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Curious Case of a Child with Wilson Disease: A Case Report

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ABSTRACT

Wilson disease is an autosomal recessive disorder occurs due to lack or dysfunction of transmembrane copper-transporting ATPase, causing accumulation of copper in liver, the nervous system, corneas, kidneys, and heart. Patient was asymptomatic at presentation even with the sign of Kayser Fleischer ring in the eye. Asymptomatic presentation of disease can have symmetric T2 and FLAIR high signal intensities in bilateral putamina in early age and absent T1 low signal intensity in these areas of the brain. Hence MRI needs to be done early to determine the disease early without considering age and symptom.Early finding of deposition of copper in brain without neurological presentation and abnormal Liver Function Test is rare and D-Penicillamine and Zinc was enough to decrease the progression of disease.

Keywords: *Case report; Child; Wilson disease.*

INTRODUCTION

Wilson disease (WD) is an autosomal recessive disorder caused by mutations of the ATP7B gene, with a reported prevalence of 1:30,000-50,000[1].ATP7B encodes an enzyme called transmembrane copper-transporting ATPase, which is essential for copper incorporation into ceruloplasmin and for copper excretion into the bile. A lack or dysfunction of this enzyme results in a progressive accumulation of copper in several organs, especially in the liver, the nervous system, corneas, kidneys, and heart.Children with WD can present with asymptomatic liver disease, cirrhosis, or acute liver failure, with or without neurological and psychiatric symptoms. Kayser–Fleischer rings are seen in most of the patients with neurologic involvement from Wilson disease. They are present in only 50% of the patients with isolated hepatic involvement and in pre-symptomatic patients[2].

Here, we report a rare case of Wilson disease diagnosed in a 13 yrs old asymptomatic male with visualization of the Kayser Fleischer ring .

CASE REPORT

A 13 years old male child referred from ophthalmology OPD with provisional diagnosis of Wilson disease (On slit lamp,greenish yellow deposition was noted on periphery of cornea on both eyes)along with complaint of dizziness. Child had visited Ophthalmology OPD for his annual eye checkup as he had been using glasses since he was 9 years for hypermetropia. He was using power +10.75(Left eye) and +9.75(Right eye) with spherical lens and -1.25 with 180 degree axis with cylindrical lens. Further evaluation regarding Wilson disease was done on Paediatric OPD. On examination, the child was active. On abdominal examination, splenomegaly was found,however, neurological examinations were normal. Child was advised for ultrasound (USG) of the abdomen and pelvis which revealed a diffusely coarse liver with irregular echotexture with irregular outline with borderline splenomegaly. Complete blood counts were within the normal reference range. His serum electrolytes, urea, creatinine and liver function test all were within normal reference range. However, "serum ceruloplasmin level was less than 0.10 g/L". 24 hours of

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urine was sent for evaluation of the amount of copper which was 825.47. Greenish yellow deposition was noted on the periphery of cornea on both eyes. With above mentioned eye finding and laboratory parameters, the patient was diagnosed as a case of Wilson's disease as per the American Association for study of Liver Disease guideline (the presence of Kayser-Fleischer rings, low serum ceruloplasmin concentration which is less than 20 mg/dL and elevated basal 24 hour urinary excretion of copper which is greater than 100 mcg/24 hours in symptomatic and greater than 40 mcg/24 hours in asymptomatic individual or children.

He then started on a copper free diet with 250 mg D-Penicillamine once a day, Zinc 20 mg twice a day. The patient's parents were advised to screen Wilson's disease.

