

## Case Report

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# Wilson's Disease Presenting with Severe Anaemia and Bleeding Manifestation: A Case Report

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### Abstract

*Wilson's disease is an inherited disorder in which defective biliary excretion of copper leads to its accumulation, particularly in liver and brain. Presentation can vary, but the key features of Wilson's disease are hepatic and neuropsychiatric disturbances, Kayser–Fleischer rings of the cornea, acute episodes of hemolysis and sometimes renal impairment. Here, we report a case of Wilson's disease in a young female having severe anaemia without other evidence of hepatic and neuropsychiatric manifestation.*

**Key words:** Wilson's disease, anemia.

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### Introduction

Wilson's disease (WD) is an autosomal recessive disorder affecting copper transport; it results in the accumulation of copper in the liver, brain and other organs. WD is the most common inherited liver disease.<sup>1</sup> An impairment in biliary excretion process leads to copper accumulation in the liver, which progressively damages the liver, leading to cirrhosis. ATP7B gene was identified as the defective gene causing the disease by three independent teams in 1993. ATP7B protein is a membrane bound copper transporting P-type ATPase which transports copper out of the hepatocytes into bile for incorporation of copper into caeruloplasmin, which is then secreted into the blood stream.<sup>2</sup> Since effective treatment is available for this disease, early and correct diagnosis is very important. Here, we report a case of WD presenting with severe anemia.

### Case Report

A 24-year-old college student presented with recurrent leg swelling for 1 year, severe generalized weakness

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for 4 months, high grade fever, vomiting, oliguria for 5 days, subconjunctival hemorrhage and excessive per-vaginal bleeding for 2 days. She had no history of joint pain or oral ulcer. She did not have history of psychosis or any other neurological symptom. There was no consanguinity of marriage of her parents. Her two sisters were in good health.

On physical examination, patient was severely anemic and there was bilateral subconjunctival hemorrhage, mild edema, hepatosplenomegaly and mild ascites. Kayser-Fleisher (KF) ring was absent on slit-lamp examination. On investigation blood picture showed Hb-6.5 mg/dl, ESR-55 mm in first hour. WBC-3000/cm<sup>3</sup>, platelet-60,000/cm<sup>3</sup>, peripheral blood film showed pancytopenia. C-reactive protein was 9.69 mg/L; direct and indirect Comb's tests were negative, reticulocyte count was 1.2%.

Her serum bilirubin was 1.7 mg/dl, serum alanine aminotransferase-49 U/L, prothrombin time-23 sec, serum albumin was 17 gm/L. She had lower normal serum ceruloplasmin (23 mg/dl)<sup>20</sup> and high urinary copper levels (1416 gm/dl) ret <100). Serum uric acid-14.21 mg/dl, serum creatinine was 2.3 mg/dl, urine routine examination was normal.

Ultrasonography showed coarse hepatic parenchyma, ascites, dilated splenic and portal veins, endoscopy revealed congestive gastropathy, anti-nuclear antibody was negative. She was tested for hepatitis viruses namely HBsAg, anti-HBc (total), anti-HCV that all were negative; ascitic fluid was transudative (SAAG was 12 gm/L) with normal white cell and differential count.

Depending up on serum ceruloplasmin, urinary copper, ultrasonography, ascitic fluid study and endoscopy reports, she was diagnosed as a case of WD.

The patient was put on copper chelation therapy with oral penicillamine and other supportive treatment. Penicillamine was initially started at 500 mg daily in two divided doses which was gradually raised to 1500 mg daily also in two divided doses. Her blood count, urine routine examination and liver function tests were routinely done and neurological functions carefully monitored. At the same time, dietary modification was done to avoid copper containing diet. Anaemia was corrected with red cell transfusion and hypoalbuminemia was corrected with albumin infusion. Oral spironolactone was given for ascites.

### Discussion

WD is a well-recognized but less frequently encountered disease entity in our clinical practice. However, there are several interesting aspects of the present case that made it worth reporting. The patient initially presented with clinical and laboratory features of anemia without stigmata of liver disease or neurological features. KF ring was absent and serum caeruloplasmin was normal. WD occurs worldwide with an average prevalence of 30 affected individuals per million population.<sup>1</sup> It can present clinically as liver disease, as a progressive neurological disorder (hepatic dysfunction being less apparent or occasionally absent), or as psychiatric illness.<sup>1</sup> WD presents with liver disease more often in children and younger adults than in older adults. Symptoms at any age are frequently nonspecific.<sup>2</sup>

There is no single specific test for the diagnosis of WD. Low serum caeruloplasmin (<20 mg/dL), high 24-h urine copper level (>100µg), high hepatic copper content (>250 µg/g of dry liver) and KF rings were found in 96%, 86%, 88% and 73% cases respectively. A combination of any 2 of the above 4 laboratory findings forms a strong support for the diagnosis of WD<sup>3</sup>, but serum caeruloplasmin was normal in our case as the patient had fever and high level of ESR and CRP which was most likely due to viral fever which subsided with supportive treatment only 2 days after hospital admission. KF rings represent deposition of copper in Descemet's membrane of the cornea. A slit-lamp examination by an experienced observer is required to identify KF rings in most patients. They are not entirely specific for WD, because they may be found in patients with chronic cholestatic diseases.<sup>4</sup> Urinary copper is a reflection of free copper in the circulation. Measuring urine copper is useful in diagnosis of WD and can be

used as a measure of compliance to therapy. Though dry weight estimation of hepatic copper is the gold standard to diagnose WD, low values due to sampling variability can occur in significant hepatic fibrosis and cirrhosis due to WD.<sup>2</sup> High values can occur in chronic cholestatic liver disorders. Moreover, the test is not available in our settings.

Acute WD may be accompanied by Coomb's test negative haemolytic anaemia due to excessive lysis of red blood cells following sudden rise in copper in blood. But, our patient had no features of haemolysis in PBF rather than pancytopenia. So, it may be due to hypersplenism.<sup>3</sup> Dietary restriction of copper is insufficient as sole therapy in WD. It is advisable to reduce consumption of food high in copper content, like shellfish, nuts, chocolate, mushrooms and organ meats.<sup>3</sup> Aim of treatment in WD is to achieve normal copper levels in the body in the shortest possible time and to maintain this. Among drugs used to treat WD penicillamine and trientine act as chelator, while oral zinc acetate reduce absorption. The commonly recommended regime is initial treatment with copper chelators like penicillamine or trientine to normalize copper levels in the body. After adequate treatment with a chelator, stable patients may be continued on a lower dosage of the chelating agents or shifted to treatment with zinc. Treatment needs to be continued lifelong. Measuring 24-hour urine copper excretion while on treatment is useful to monitor compliance. Liver transplantation is the ultimate treatment for decompensated cirrhosis with WD.<sup>6</sup> So, WD should be suspected in any individual with liver dysfunction of uncertain cause at any age and high degree of clinical suspicion is needed for the diagnosis of WD.

**Conflict of interest:** None

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