second admission after a week of discharge revealed worsening ascites and spontaneous bacterial peritonitis with polymicrobial growth, requiring escalation of antibiotics. Further investigation showed progressive decline in hepatic function.

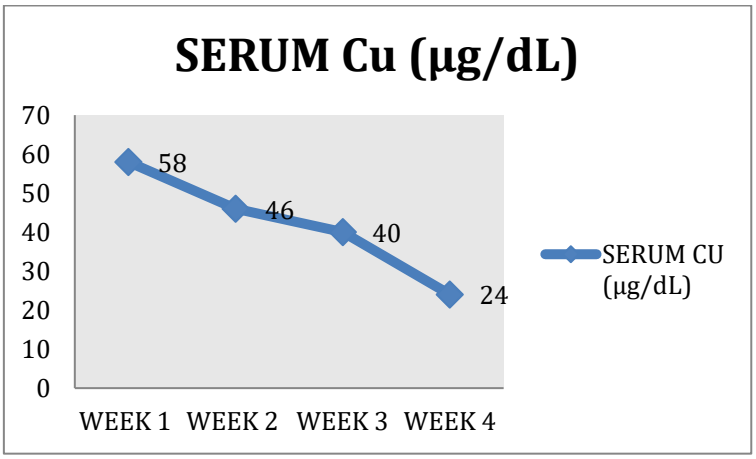

Figure 1: Serum Cu (µg/dL)

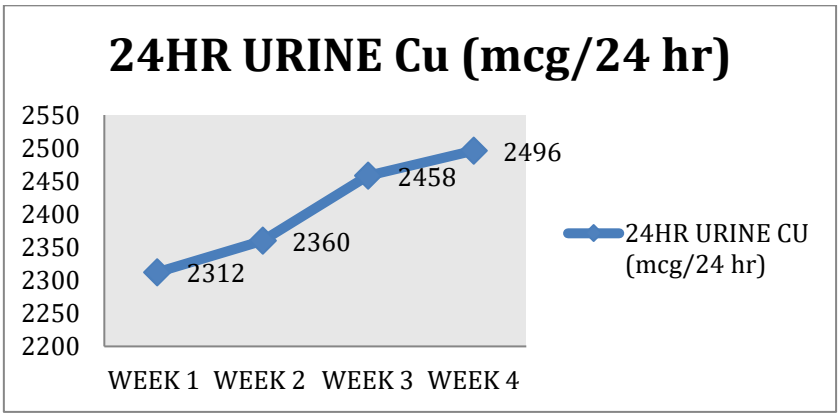

Figure 2: 24hr Urine Cu (mcg/24 hr)

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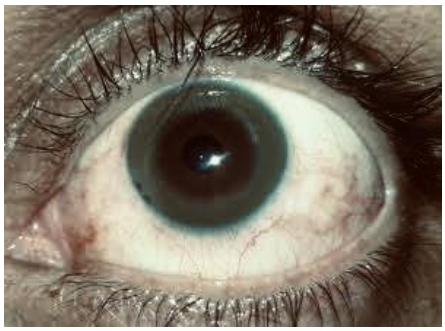

Figure 3: Kayser-Fleischer ring

Table 1 : weekly lab values timeline

	WEEK 1 (INITIAL ADMISSION)	WEEK 2	WEEK 3 (RE-ADMISSION)	WEEK 4
CBC				
RBC (10^6/µL)	3.06	2.89	2.9	3
HB (g/dL)	8.4	8.6	9	9
WBC (10^3/µL)	6.3	11.2	4.2	4.1
PCV (%)	25.4	26.3	26	27.4
PLAT (10^3/µL)	116	111	55	90
PT TEST	26.1	24	27	24
RENAL FUNCTION TEST				
CREATININE (mg/dL)	0.65	0.58	0.5	0.6
UREA (mg/dL)	6	11	10	12
NA (mEq/L)	132	132	134	136
K (mEq/L)	2.96	3.2	3.1	3.7
LIVER FUNCTION TEST				
TOTAL BILIRUBIN (mg/dL)	6.4	8	6.2	1.9
DIRECT BILIRUBIN (mg/dL)	2.6	4.6	2.6	1.3
INDIRECT BILIRUBIN (mg/dL)	3.8	3.4	3.6	0.6
SGPT (U/L)	203	196	157	65
SGOT (U/L)	717	502	429	135
ALBUMIN (g/dL)	2.5	2.1	2.4	2.5
GLOBULIN (g/dL)	4.5	4.4	3.6	4.2
GGT (U/L)	127	95	84	41
COPPER RELATED TEST				
24HR URINE CU (mcg/24 hr)	2312	2360	2458	2496
SERUM CU (µg/dL)	58	46	40	24
CERULOPLASMIN (mg/dL)	7	11	9	8
OTHER TEST				
FIBRINOGEN TEST (mg/dL)	-	-	61	-
D DIMER (ng/mL)	-	-	4.57	-

