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Internal Medicine

WILSON'S DISEASE UNCOVERED IN AN ASYMPTOMATIC INDIVIDUAL : A CASE REPORT

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ABSTRACT Wilson's disease is an autosomal recessive disorder resulting in defective copper metabolism due to mutation in ATP7B gene [1]. It is a debilitating disease that can be fatal if left untreated [2]. In India, nearly 50% of Wilson's disease cases have a positive family history, with a high rate of consanguinity [1]. Asymptomatic patients may already have copper-induced damage in the liver and other organs and are at risk of progressing to symptomatic Wilson's disease unless treated [3]. The management of Wilson's disease involves early diagnosis, timely initiation of appropriate treatment, lifelong monitoring of patient adherence, and screening for adverse effects and treatment efficacy [4]. This report describes the case of a 38-year-old asymptomatic female who, while being evaluated as a potential liver donor for her elder brother with a known diagnosis of Wilson's disease, was unexpectedly diagnosed with the condition.

KEYWORDS : WILSON'S DISEASE, ASYMPTOMATIC, FAMILY SCREENING.

INTRODUCTION:

Copper is an essential metal necessary for the proper function of numerous metalloproteins [3]. About 50 to 75% of ingested copper is absorbed, then transported to the liver, where it is incorporated into enzymes and proteins, including apoceruloplasmin, which is subsequently converted into ceruloplasmin [4]. When copper levels in the liver exceed safe thresholds, the ATP7B protein loads copper into ceruloplasmin and promotes its secretion into the plasma [4]. In the cytoplasm of hepatocytes, ATP7B transports excess copper into vesicles and excretes it through bile via exocytosis [4]. Wilson's disease is an autosomal recessive disorder of hepatocyte copper trafficking due to impaired function of the P-type adenosine triphosphatase (ATP7B), encoded by the ATP7B gene on chromosome 13q14[5]. To date, over 750 mutations in the ATP7B gene have been identified [1]. Common sites of copper accumulation include the brain, cornea, eyes, and kidneys [4].

The first case of Wilson's disease was reported by Friedrich Theodor von Frerichs in 1861, but it was Alexander Kinnier Wilson's detailed documentation of multiple cases in 1912 that brought widespread recognition to the condition [6]. In 1963, Wadia and Dastur reported the first case of Wilson's disease from India [1]. The World Health Organization estimates the global prevalence of Wilson's disease to be 30-100/ million people [1]. Approximately 30% of individuals with Wilson's disease are asymptomatic andare primarily diagnosed through family screening [7]. In India, up to two-thirds of Wilson's disease cases may be initially misdiagnosed, with an average diagnostic delay of up to two years [1].

Case Report:

A 38-year-old woman presented to the hospital for evaluation as a liver donor for her elder brother, who had been diagnosed with Wilson's disease due to liver dysfunction. The patient had no history of yellowish discoloration of skin or sclera, behavioural changes, or movement disorders. On examination, she was alert, oriented, and moderately nourished, with no signs of jaundice, hepatosplenomegaly, or Kayser-Fleischer rings on slit-lamp examination. Routine investigations showed normal liver and renal function tests. However, her serum ceruloplasmin (8.46 mg/dl) and copper (26.4 MCG/dl) levels were low. Further evaluation with a 24-hour urinary copper test revealed elevated copper levels (223 mcg/dl).

An abdominal ultrasound showed features of fatty liver, but there was no evidence of cirrhosis or hepatomegaly.

Given her positive family history, elevated urinary copper, and low serum ceruloplasmin levels, she was diagnosed with Wilson's disease. Treatment was initiated with copper restriction in her diet, along with copper chelating agents, including penicillamine and zinc. She was advised to follow up regularly to monitor the progression of the disease and her response to therapy.

