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General Medicine

WILSON'S DISEASE: A RARE DISEASE WITH A CHALLENGING DIAGNOSIS: A CASE REPORT.

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ABSTRACT This case study is about a 15-year-old girl who has been diagnosed with portal hypertension and chronic liver disease (CLD). Over a period of approximately 2 weeks, the patient noticed generalised swelling of her body, including her lower limbs, abdomen, and her face. Her past featured a recurrence of comparable symptoms and the habit of eating raw, uncooked rice. Pedal oedema, moderate splenomegaly, and mild icterus were found on physical examination. Hepatitis panels and autoantibody tests came back negative, but laboratory examinations revealed anaemia, abnormal liver enzymes, and hypoalbuminemia. Imaging tests verified portal hypertension, splenomegaly, and CLD. Urinary copper levels were raised and ceruloplasmin was on the higher end of normal, supporting the diagnosis of decompensated CLD with portal hypertension, most likely caused by hepatic Wilson's disease. Nutritional supplements and diuretics were used in supportive care. In addition to highlighting the need of early identification and comprehensive care to stop the progression of the disease and improve outcomes, this case emphasizes the significance of taking CLD and portal hypertension into account in young patients with unexplained oedema and abdominal distension.

KEYWORDS : Hepatolenticular degeneration, Copper chelators, Decompensated chronic liver disease

INTRODUCTION

Decompensated chronic liver disease, also known as decompensated cirrhosis is a condition in which there is a very advanced stage of liver failure. This leads to the apparent symptoms of generalized edema, hematemesis and in a few cases neuro-psychiatric manifestations. At a young age, it can occur due to a variety of causes. Some of the well-known causes are Autoimmune hepatitis, Viral hepatitis, Alpha 1 antitrypsin deficiency, Wilson disease and Non-Alcoholic fatty liver disease. In this case we find that the female developed chronic decompensated liver failure due to underlying Wilson disease. Wilson disease is a very uncommon hereditary disorder which develops due to deficiency of ATP7B gene defect [1]. This leads to copper accumulation initially in the liver and later in the other tissues leading to a very varied presentation [2].

Case Report

A 15-year-old female presented with insidious onset, gradually progressive pedal oedema and abdominal distension with facial puffiness. She has a history of similar complaints 4 months ago with no history of jaundice, melena, fever, and decreased urine output.

At her initial presentation, patient is conscious and coherent and vitals were normal. On examination mild icterus and pedal oedema was present. She had no problem with her vision and Kayser-Fleisher rings were absent.

Laboratory tests showed abnormal liver function tests with elevated bilirubin from 2.0 mg/dl to 3.9 mg/dl, elevated SGOT/SGPT (Asparatate transaminase/Alanine transaminase) 202/96, ALP 310 U/L and Serum Albumin 2.0 g/L. Her Gamma glutamyl transpeptidase is 107 U/L and SAAG is 1.5. Hepatitis B and C serology is negative. Additionally, her urinary copper levels were elevated and were equal to 62mg/day and serum ceruloplasmin level of 25mg/dl (Table 1).

Table 1:

INVESTIGATION	RESULTS	NORMAL RANGE
HEMOGLOBIN	8.4 g/dl	13 - 16 g/dl
WBC	5200 per micro lt	4500 -11000 per micro lt
PLT	170000 per micro lt	150000 - 400000 per micro lt
Sr CERULOPLASMIN	25 mg/dl	20 -35 mg/dl
DIRECT BILIRUBIN	1.6 mg/dl	< 0.3 mg/dl
INDIRECT BILIRUBIN	2.3 mg/dl	0.2 - 0.8 mg/dl
SGOT/SGPT	287/114	
ALP	450 IU/L	44 - 140 IU/L
Sr ALBUMIN	2.0 g/dll	3.4 - 5.4 g/dl
24 HR URINE COPPER	62 mcg/day	10 - 30 mcg/day

Her USG (Ultrasound) and MRI abdomen were suggestive of chronic liver disease with ascites and portal hypertension, moderate splenomegaly, hypoplastic uterus, panniculitis, multiple enlarged peri pancreatic lymph nodes and coarse echogenic irregularities. Her MRI brain (Figure 1) was indicative of symmetrical T1 hyperintensities in bilateral basal ganglia due to hepatic dysfunction. Her upper GI endoscopy was indicative of grade 2 oesophageal varices. Liver biopsy showed histopathological features of Chronic Hepatitis with Cirrhosis and copper deposition (Figure 2). Genetic testing for ATP7B gene mutation is negative.

