

Silent Wilsons Disease Unmasked By Hepatitis E- Case Study

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Abstract: *Wilson disease is a rare autosomal recessive inherited disorder of copper metabolism that is characterized by excessive deposition of copper in the liver, brain, and other tissues. Hepatitis E is a viral hepatitis caused by infection with a virus called hepatitis E virus. It is one of five known human hepatitis viruses. Although hepatitis E often causes an acute and self-limiting infection with low mortality rates in the western world, it bears a high risk of developing chronic hepatitis in immune compromised patients with substantial mortality rates. Reveal of Wilson's disease with viral hepatitis is reported earlier in the literature as a rare association. Here we report a case of report 24 year old female patient with biochemical, serological, hematological and histopathological evidence of underlying Wilson's disease complicated by hepatitis E virus infection. In this case the patient developed acute hepatic decompensation indicating that HEV plays a part in the acute hepatic decompensation seen in cases of unrecognized Wilson's disease.*

Keywords: Wilsons Disease, Hepatitis E.

1. 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 disease¹. J. N. Cumings first elucidated the link between copper and Wilson's disease in 1948². 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 1993³⁻⁵. 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. H1069Q, the most common ATP7B mutation in the Caucasian population⁶.

HEV infection remains either asymptomatic or resolves with mild symptoms without development of chronic disease. However, once it occurs as a co-infection with other viruses, it may develop serious disease. Management of hepatitis E may present several diagnostic challenges. This is a case of report 24 year old female patient with biochemical, serological, hematological and histopathological evidence of underlying Wilson's disease complicated by hepatitis E virus infection. In my case the patient developed acute hepatic decompensation and it indicates that HEV plays a part in the acute hepatic decompensation seen in cases of unrecognized Wilson's disease. Also persistent asymptomatic elevation of liver enzymes, the presence of hemolytic anemia in conjunction with the hepatic dysfunction, or elevation of unconjugated (indirect) bilirubin, should warrant the clinician to the possibility of Wilson's disease. This can lead to early intervention to avoid progressive development of cirrhosis and fulminant liver failure.

2. Case Report

24 year old female patient presented with the complain of abdominal distention, abdominal pain, vomiting, yellow colour urine and yellow colour sclera since 7-8 days. No neuropsychiatry symptoms. She had no history of intake of any drug with known hepato-toxicity in the last three months and was non-alcoholic. Her parents were non-consanguineously married and neither she nor her one sibling had history of any hepatic or neurological manifestation suggesting Wilson's disease. There was no history suggestive of copper intoxication and dietary intake of copper was normal. There was a history of 2 episode of jaundice in past 1 year.

On physical examination the patient was icteric, pallor and had tender, hepatomegaly, however she did not have any stigmata of chronic liver disease. Ophthalmologist identified classic Kayser-Fleischer rings on slit lamp examination.

Hematological examinations revealed anemia (hemoglobin: 8.05 gm/dL), MCV: 92.2, MCH: 37.3, MCHC: 40.2, RDW: 17.2 with slight anisocytosis and poikilocytosis. The platelets and WBC counts were normal and no parasites were detected on the peripheral blood smear examination.

The peripheral smear also had 18% of normoblast and spherocytosis indicative of hemolytic anemia. Serum biochemistry investigations revealed deranged liver function [Total serum bilirubin of 22.6 mg/dL, direct bilirubin of 8.8, and indirect bilirubin of 13.8, elevated liver enzymes, [SGOT: 122, SGPT: 234].

Serological tests for anti HEV IgM were positive (ELISA), while hepatitis B (HBsAg Virucheck), hepatitis A, human immunodeficiency virus I and II (HIV Tridot), IgM for dengue fever were negative. There were no serological

features of autoimmune hepatitis (anti-nuclear antibody negative).

Serum copper levels were high 255.5 mcg/dL (n=70-140 mcg/dL). Urine copper levels in 24 hours were elevated to 403µg/24 hours (24 hours urine volume 3600 ml). Serum ceruloplasmin levels turned out to be 56.21 mg/dL (n=15-30 mg/dL). Core biopsy of the liver was obtained. Microscopic examination revealed distortion of basic architecture in liver tissue. Liver parenchyma showed nodule formation surrounded by fibrosis and chronic inflammation. Hepatocytes showed micro vesicular steatosis, and intracellular yellowish brown pigment accumulation.

Considering the clinical presentation, positive hepatitis E antibody, high serum and urinary copper, presence of Kayser-Fleischer ring with a background of a hemolytic anemia, diagnosis of a hepatitis E superimposed on Wilson's disease was established.

Abdominal ultrasonography revealed hepatomegaly with echo poor echo pattern and marked peri-portal echogenicities. All these findings were consistent with acute hepatitis.

Her sibling 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 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. 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.

3. Discussion

From the case discussed above, the patient was suffering from underlying Wilson's disease (WD) and diagnosis came into picture with hepatitis E super infection.

Wilson's disease is caused by defective copper excretion through biliary channels and incorporation into apoceruloplasmin due to ATP7B protein deficiency (gene at chromosome 13) leading to accumulation of copper mainly in liver and brain⁷. WD may present at any age but mainly children and young adults, 3% patients are of more than 40 years at the age of presentation⁸. The disease is characterized by acute liver failure to cirrhosis, neuropsychiatric abnormalities, haemolysis, K-F ring in Descemet's membrane of cornea, sunflower cataract⁹.

Hepatitis E has highest prevalence in the East and South Asia, with 60% of hepatitis E global incidence and 65% of global deaths. Among the Indians, there is low seroprevalence until the age of 15 years, 40% in young adults. HEV infection is the more important cause of epidemic hepatitis than HAV, common among children¹⁰. The virus is

transmitted via feco-oral route and causes only acute illness with hepatic involvement. Sometimes it may cause severe DE compensation of chronic liver disease¹¹.

Now if we look back into the previous literatures, such event had been reported by many authors¹²⁻¹⁴. In 1994, Sallie, et al. documented the first case in this regard in a 6 years old girl with histological evidence of hepatic copper deposition and hepatitis E virus in nested PCR. In 2013, Kumari, et al. showed decompensation of liver failure by hepatitis E infection in a 25 years old male with WD. In 2015, Kiran, et al. reported coexistence between hepatitis E and underlying WD in a 10 years old girl by 24 hours urine copper before and after penicillamine challenge and HEV RNA detection.

4. Conclusion

From this case we can conclude that HEV plays an important part in the acute hepatic decompensation in cases of unrecognized Wilson's disease.

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