DISCUSSION

Hepatolenticular degeneration, also known as Wilson's disease (WD), develops as a result of dyshomeostasis of copper. The amount of copper ingested with food and absorbed through the intestinal wall highly exceeds the demand of an organism. In healthy individuals, *ATP7B* protein, a specialized P-type ATP-ase, regulates and maintains the proper concentration of copper through its excretory activity. It is a transmembrane protein with several characteristic regions necessary for transport. Its cytosolic N-terminal domain can bind up to six Cu^{+} ion.[3] Mutation of the *ATP7B* alleles, which is the genetic background of WD, results in the formation of a defective protein leading to ineffective biliary excretion of copper and impaired ceruloplasmin synthesis (a major copper-transporting serum protein.[4] In the liver, a major copper excretory organ, copper is involved in the holo-ceruloplasmin synthesis. For both the delivery of copper to apoceruloplasmin and excretion of copper to bile, the activity of ATP7B protein is crucial. In WD, inherited dysfunctional ATP7B is responsible for the accumulation of copper in the liver, oxidative stress, and cellular damage that triggers inflammation. This may result in acute liver failure or fibrosis often progressing to cirrhosis, while in the case of the brain, this condition may result in the development of neurological and psychiatric symptoms.[5] The birth prevalence of the disease is currently estimated to be about 30 per million worldwide.[5]

include mild-to-aggressive and recurrent hepatitis, fulminant hepatic failure, hemolysis, and neurological or psychiatric symptoms such as an akinetic–rigid syndrome similar to Parkinson's disease, tremor, ataxia, dystonic syndrome, insomnia, seizures, depression, anxiety, and psychosis.[6,7] In our case patient was asymptomatic. Corneal deposits of copper, often observed in the patients with neurological manifestation of WD during clinical examination.[8] Our patient also presented with signs of deposition of copper in cornea, however neurological manifestation was absent. The estimated prevalence ranges from 1 in 30,000 to 1 in 100,000 live births.[1] In some cases, there may not be a family history of the disease or the disease may be caused by a de novo mutation. In these cases, a thorough clinical evaluation and genetic testing may be necessary to confirm the diagnosis.[9] Our case also did not have family history , so we advised the family to screen. In pediatric patients with WD, liver disease often presents as jaundice, abdominal enlargement, and abnormal liver function. Our case patient was asymptomatic. First, children may present with different symptoms than adults, such as failure to thrive, developmental delay, and behavioral changes, which can be easily misinterpreted as other conditions. Second, the onset of symptoms can be insidious, with some children remaining asymptomatic for years, making it difficult to link symptoms to WD.[9] There was no history of developmental delay, failure to thrive in our case, however he was asymptomatic. More than 90% of patients with a neurological presentation have Kayser-Fleischer rings, but less than 50% of cases show a hepatological presentation.[10] In our case, In our case, the Kayser-Fleischer corneal ring was present, however neurological symptoms were absent. Ceruloplasmin is an acute-phase reactant and its levels may be elevated in response to liver injury, making it difficult to interpret the results.[10] Approximately 5–20% of cases can have normal levels of ceruloplasmin due to elevation in response to inflammation or infection.[11] In our case even the patient was asymptomatic, KF ring found by ophthalmologist during annual eye examination for hypermetropia, suspect the provisional diagnosis of Wilson disease that made paediatrician to investigate in the view of Wilson disease where serum ceruloplasmin and 24 hrs urinary copper were sent decreased and raised respectively. MRI showed Symmetric T2/FLAIR high signal intensities are seen in bilateral putamina. No significant signal alteration noted in T1 weighted images. No abnormal signal changes seen in other deep gray matter nuclei, brainstem and rest of the brain. These findings are consistent with early neurological manifestations of WIlson's. High T2 signal in putamina is the most common signal abnormality seen in Wilson's disease.[12] Studies have found T1 low signal intensity to be present in these areas of signal changes in patients presenting with neurological manifestations, which is not seen in our patients. Furthermore, in patients presenting with hepatic dysfunction, manganese deposition will lead to T1 high signal intensity. This will depend on the degree of hepatic dysfunction.[12,13]

Although genetic testing has become a more important diagnostic tool for WD, the diagnosis remains based on both clinical features and laboratory investigations. The aims of treatment are to reduce copper levels and prevent its accumulation in the liver and other organs, especially in the central nervous system.[1] For WD patients

treated with chelating agents, adherence to the therapy is essential for long-term success.[1] Here in our case management was done in line of reducing copper levels and preventing its accumulation by D-Penicillamine and zinc. Patient is on regular outpatient follow up.

CONSENT

Case Report Consent Form was signed by the patient.

