Research Article

# Wilson's Disease: Timely Diagnosis Is Real Challenge

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**ABSTRACT**

**Introduction**-Wilson's disease (WD) is a potentially fatal rare copper metabolism disorder which leads to copper accumulation in organs such as liver, brain, and cornea. Prompt diagnoses and treatments help prevent complications, improve patients' quality of life, and ensure a normal life expectancy. The clinical presentations and outcomes of WD can vary within a single family.
**Case Report-** A fourteen-year-old male presented with headache, generalized weakness and low mood level for last six months. He was seen by some local physician first who advised for routine labs and ultrasonogram (USG) abdomen which revealed mild transaminitis with normal USG. At this point, patient was referred to our department. On clinical examination, he had mild pallor, local eye examination showed suspected Kayser -Fleischer ring. The systemic examination including cardiovascular, chest, neurological and per-abdominal examination was essentially normal. The MRI brain showed bilateral basal ganglia calcification. The 24- hour urinary copper excretion was raised with low serum ceruloplasmin level. The fundus examination confirmed K-F rings. The upper gastro-intestinal endoscopy was normal and Fibroscan score was 9.2 Kpa, suggestive of significant fibrosis (F3) pattern. He was started on D-penicillamine (20 mg/Kg body weight) and 25 mg tid zinc and was symptomatically and biochemically better on follow up after three months.
**Conclusion-** Wilson's disease can have varied manifestations and can be easily missed in early stages. The timely diagnosis and initiation of management can lead to significant fibrosis reversibility. Early diagnosis and family awareness can prevent fatal outcomes.

**Keywords-** Wilson's disease, Pediatric, Fibrosis regression, D- penicillamine, Kayser-Fleischer rings, Exome sequencing.

## INTRODUCTION

Wilson's disease (WD) is caused by an inborn error of copper metabolism. The estimated prevalence in Europe, Asia, and the United States varies between 1:30000 to 1:50000 inhabitants but certain regions show higher estimated prevalence due to increased frequencies of disease-causing mutations and consanguinity [1]. WD is a monogenic autosomal recessive disorder, with a genetic defect on chromosome 13q14.3. More than a thousand mutations of the ATP7B gene are there which cause alteration of the copper-transporting ATPase beta protein, and modifying copper homeostasis [2]. Hepatic manifestations of WD range from asymptomatic presentations to acute liver failure and clinical findings include hepatomegaly, steatosis, or incidental elevations in aminotransferases and are common at the time of diagnosis. Neurological manifestations are varied and include dysarthria, gait disturbances, ataxia, dystonia, parkinsonism, and tremors. Psychiatric symptoms comprise personality and behavioural changes, depression, cognitive problems, and bipolar and psychotic disorders [3,4]. Kayser–Fleischer rings (K-F rings), observed upon slit lamp examination, are considered pathognomonic for WD; they result from copper deposition on Descemet's membrane, and are visualized as a brown or golden pigment [4-6]. Diagnostic and therapeutic delays are common, leading to neurological disability and hepatic complications. The diagnosis, on the basis of the Leipzig scoring criteria, involves both clinical and laboratory examination results. Brain magnetic resonance imaging (MRI) is valuable for visualizing copper deposition on damaged areas especially the basal ganglia. The 'face of the giant panda' sign is another finding considered pathognomonic for WD [3-6]. WD requires a lifelong treatment with a combination of oral pharmacotherapy and a copper-restricted diet, recommended for both symptomatic and asymptomatic patients. Treatment with chelating agents, such as D-penicillamine (DPA) or trientine, is recommended initially for patients with active disease, and an oral chelator at a reduced dose or zinc may be indicated for maintenance therapy [4]. Liver transplantation is reserved for specific cases, such as patients with progressive chronic liver failure resistant to pharmacotherapy and acute liver failure [4]. Children often present with acute liver injury or cirrhosis. Fibrosis regression is possible with prompt chelation, yet family history of early death emphasizes screening urgency.

## CASE REPORT

A fourteen-year-old male presented with headache, generalized weakness and low mood level for last six months. He was seen by some local physician first who advised for routine labs and ultrasonogram (USG) abdomen which revealed mild transaminitis with normal USG. At this point, patient was referred to our department. On clinical examination, he had mild pallor, local eye examination showed suspected Kayser -Fleischer ring. The systemic examination including cardiovascular, chest, neurological and per-abdominal examination was essentially normal. He had anemia with haemoglobin level of 9.3 g/dL which on evaluation was confirmed to be Coombs-negative haemolytic anemia. The total serum bilirubin was 1.7 mg/dL with AST 104 U/L and ALT 120 U/L. The alkaline phosphatase level was 223 U/L. The viral screen and autoimmune profile were negative. The MRI brain showed bilateral basal ganglia calcification. The 24- hour urinary copper excretion was raised to 3100 µg/day to with low serum ceruloplasmin level of 12 mg/dl. The fundus examination confirmed K-F rings. The upper gastro-intestinal endoscopy was normal and Fibroscan score was 9.2 Kpa, suggestive of significant fibrosis (F3) pattern. He was started on D-penicillamine (20 mg/Kg body weight) and 25 mg tid zinc and was symptomatically and biochemically better on follow up after three months.

