Case Report

Haemolytic anaemia – Initial presentation of Wilson Disease

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Abstract:
Wilson disease is an autosomal recessive inborn error of copper metabolism characterized by toxic accumulation of copper in liver, brain, cornea and other tissues. It usually presents with hepatic dysfunction or neuropsychiatric manifestations. Hemolytic anemia is an uncommon presenting manifestation of Wilson disease. We present a case of a child who presented with hemolytic anemia and was subsequently diagnosed as Wilson disease.

Keywords: Hemolytic anemia, Wilson disease, first manifestation

Introduction
Wilson disease is an autosomal recessive inborn error of copper metabolism characterized by toxic accumulation of copper in liver, brain, cornea and other tissues. It usually presents with hepatic dysfunction or neuropsychiatric manifestations. Hemolytic anemia is an uncommon presenting manifestation of Wilson disease. We present a case of a child who presented with hemolytic anemia and was subsequently diagnosed as Wilson disease.

Case Report:
A six years old male child presented with history of jaundice since five days and acute onset of breathlessness for the past two days. There was no history of fever, abdominal pain or distension, vomiting, high coloured urine or bleeding manifestations. There was no past history of jaundice or blood transfusion. The child was very pale and icteric. He had signs of congestive cardiac failure in the form of facial puffiness, pedal edema, and raised jugular venous pressure. On abdominal examination, we found the liver to be enlarged; it was five centimetres below the costal margin and of firm consistency. The spleen was also enlarged; it was two centimetres below the costal margin. We also found shifting dullness and a hemic murmur in the patient. We did not detect any other clinical abnormalities. Based on the clinical examination, we made a provisional diagnosis of severe hemolytic anemia in congestive cardiac failure.

We then performed haematological and serological investigations in the patient. The haemoglobin level was 7.1 gm% and the total white blood cell count was 15,400/mm$^3$. The differential white blood cell was 40% polymorphonuclear cells, 38% lymphocytes, and 11% eosinophils. We did not detect any malarial parasite on examination of blood smears. The reticulocyte count was 17% (corrected reticulocyte count 8.5%). In addition, Coombs' test was negative and Glucose-6-Phosphate dehydrogenase level was normal.
We also did liver function tests in view of firm hepatomegaly. In these tests, total serum bilirubin was 14 mg% and the direct fraction was 4.4 mg%. Additionally, total proteins were 5.2 gm%, serum
albumin was 3 gm%, and aspartate aminotransferase was 107 IU. The prothrombin time was 27 seconds for a control of 14 seconds. We also found that the viral markers were negative for Hepatitis A, B, and E. Since, the child had firm hepatomegaly with deranged liver function and a Coombs’ negative hemolytic anemia, we investigated him further for Wilson disease.

We found a Kayser Fleischer ring on slit lamp examination. In addition, the patient also had a sunflower cataract (Figure 1). The serum ceruloplasmin was levels were very low - 9.17 mg/dl and the 24 hour urinary copper excretion was very high - 2463 micrograms in 24 hours. Based on the above investigations, we diagnosed Wilson disease in the patient. An upper gastrointestinal endoscopy also showed Grade 2 varices. We transfused packed red blood cells in the patient. After stabilisation, D-penicillamine treatment was started and oral zinc was subsequently started in the patient. We also supplemented the child with Vitamins A, D, E and K. Due to presence of oesophageal varices, we started the child on oral propranolol. We also vaccinated the child for Hepatitis A and B. The family screening for Wilson disease was normal.

The child has been on a regular follow up for the past three years. His liver function test parameters have become normal and there have been no further episodes of hemolytic anemia. Furthermore, prothrombin time has also become normal. The child is presently doing well on oral penicillamine and zinc therapy, and no side-effects have been reported so far.

**Discussion:**

Classic Wilson disease with hepatic involvement has been described as a patient with liver disease who is at least 5 years old, with decreased serum ceruloplasmin and detectable KF ring in the cornea. Although liver disease is the predominant presenting clinical manifestation in children, atypical presenting manifestations are known. Coombs’ negative hemolytic anemia can be one such initial presenting feature. In a Mayo series of 58 patients, only one patient had a hemolytic anemia like presentation. In another series of 17 cases by Guan and co-workers, two patients presented with hemolytic anemia. In a retrospective Brazilian study of 28 pediatric patients with Wilson’s disease, one presented with fulminant hepatitis with hemolytic anemia. In another study from Australia, the authors report their experience with Wilson’s disease patients over three decades in which one out of 30 patients presented with hemolysis as the initial presentation.

Hemolytic anemia in Wilson disease is Coombs’ negative and intravascular. The release of large quantities of inorganic copper from the liver into the bloodstream has been postulated as the cause. The exact mechanism is, however, not known. When the hepatic binding sites are saturated with copper, the excess copper is gradually released into circulation. In some patients, however, the release of copper into the bloodstream is sudden causing large amounts of copper being taken up by erythrocytes. Oxidative damage to the red cells occurs due to high intra-erythrocytic concentration of copper which results in acute intravascular hemolysis.

Wilson disease has a diverse spectrum of clinical manifestations. Thus, liver function tests should be performed in young patients presenting with hemolytic anemia so as not to delay the diagnosis of Wilson disease. Furthermore, Wilson disease should be considered as one of the differential diagnosis in
patients presenting with unexplained hemolytic anemia and liver disease.

![Figure 1: Figure showing sunflower cataract in a patient with Wilson disease](image)

**Figure 1: Figure showing sunflower cataract in a patient with Wilson disease**

**References:**