# Wilson's Disease Presenting with Severe Hemolytic Anemia

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Wilson' s disease or progressive hepatolenticular degeneration, originally described by Wilson in 1912, is a disorder of copper metabolism generally characterized by hepatic and / or neurological symptoms. Other findings include Kayser-Fleischer rings, hypoceruloplasminemia, hypocupremia, and hypercupriuria. Initial hematological manifestations are rare (1-3). We herein report a case of Wilson' s disease presented with severe hemolytic anemia as an uncommon initial manifestation.

## Case report

A 9 year-old girl was admitted to hospital presenting with abdominal distention, fatigue and pallor for two weeks. In family history, the parents were cousins and the patient' s sister died of cirrhosis of unknown aetiology at the age of 4. Three other siblings were normal. On the physical examination, the patient was pale and mildly icteric and prominent hepatomegaly was present. The vital signs were within normal levels. Complete blood count showed decreased hemoglobin concentration (3.6g/dl), increased white blood cell count (55000/mm$^{3)}$, normal platelet count (349000/mm$^3$) and increased mean corpuscular volume (137fl). The blood smear revealed normochromic and normocytic red blood cells, increased normoblasts (4%) and increased reticulocyte count. Urine analysis was normal. Direct Coombs test was negative. Serum transaminases and bilirubin levels were mildly elevated (AST 67 IU/l, ALT 75 IU/l, total bilirubin 3.2 mg/dl, indirect bilirubin 3.1 mg/dl). Serum LDH was elevated (897 IU/l) and haptoglobulin concentration was low (6 mg/dl). On further investigation, the level of serum ceruloplasmin was found to be low (2 mg/dl) and urinary copper excretion was markedly elevated (338 micrograms per day). Serum copper level was normal (89 micrograms/dl). Slit-lamp examination of both corneas revealed obvious Kayser-Fleischer rings. Liver biopsy showed features of chronic active hepatitis (Fig. 1). The biochemical examination of liver tissue showed an elevated copper concentration of 690 micrograms/gm dry weight. These findings suggested that the patient's hemolytic anemia was due to the abnormal copper metabolism associated with Wilson' s disease. After an initial transfusion the patient has been treated so far with oral D-penicillamine ( 1 g per day) and oral zinc sulphate (150 mg of elemental zinc daily). Since the initial diagnosis, the patient has been very well for two years with no evidence of symptoms related to Wilson's disease.

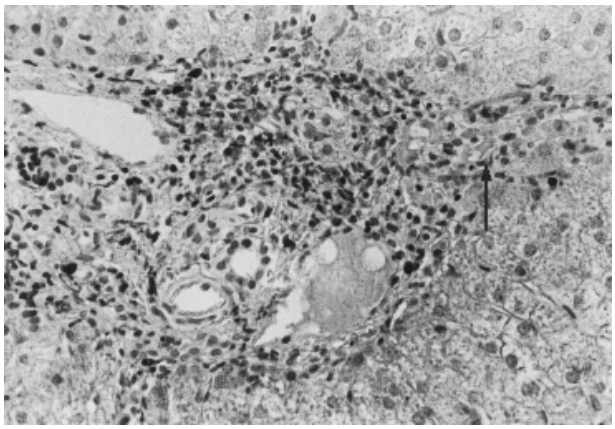

Figure 1. Histologic appearance of chronic active hepatitis. Mononuclear inflammatory infiltrate in the portal tract and piecemeal necrosis (black arrow). H&E staining, 100x.

## Discussion

Wilson's disease is an autosomal recessive disorder and occurs between the ages of 6 to 60 years. Although the underlying basic defect begins at birth, patients with Wilson' s disease present with symptoms during the second or third decade of life. The clinical findings are characterized by toxic accumulation of copper in the liver and subsequently in the brain and other organs (4).

The diagnosis of Wilson's disease is frequently overlooked. Non-specific symptoms and multisystem involvement may mimic other disease states, such as neurological or psychiatric disorders, and hemolytic anemia. The initial clinical manifestations are of hepatic origin in 42% of cases, neurological in 34%, psychiatric in 10%, hematological and endocrinological in 12%, and renal in 1%. Approximately 25% of patients have evidence of involvement of more than one organ at presentation (5).

Wilson's disease in children has several characteristics distinct from those seen in adults. In children, hepatic manifestations predominate. Manifestations of liver disease are greatly variable and mimic all forms of liver disease. It is common for the hepatic manifestations to precede neurological manifestations by years (6).

Although the specific underlying biochemical defect remains to be defined, specific therapy is available and is

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usually successful. Early recognition of this condition is very important, because early diagnosis and treatment prevent brain and liver damage (7).

We report here a patient presenting with severe hemolytic anemia as an initial manifestation of Wilson' s disease. Further investigations revealed features of Wilson's disease including Kayser-Fleischer rings, hypoceruloplasminemia, hypercupriuria, elevated hepatic copper content. The diagnosis of Wilson' s disease in the present patient might suggest that, due to its inheritance pattern, her sister might have been died of the same disease.

Coombs-negative hemolytic anemia of unknown etiology, a hematological manifestation of Wilson's disease, may be the initial manifestation of the disease in 10% to 15% of cases . Severe hemolysis may also be detected in the fulminant hepatitis type of presentation of Wilson' s disease. This is probably due to rapid release of copper from necrotic hepatocytes and subsequently oxidative damage to erythrocytes by the excessive copper (7-9). This hypothesis might explain the occurrence of hemolytic anemia in the present patient. In addition, the histological and laboratory findings and hepatosplenomegaly might be related to hepatocytic injury possibly due to the excessive copper.

To conclude, the present report underscores the importance of considering Wilson's disease as a cause of hemolytic anemia of unknown aetiology in children. The treatment in the early stages is very successful, and early recognition of the disease may prevent further organ injury and the requirement of liver transplantation.

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