

# A CASE OF WILSON'S DISEASE PRESENTING AS ACUTE HEPATITIS

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## ABSTRACT

*In Bangladesh and in most parts common causes of acute hepatitis include hepatitis viruses, alcohol and drugs. However less common aetiologies like Wilson's disease must be kept in mind and looked for, whenever there is strong suspicion. Here we present a young male who presented to us with classic features of acute hepatitis including prodrome and on evaluation was diagnosed as a case of acute Wilson's disease.*

**Key Words:** Wilson's disease, acute hepatitis.

*This article may be cited as:* Choudhury N, Mamun-Al-Mahtab, Rahman S. A case of Wilson's disease presenting as acute hepatitis. KUST Med J 2011;3(2): 64-66.

## INTRODUCTION

In 1912, a Neurology resident described cirrhosis and lenticular degeneration occurring in families and this disease has since been named after him as Wilson's disease<sup>1</sup>. J. N. Cumings first elucidated the link between copper and Wilson's disease in 1948<sup>2</sup>. This is an inherited disorder of copper metabolism manifesting typically as hepatic disease in children and as neurological disease in older children and young adults.

Copper overload in Wilson's disease occurs due to reduced biliary excretion of copper. ATP7B gene was identified as the defective gene causing the disease by three independent teams in 1993<sup>3-5</sup>. 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 ceruloplasmin, which is then secreted into the blood stream. H1069Q, the most common ATP7B mutation in the Caucasian population<sup>6</sup>.

## CASE REPORT

The patient, an 18 year old male, college student presented to us with classic features of prodrome including jaundice, nausea, vomiting and loss of appetite for one week. He had no history of intake of any drug with

known hepato-toxicity in the last three months and was non-alcoholic. His parents were non-consanguineously married and neither he nor his three siblings had history of any hepatic or neurological manifestation suggesting Wilson's disease.

On physical examination the patient was icteric and had tender, hepatomegaly; however he did not have any stigmata of chronic liver disease. On investigation his total serum bilirubin was 14.4 mg/dl (conjugated serum bilirubin 11.2 mg/dl and unconjugated serum bilirubin 3.2 mg/dl), serum alanineaminotransferase 1270 U/L and INR 2.11.

His peripheral blood film showed non specific morphology and his haemoglobin was 14.6 mg/dl. Capillary electrophoresis was done and showed HbA 97.5% and HbA2 2.5%. He tested negative for all hepatitis viruses, namely anti-HEV IgM, anti-HAV IgM, HBsAg, anti-HBc IgM, anti-HCV, anti-CMV IgM, anti-Dengue IgM and anti-HSV 1 & 2 IgM by ELISA.

He also tested negative for ANA, ASMA, anti-LKM1, AMA (M2) antibodies by ELISA and his serum iron profile was normal. On further investigation his urinary copper was 1140 microgm/L. His serum ceruloplasmin was however raised (440 mg/ml) and he had no KF ring on slit lamp Ophthalmic examination.

Abdominal ultrasonography revealed hepatomegaly with echo poor echo pattern and marked peri-portal echogenicities. Gall bladder was contracted even after over night fasting. All these findings were consistent with acute hepatitis. Subsequently an upper gastrointestinal tract (GIT) endoscopy showed normal upper GIT. His siblings were screened for Wilson's disease with serum ceruloplasmin, urinary copper and slit lamp examination for KF ring, but all were found to be normal.

The patient was put on copper chelation therapy with oral penicillamine and zinc along with supportive treatment. It was started at 500 mg penicillamine daily in two divided doses which was gradually raised to 1500

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**Date Submitted:** October 16, 2011

**Date last Revised:** November 19, 2011

**Date Accepted:** November 22, 2011

mg daily also in two divided doses. His blood count, urine routine examination and liver function tests were routinely done and neurological functions carefully monitored. The patient underwent eventless recovery and is currently on maintenance copper chelation therapy with 750 mg penicillamine daily in two divided doses and oral zinc.