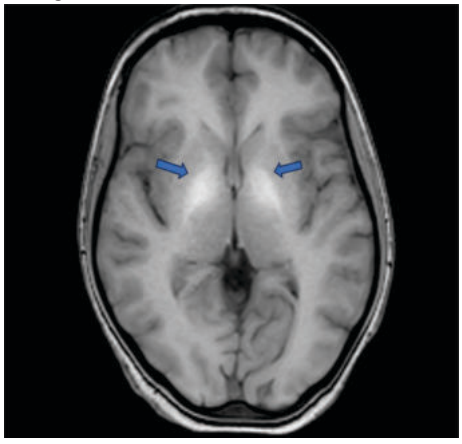

Figure 1: T1 Hyperintensities In The Globus Pallidus.

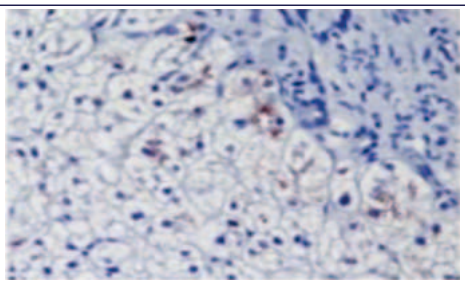

Figure 2: Rhodanine Stained Hepatic Tissue Showing Copper Deposition. Original Magnification Used Was 100x.

During her hospitalization she was initially given supportive care with Diuretics, Hepamerz (Hepatoprotective) and Piperacillin-Tazobactam. Even though her genetic testing was negative, taking into consideration her urinary copper levels and the copper deposition in the hepatocytes, the patient was eventually started on Penicillamine, Vitamin B6 and zinc. She and her family were counselled on the importance of treatment compliance, as lifelong treatment is required. They were also counselled on the importance and requirement of liver transplant in the long run.

DISCUSSION

Wilson's disease, also known as the hepatolenticular degeneration, is a rare genetic disorder which is autosomal recessive in inheritance. It usually presents with damage to the liver and the neurological manifestations like dystonia, dysarthria, and Parkinson disease like features [5]. The struggle has always been there in trying to meet the gap between onset of symptoms and in reaching the diagnosis [3]. The pathogenesis of Wilson's disease in recent studies shows that, not just copper accumulation, but free radical formation and iron deposition in liver and other tissues leading to ferroptosis could be a potential cause of cellular death [4]. ATP7B is a copper transporter which helps in incorporation of copper into the ceruloplasmin and the biliary excretion of the excess amount of copper. If this becomes defective, the excess copper is either deposited in different body tissues or is excreted in the urine [6]. However, there are certain pathogenic mutations which result in normal production of ATP7B gene but it will be non-functional. So, then we need to depend on the laboratory and biopsy results to reach the diagnosis of Wilson's disease [12]. Fleisher rings are seen in approximately 95% of the patients with neurological disease, but in younger age groups its quite a rare finding and often it is absent [7]. Diagnosis of Wilson's disease is typically based on the clinical presentation of the patient which should go hand-in hand with the lab investigations like 24-hour urinary copper levels, ceruloplasmin levels in plasma, liver biopsy which shows copper deposition and molecular analysis. A multidisciplinary team of hepatologists, nephrologists, rheumatologists, neurologists, and ophthalmologists are required for a wholesome management of the patients [8,9]. Hepatolenticular degeneration can be effectively treated if diagnosed at an early stage. It is of high importance to recognize the disease at an early stage so that timely treatment is given and complications are prevented [10]. De-coppering treatment is the cornerstone of the management. Chelating agents like penicillamine and trientine are commonly used for treatment along with Zinc [10,11].

CONCLUSION

Wilson's disease is a rare kind of genetic disorder which primarily affects the copper metabolism. However, this patient did not have the classic decrease in the ceruloplasmin levels which is usually suspected nor the mutated ATP7B gene. Studies have shown that even in the absence of mutated ATP7B gene, if the patient has abnormal copper levels and copper deposition it can still be considered as Wilson's disease because the gene remains may remain nonfunctional.

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