

Case Report

Wilson's disease presenting as acute hepatic failure: A case report

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Introduction

Wilson disease (WD) was first described in 1912 by Kinnear Wilson as "progressive lenticular degeneration," a familial, lethal neurological disease accompanied by chronic liver disease leading to cirrhosis.¹ J N Cumings first elucidated the link between copper and Wilson's disease in 1948.² 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 WD occurs due to reduced biliary excretion of copper. ATP7B gene was identified as the defective gene causing the disease by three independent teams in 1993.³⁻⁵ 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. Absent or reduced function of ATP7B protein leads to decreased hepatocellular excretion of copper into bile. This results in hepatic copper accumulation and injury. Eventually, copper is released into

the bloodstream and deposited in other organs, notably the brain, kidneys, and cornea. WD presents with liver disease more often in children and younger adult patients than in older adults. Symptoms at any age are frequently nonspecific.

Case report

A 35 years old man presented to us with features of prodrome includes abdominal pain, nausea & vomiting for twelve days and altered sleep pattern for three days. He had no history of intake of any drug with known hepatotoxicity in the last three months and was non-alcoholic. His parents were 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 severely icteric, all neurological exam was normal except flapping tremor and had tender hepatomegaly.

On investigation his total serum bilirubin was 25 mg/dL, SGPT 1779 U/L, SGOT 256 U/L, Alkaline phosphatase 129 U/L, INR 1.65, serum albumin 3.5gm/dL. His haemoglobin was 13 mg/dL, platelet count 2,40,000/cmm and peripheral blood film showed nonspecific morphology. Haemoglobin electrophoresis was done and showed to be normal.

He was found to be negative for anti-HEV IgM, anti-HAV IgM, HBsAg, anti-HBc IgM, anti-HCV, anti-CMV IgM, anti-Dengue IgM and anti-HSV 1 (IgM) & anti-HSV 2 (IgM) by ELISA. He was also found to be 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 188.48 microgm/24h. His serum ceruloplasmin was near the lower end of normal reference (31 mg/dL) and he had bilateral KF ring on slit lamp ophthalmic examination.

Abdominal ultrasonography revealed hepatomegaly with poor echo pattern and marked periportal echogenicities. Gallbladder was contracted even after overnight fasting. All these findings were consistent with fulminant hepatic failure. Upper gastrointestinal tract (GIT) endoscopy was normal. His siblings were screened for Wilson's disease with

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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 along with supportive treatment. It was started at 500 mg penicillamine daily in two divided doses which were gradually raised to 1000 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 1000 mg penicillamine daily in two divided doses.

Discussion

WD occurs worldwide with an average prevalence of around 30 affected individuals per million population.⁶ Wilson's disease is rare but important genetic disease in young patient. It is a well-recognized and often encountered in our clinical practice. Several aspect of current case make it worth reporting.

Firstly, Wilson's disease usually present in children and young adult, although presentation up to 70 years has been reported. Secondly, Wilson's disease usually manifests as a chronic disease in its hepatic and/or neurological form(s). Acute presentation of the disease is infrequent and increasingly diagnosed in children younger than 5 years old, with atypical findings as acute liver failure.⁷ Current case is middle aged with presentation as acute liver failure. Thirdly, 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. 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. Fifthly, a slit-lamp examination by an experienced observer is required to identify Kayser-Fleischer rings in most patients. They are not entirely specific for WD, because they may be found in patients with chronic cholestatic diseases⁸⁻¹⁰. In our case bilateral KF ring are present due to WD as chronic cholestasis excluded. Finally, it is expected that parents of Wilson's disease will be consanguineously married and one or more siblings will also be affected. In our case, though parents are consanguineously married, siblings are not affected.

Diagnosis of Wilson's disease depends on its variable presentation and a number of investigations including

presence of KF ring, high 24hrs urinary copper and normal level of ceruloplasmin as ceruloplasmin is acute phase protein.

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 monitoring and 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.¹¹ High values can occur in chronic cholestatic liver disorders.

Drug therapy aimed to reduce/abolish symptoms, prevent development of permanent liver damage and normalized serum and urinary copper level. 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 intestine¹². Recommended first line regime is treatment with copper chelators like penicillamine or trientine to normalize 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, and 24 hour urine copper become 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 limited¹³. Though it is not necessary in our patient as neurological manifestation due to acute liver failure with encephalopathy not due to WD itself. Antioxidants such as vitamin E may be useful adjuncts to treatment.¹⁴

Fulminant hepatic failure and in patients with decompensated cirrhosis, due to Wilson's disease non-responsive to medical therapy, liver transplantation is treatment of choice. Following liver transplantation hepatic insufficiency is corrected and neurological manifestations improve in up to 80% cases & survival at 1 year is about 80%.¹⁵

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