CONFLICT OF INTEREST

None

REFERENCES

1. Chanpong A, Dhawan A. Wilson disease in children and young adults - State of the art. Saudi J Gastroenterol. 2022 Jan-Feb;28(1):21-31. doi: 10.4103/sjg.sjg_501_21. PMID: 35042319; PMCID: PMC8919932.
2. Pandey N, John S. Kayser-Fleischer Ring. 2022 Jun 21. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–. PMID: 29083643.
3. Lutsenko S, Barnes NL, Bartee MY, Dmitriev OY. Function and regulation of human copper-transporting ATPases. Physiol Rev. 2007;87(3):1011–1046. doi: 10.1152/physrev.00004.2006. [PubMed] [CrossRef] [Google Scholar]
4. Terada K, Schilsky ML, Miura N, Sugiyama T. ATP7B (WND) protein. Int J Biochem Cell Biol. 1998;30(10):1063–1067. doi: 10.1016/s1357-2725(98)00073-9. [PubMed] [CrossRef] [Google Scholar]
5. Hadrian K, Przybyłkowski A. Toxic milk mice models of Wilson's disease. Mol Biol Rep. 2021 Feb;48(2):1903-1914. doi: 10.1007/s11033-021-06192-5. Epub 2021 Feb 15. PMID: 33590415; PMCID: PMC7925478.
6. Gheorghe L, Popescu I, Iacob S, Gheorghe C, Vaidan R, Constantinescu A, Iacob R, Becheanu G, Angelescu C, Diculescu M. Wilson's disease: a challenge of diagnosis. The 5-year experience of a tertiary centre. Rom J Gastroenterol. 2004;13(3):179–185. [PubMed] [Google Scholar]
7. Svetel M, Potrebic A, Pekmezovic T, Tomic A, Kresojevic N, Jesic R, Dragasevic N, Kostic VS. Neuropsychiatric aspects of treated Wilson's disease. Parkinsonism Relat Disord. 2009;15(10):772–775. doi: 10.1016/j.parkreldis.2009.01.010. [PubMed] [CrossRef] [Google Scholar]
8. Kayser B. Uber einen Fall von angeborener Grunlicherverfarbung der Cornea. Kiln Mbl Augenheilk. 1902;40:22–25. [Google Scholar]
9. Ungureanu IM, Iesanu MI, Boboc C, Cosoreanu V, Vatra L, Kadar A, Ignat EN, Galos F. Addressing the Challenges in the Diagnosis and Management of Pediatric Wilson's Disease-Case Report and Literature Review. Medicina (Kaunas). 2023 Apr 18;59(4):786. doi: 10.3390/medicina59040786. PMID: 37109744; PMCID: PMC10144359.
10. Gulhar R., Ashraf M.A., Jialal I. StatPearls. StatPearls Publishing; Treasure Island, FL, USA: 2023. Physiology, Acute Phase Reactants. [PubMed] [Google Scholar]
11. Menkes J.H. CHAPTER 108—WILSON DISEASE. In: Schapira A.H.V., Byrne E., DiMauro S., Frackowiak R.S.J., Johnson R.T., Mizuno Y., Samuels M.A., Silberstein S.D., Wszolek Z.K., editors. Neurology and Clinical Neuroscience. Mosby; Philadelphia, PA, USA: 2007. pp. 1447–1453. [Google Scholar]
12. Kim TJ, Kim IO, Kim WS, Cheon JE, Moon SG, Kwon JW, Seo JK, Yeon KM. MR imaging of the brain in Wilson disease of childhood: findings before and after treatment with clinical correlation. AJNR Am J Neuroradiol. 2006 Jun-Jul;27(6):1373-8. PMID: 16775300; PMCID: PMC8133926.
13. King AD, Walshe JM, Kendall BE, Chinn RJ, Paley MN, Wilkinson ID, Halligan S, Hall-Craggs MA. Cranial MR imaging in Wilson's disease. AJR Am J Roentgenol. 1996 Dec;167(6):1579-84. doi: 10.2214/ajr.167.6.8956601. PMID: 8956601.