## DISCUSSION

Our case highlights the early presentation of Wilson's disease, its timely diagnosis and initiation of treatment which is cornerstone and key to success in management. The main target is to catch patient early before development of cirrhosis and neurological involvement. The importance of family screening and multimodal approach cannot be denied. In our case, patient had only generalized weakness, low mood level, mild transaminitis and F3 fibrosis. The noticeable point was still not going in cirrhosis even at 14 years of age and prescence of K-F ring which is seen only in 5% of cases at this stage. The authors have already reported case series of Wilson's disease **[7]**. Wilson disease can have varied manifestations ranging from asymptomatic, acute or chronic hepatitis, cirrhosis, coomb's negative haemolytic anemia or neurological features. Hence, the treating Physicians, Gastroenterologist or Hepatologist should have broader vision for timely and proper evaluation of both typical and atypical findings of WD.

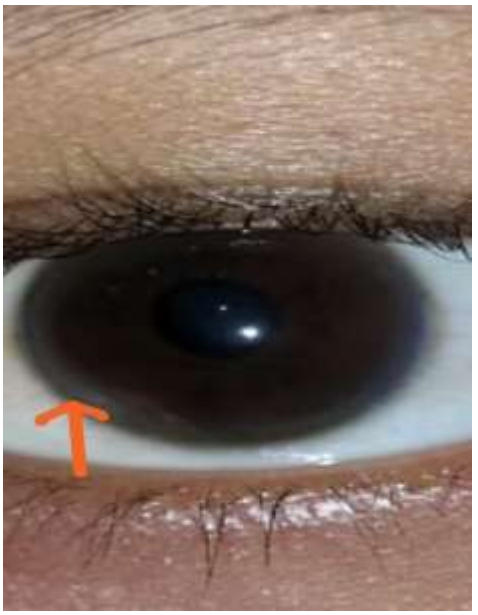

**Figure 1** – K-F Ring in Eye

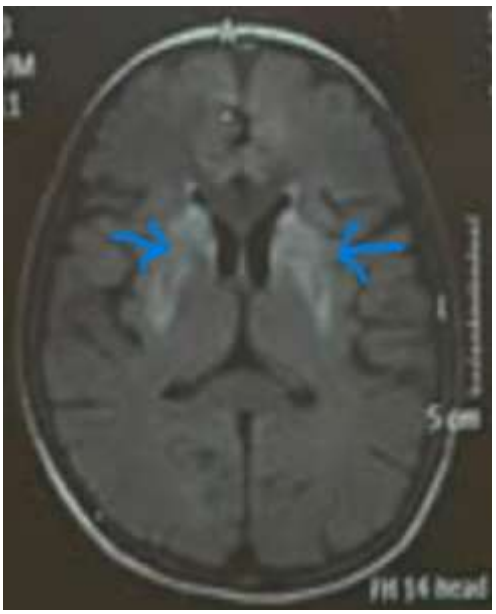

**Figure 2-** MRI Showing basal ganglia Calcification

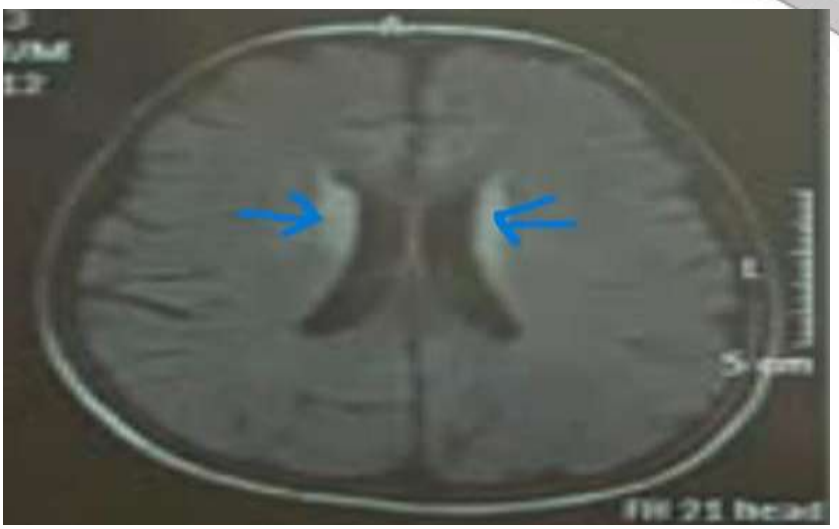

**Figure 3-** MRI brain showing calcification in peri-ventricular area

## CONCLUSION

Wilson's disease can have varied manifestations and can be easily missed in early stages. The timely diagnosis and initiation of management can lead to significant fibrosis reversibility. Early diagnosis and family awareness can prevent fatal outcomes.

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