3.1 MULTIDISCIPLINARY EVALUATION FOR TRANSPLANTATION:

Given the progressive decline in her liver function and high prognostic scores, she was evaluated by a multidisciplinary transplant team:

Cardiology: Electrocardiogram and echocardiogram were normal with preserved LV function (EF: 63%), no ischemia on Tread Mill Test.

Pulmonology: Pulse oximetry (98%) and Chest XRay were normal. ABG showed mild respiratory alkalosis.

Nephrology & Neurology: USG Doppler and CT brain were normal. No contraindications from nephrology or neurology.

ENT & Dental: No active infection. Dental scaling completed.

Other Evaluations:

- **Psychiatry:** No contraindications.
- **ID Specialist:** Vaccination complete.
- **Dermatology:** No skin lesions at surgical site.
- **Anesthesia:** Patient cleared for surgery.

3.2 GENETIC COUNSELLING AND FAMILY PLANNING:

Recognizing the hereditary nature of WD, the family was counseled on genetic transmission risks. Testing was advised for her siblings, and her husband was advised to postpone conception plans until further genetic evaluation was completed. The family expressed full consent for proceeding with transplantation; her mother was evaluated and accepted as a living donor, with imaging confirming suitable liver volume and anatomy for donor hepatectomy.

4. DISCUSSION:

WD is a rare autosomal recessive disorder of copper metabolism that often presents with hepatic, neurologic, or psychiatric manifestations. In this case, a 21-year-old female presented with signs of advanced liver failure including jaundice, ascites, coagulopathy, and pedal edema. The absence of prior liver disease made the diagnosis challenging; however, classic findings such as low serum ceruloplasmin, markedly elevated 24-hour urinary copper, and Kayser-Fleischer rings led to the diagnosis. The patient's rapid clinical deterioration, elevated Nazer and New Wilson's Index scores, and signs of intravascular hemolysis (e.g., DAT positivity and low haptoglobin) are consistent with acute decompensated hepatic WD, a condition known to carry a poor prognosis without transplantation.

Despite the initiation of chelation therapy with trientine and zinc, the patient's worsening liver function and the onset of spontaneous bacterial peritonitis emphasized the aggressive course of the disease. This case highlights the importance of maintaining a high index of suspicion for WD in young adults with unexplained liver dysfunction, even in the absence of neurological symptoms. Early diagnosis through targeted investigations and timely initiation of disease-specific therapy are essential to prevent irreversible damage and improve outcomes.

5. CONCLUSION:

This case underscores the aggressive nature of WD when presenting predominantly as advanced hepatic decompensation. The rapid progression to liver failure—evidenced by marked biochemical derangements, coagulopathy, and hemolysis—highlights the critical importance of early, targeted diagnostic workup in young adults with unexplained liver dysfunction. Despite the initiation of

chelation therapy with trientine and zinc, the severity of the hepatic injury necessitated urgent liver transplantation, which remains the definitive treatment in cases where conventional therapy fails to halt progression.

Ultimately, this report illustrates that a high index of clinical suspicion, prompt diagnosis, and early intervention are paramount in improving outcomes for patients with WD. The case serves as a reminder that timely escalation to liver transplantation can be lifesaving in the context of fulminant hepatic failure and reinforces the need for continuous research into more effective early diagnostic and therapeutic strategies for this complex disorder.

6. ACKNOWLEDGEMENT:

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7. DECLARATIONS

Funding: No funding sources.

Conflict of interest: The authors declare that there is no conflict of interest.

Ethical approval: This study was approved by the Institutional Ethics Committee of PSGIMS&R.

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	Corresponding Author:Mrs. Subadradevi J, M Pharm, Assistant professor,Department of Pharmacy Practice, PSG College of Pharmacy,Coimbatore- 641004.
	Dr. Shiv Sundar S, Pharm D Department of Pharmacy Practice, PSG College of Pharmacy, Coimbatore- 641004.
	Dr. Vaikunda John J, Pharm D, Department of Pharmacy Practice, PSG College of Pharmacy, Coimbatore- 641004.
	Dr. Lydia James P, Pharm D, Clinical Pharmacist,Department of Gastroenterology, PSG Hospitals,Coimbatore- 641004.

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