## DISCUSSION

Wilson's disease is a well recognized and frequently encountered disease entity in our clinical practice. However there are several interesting aspects of the present case that make it worth reporting. Firstly, Wilson's disease usually manifests as a chronic disease in its hepatic and/ or neurological form(s). Acute presentation of the disease is infrequent. Secondly, unlike in chronic Wilson's disease, in its acute form, serum ceruloplasmin is expected not to be low, but rather to be normal or raised as in our case, since ceruloplasmin is an acute phase protein. This can make the diagnosis of Wilson's disease difficult. Thirdly, in acute Wilson's disease, KF ring, which frequently accompanies chronic Wilson's disease as a diagnostic criteria, is likely to be absent. This is because KF ring results from excessive deposition of copper in the cornea of Wilson's disease patients, which does not happen in the acute form of the disease. This also adds to the diagnostic dilemma. Fourthly, acute Wilson's disease 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. Our patient fortunately did not have this complaint. And finally, it is expected that parents of Wilson's disease will be consanguineously married and one or more siblings will also be affected. Neither of this however happened in our case.

Symptomatic Wilson's disease typically presents in children and young adults, though it has been reported from 2-70 years of age. The prevalence of Wilson's disease is estimated to be 1 in 50,000 in general population<sup>7</sup>. Diagnosis of Wilson's disease involves a number of investigations. In Wilson's disease incorporation of copper into ceruloplasmin is impaired accounting for reduced serum ceruloplasmin levels. Ceruloplasmin is however an acute phase reactant and thus serum levels can go up in inflammatory states including acute hepatitis, as in case of our patient.

Dietary restriction of copper is insufficient as sole therapy. It is advisable to reduce consumption of foods high in copper content, like shellfish, nuts, chocolate, mushrooms and organ meats. Serum copper levels are usually reduced in Wilson's disease, in proportion to reduced serum ceruloplasmin. However free copper level, which is not bound to ceruloplasmin, is high in most patients with Wilson's disease.

Urinary copper is a reflection of free copper in the circulation. Measuring urine copper is useful in diagnosis of Wilson's disease and can be used as a measure of

compliance to therapy. Though dry weight estimation of hepatic copper is the gold standard to diagnose Wilson's disease, low values due to sampling variability can occur in significant hepatic fibrosis and cirrhosis due to Wilson's disease<sup>8</sup>. High values can occur in chronic cholestatic liver disorders.

Aim of treatment in Wilson's disease is to achieve normal copper levels in the body in the shortest possible time and to maintain this. Of the drugs used to treat Wilson's disease, penicillamine and trientine mainly act by increasing cupriuresis, while oral zinc mainly acts by inhibiting copper absorption from the intestine<sup>9</sup>. The commonly recommended regime is initial treatment with copper chelators like penicillamine or trientine to normalise copper levels in the body, followed by maintenance treatment with lower dose of copper chelators or zinc.

Transition from the initial high dose chelator therapy to maintenance therapy is made once patient is clinically well, has normal liver function tests, normal non-ceruloplasmin bound copper level and 24 hour urine copper of 200-500 µgm per day on treatment. Treatment needs to be continued lifelong. Measuring 24 hour urine copper excretion while on treatment is useful to monitor compliance. Ammonium tetrathiomolybdate appears to be useful as initial therapy in neurological Wilson's disease, however experience is very limited<sup>10</sup>. Antioxidants such as vitamin E may be useful adjuncts to treatment<sup>11</sup>. Dimer-caprol (British anti-Lewisite), the first drug used to successfully treat Wilson's disease, is rarely used now.

Liver transplantation is treatment of choice in fulminant Wilson's disease and may be considered in patients with decompensated cirrhosis, non-responsive to medical therapy. Following liver transplantation hepatic insufficiency is corrected and neurological manifestations improve in upto 80% cases. Survival at 1 year is about 80%<sup>12</sup>.

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- CONFLICT OF INTEREST**  
Authors declare no conflict of interest  
**GRANT SUPPORT AND FINANCIAL DISCLOSURE**  
NONE DECLARED

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