DISCUSSION:

Wilson's disease is most diagnosed between the ages of 5 and 35 [4]. In children, liver involvement is the most frequent presentation, typically around 15 years of age, while neurological symptoms tend to manifest on average at 20 years [2]. Pure psychiatric manifestations are commonly seen in the third decade of life [1]. Around 50% of individuals with Wilson's disease present with liver involvement [4]. Viral hepatitis can trigger or reveal Wilson's disease [1]. The condition may manifest with a variety of symptoms, ranging from asymptomatic liver disease to cirrhosis, chronic hepatitis, and acute liver failure [4]. Neurological disorders are the second most common clinical manifestation of Wilson's disease, following liver involvement [4]. The basal ganglia and brain stem are the most susceptible sites to copper toxicity [4]. Approximately 30 to 60 percent of patients with Wilson's disease exhibit psychiatric symptoms at presentation [7].

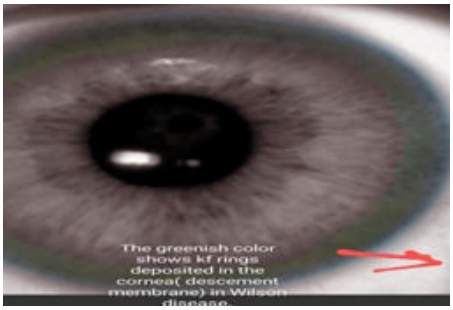

Figure:1 Kayser -fleischer Ring In Wilsons Disease

Copper deposition in Descemet's membrane leads to the formation of Kayser-Fleischer rings, which typically do not impair vision [7]. These rings are present in 95% of patients with Wilson's disease who exhibit neurological symptoms [4]. However, they may be absent in up to 50% of those with isolated hepatic disease [4]. Renal tubular acidosis is observed in more than half of these patients, particularly in those with hepatic Wilson's disease of longer duration [1]. This condition can lead to renal impairment resembling Fanconi syndrome [4]. Coombs-negative autoimmune haemolytic anaemia occurs in approximately 10 to 15% of Wilson's disease cases [4]. Radiological osteoporosis is observed in nearly 40% of Wilson's disease cases. Cardiac arrhythmias, cardiomyopathy, autonomic dysfunction, menstrual irregularities, and non-hepatic malignancies such as retinoblastoma, leukaemia, basal cell carcinoma, and glioblastoma have also been reported in patients with Wilson's disease [1].

Serum ceruloplasmin levels below 10 mg/dL in clinically suspected cases are highly indicative of Wilson's disease [1]. A 24-hour urinary

copper excretion which usually exceeds 100 micro-grams per 24 hour in adults and 40 microgram per 24 hour in children confirms the presence of Wilson's disease [4]. The evaluation of Kayser-Fleischer rings using a slit lamp is a fundamental aspect of the clinical diagnosis of Wilson's disease [5]. "Face of the giant panda" sign in the midbrain is a characteristic feature in MRI brain [5]. Hepatic copper estimation with liver biopsy, a level more than 250 microgram per gram of dry weight is suggestive of Wilson's disease [1]. Sequencing the entire ATP7B gene is recommended for individuals where the diagnosis of Wilson's disease is challenging to confirm through clinical and biochemical tests [3]. It is also a valuable tool for screening first-degree relatives of affected patients [3].

The cornerstone of Wilson's disease treatment includes dietary copper restriction and lifelong oral pharmacotherapy [3]. Copper-chelating agents such as D-penicillamine and trientine are the first-line therapy for symptomatic patients with Wilson's disease, as both facilitate urinary copper excretion [4].

Zinc inhibits intestinal copper absorption by inducing intracellular metallothionein and promotes hepatocellular metallothionein production, potentially enhancing liver protection [3]. The only indication for discontinuing therapy is liver transplantation [4]. Liver transplantation is performed in above 5% of the patients, who present with acute liver failure at first disease presentation, or with signs of decompensations during liver cirrhosis [4].

First-degree relatives of individuals with newly diagnosed Wilson's disease should be screened for the condition [3]. Siblings of the proband have a 25% risk, while offspring and parents have a 0.5% risk of developing Wilson's disease [1]. Even if the diagnosis is ruled out during the initial screening, it is recommended that they should be monitored for symptoms of Wilson's disease every 6 to 12 months [1].

CONCLUSION:

This case highlights the critical need for systematic screening of family members of individuals affected by Wilson's disease. Clinicians should maintain a high index of suspicion, even in asymptomatic individuals, to facilitate early detection, prevent disease progression, and improve patient outcomes.

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