Available online at **www.ijmrhs.com**

ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2017, 6(9): 59-61

The Silent Wilson's Disease Unmasked by Hepatitis E Infection - A Case Report and Review of Literatures

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ABSTRACT

Reveal of Wilson's disease with viral hepatitis is reported earlier in the literature as a rare association. Here we have reported a case of late onset Wilson's disease diagnosed after hepatitis E infection in a 45 years old male who had no manifestation of liver disease before the infection and rapid deterioration thereafter.

Keywords: Wilson's Disease (WD), Late onset, Hepatitis E, Rapid deterioration

Abbreviations: ANA: Antinuclear Antibodies; ASMA: Antismooth Muscle Antibodies; AMA: Antimitochondrial Antibody; LKM: Antiliver-Kidney Microsome; GCS: Glasgow Coma Scale

INTRODUCTION

Wilson's disease is caused by genetic defect of copper metabolism and affection of liver, brain due to deposition, also lysis of RBCs due to free radicular injury by excess copper in the circulation. It manifests as chronic hepatic failure, sometimes with fulminant disease, also in the form of neuropsychiatric complications, Coomb's negative haemolytic anaemia, ophthalmologic complications (cataract, K-F ring) [1]. Besides the acute manifestation of Wilson's disease, a trigger may provoke the underlying disease to come in front [2]. Cases have been highlighted with such incidences earlier, but in this case, there was no evidence of Wilson's disease till 45 years of age and manifested after hepatitis E virus infection both clinically and on investigations, severity and rapid progression resulted unfortunate death of the patient.

CASE REPORT

Patient's profile

A 45-year-old non-diabetic non-hypertensive male patient presented with yellowish discolouration of urine and white part of sclera and gradually increasing abdominal swelling since last 1 month following low grade fever for 6-7 days (with no chill and rigor) and decreased appetite, nausea, weakness, body ache, vague abdominal pain. There was no history of shortness of breath, palpitation, cough, blood vomiting, blood in stool, urinary disturbances, long standing diarrhoea, behavioural abnormalities, abnormal position and movements of limbs, performance inability.

There was no previous history similar illness. Patient declared no addiction for alcohol and didn't elicit any significant and regular drug intake before the start of symptoms. No family member had undergone same illness. Patient was married, had one son. There was no history of impotence.

On general examination, patient's built was average, mild pallor, icterus was present, bipedal swelling was there. Hair nails were normal, skin colour was yellowish on fare complexion, no other abnormal findings. There was no clubbing, no enlarged lymph nodes, no engorged neck veins (Table 1).

Table 1 Patient's vitals

Patient's vitals	Values
GCS=13	M3, V4, E6 (motor, verbal and eye-opening responses)
Pulse Rate (PR)	70/minute
Blood Pressure (BP)	110/72 mmHg
Respiratory rate (RR)	20/minute
SpO_2	96% on room air

On per abdominal examination abdomen was hugely distended, umbilicus was on midline but protruded; liver was palpable 4 cm from right costal margin (span - 16 cm), firm, regular margin. Spleen was not palpable but percussion of Traube's space was dull. Fluid thrill and shifting dullness were present. No bruit was heard on auscultation.

Findings of cardiovascular, respiratory, nervous system, genitourinary systems were unremarkable. Peripheral blood smear revealed normocytic normochromic anaemia. Kidney function tests and electrolytes were within normal range. Parameters of lipid profile were normal (Table 2).

Table 2 Haematological investigation

Laboratory findings	Values
Haemoglobin	9.0 g/dL
TLC	7300/mm^3
Neutrophils	73%
Lymphocytes	21%
Monocytes	4%
Eosinophils	2%
Basophils	0%
Reticulocyte count	5%
Platelet count	2,00,000/mm^3
Coagulation factors	
Prothrombin time	32 secs with control 13 sec
International Normalized Ratio (INR)	2.49
activated Partial Thromboplastin Time (aPTT)	76.8 sec

Anti HEV IgM was positive (10.97 A/C.O.). Other virological markers in relation to cause acute hepatitis were negative.

After the acute phase, serum ceruloplasmin - 0.099 g/L (normal plasma level of ceruloplasmin is 0.2-0.6 g/L), urinary copper - 112 µg/24 hours (normal urine copper range 20-50 µg/24 hours). Kayser-Fleischer ring was detected in both eyes on slit lamp examination. Liver autoimmune profile (ANA, ASMA, AMA, LKM) were negative.

Ascitic fluid study revealed no evidence of bacterial peritonitis. Abdominal ultrasound revealed gross ascites with hepatomegaly and sludge and calculi in gall bladder. Brain MRI was normal.

Patient was on supportive therapy with prophylaxis of encephalopathy, bacterial peritonitis and measures to reduce abdominal discomfort. Patient relatives were explained for the prognosis and advised for liver transplantation but they were unable to do the same for financial weakness.

Acute phase was over but the patient's condition was deteriorating in due course and unfortunately died after 1 month of admission.

DISCUSSION

From the case discussed above, impression can be drawn that the patient was suffering from underlying Wilson's disease (WD) and diagnosis came into picture with hepatitis E super infection. Diagnosis of WD was according to Leipzig criteria in 2001 [3], score was 5 (KF ring - 2, serum ceruloplasmin - 2, 24 hours urinary copper - 1). Our hospital does not have the facility for Coombs test and genetic mutation analysis thus could not be done. Liver biopsy was not possible due to derangement of coagulation profile.

Wilson's disease is caused by defective copper excretion through biliary channels and incorporation into apo-ceruloplasmin due to ATP7B protein deficiency (gene at chromosome 13) leading to accumulation of copper mainly in liver and brain [1]. WD may present at any age but mainly children and young adults, 3% patients are of more than

40 years at the age of presentation [4]. The disease is characterized by acute liver failure to cirrhosis, neuropsychiatric abnormalities, haemolysis, K-F ring in Descemet's membrane of cornea, sunflower cataract [5].

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 sero-prevalence until the age of 15 years, 40% in young adults. HEV infection is the more important cause of epidemic hepatitis than HAV, common among children [6]. 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 disease [7].

Diagnosis of WD on setting of acute hepatitis is misleading with increased urinary copper excretion from depleted store due to hepatocytes injury and elevated serum ceruloplasmin level as an acute phase reactant. Liver biopsy may not be possible with highly altered coagulation profile. So, it is better to continue supportive therapy till the acute phase gone (high bilirubin with less pronounced enzyme levels) and search for the underlying chronic event.

Now if we look back into the previous literatures, such event had been reported by many authors [8-10]. 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.

Keeping the data in mind, our case is different from the aforementioned ones in the age of presentation and diagnosis.

For the management of Wilson's disease, Dhawan's modification of prognostic index is used [11]. A score of 11 or more indicates need for liver transplantation. Here in this case score was 13 and planned for transplantation.

CONCLUSION

From the rising incidence, it can be concluded that WD may run as asymptomatic with no clinical pictures suggestive of and an acute event other than WD may pull out the diagnosis. Exact pathogenesis is yet to be enlightened.

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