Indian Journal of Basic and Applied Medical Research; March 2021: Vol.-10, Issue- 2, P. 28 - 32
DOI: 10.36848/IJBAMR/2020/26215.55562

Case Report:

Wilson disease: an unusual presentation- a case report

Ahmed S[1], Jannawar SB[1], Ambike DA[2], Maheshgauri R[3]

[1]Post-graduate student, Department of Paediatrics, PCMC's Post-graduate Institute, Yashwantrao Chavan Memorial Hospital, Pimpri, Pune, India

[2] Professor & Head of the Department, Department of Paediatrics, PCMC's Post-graduate Institute, Yashwantrao Chavan Memorial Hospital, Pimpri, Pune, India

[3] Professor & Head of the Department, Department of Ophthalmology, PCMC's Post-graduate Institute, Yashwantrao Chavan Memorial Hospital, Pimpri, Pune, India

Address for Correspondence:

Dr Deepali Ambike, Professor & Head, Department of Pediatrics, Postgraduate Institute & Yashwantrao Chawan Memorial Hospital, Pimpri, Pune, Maharashtra, India.

Email: ambikedeepa@gmail.com

Abstract:

Wilson disease, also known as hepato-lenticular degeneration, is an autosomal recessive genetic disorder due to a mutation of the ATP7B gene resulting in impaired hepatic copper excretion and copper accumulation in different organs. It is associated with the classic triad of cirrhosis, neurological manifestations, and the ocular finding of Kayser-Fleischer rings; however, the clinical presentation can vary greatly from incidental findings of abnormal liver enzymes to acute liver failure necessitating liver transplant. Paediatric patients may present with subtle findings including asymptomatic hepatomegaly, changes in behavior, movement disorders, or school failure. The general paediatrician may be the first to recognize these symptoms and should consider Wilson disease in their differential diagnosis. Wilson disease can be managed with lifelong chelation or zinc therapy in patients who present early in the disease. Hepatic manifestations tend to occur in the first decade and neurological symptoms in the third decade. Neurological manifestations are said to worsen with chelation therapy. In the case reported here, child presented with K-F rings without any neurologic symptoms which is seen on very rare occasions.

Key words: Wilson disease, Copper metabolism, Kayser-Fleischer rings

Introduction:

Wilson disease is a rare autosomal recessive disorder of copper metabolism, with a prevalence of about 1 in 30 000 people. It is characterised by a decreased biliary copper excretion and a defective incorporation of copper into ceruloplasmin, leading to copper accumulation in the liver, brain, cornea and kidneys.[1, 2] In 1993, the Wilson disease gene ATP7B was cloned. This gene codes for a membrane-bound, P-type copper-transporting ATPase expressed primarily in the liver.[3,4] Wilson disease may exhibit a variety of clinical symptoms, the most common being liver disease and neuropsychiatric disturbances.[5,6,7] Wilson disease typically begins with a presymptomatic period, during which copper accumulation in the liver causes subclinical hepatitis in the first decade, and progresses to liver cirrhosis and development of neuropsychiatric symptoms in 2nd and 3rd decades of life. The type of hepatic and neurological symptoms can be highly variable.Ophthalmic findings include K-F rings and sunflower cataracts[8].They do not impair vision. Other less common findings include night blindness,

exotropic strabismus, optic neuritis, and optic disc pallor[9].Wilson disease may also present as fulminant hepatic failure with an associated Coombs-negative haemolytic anaemia and acute renal failure.

Wilson disease invariably results in severe disability and death if untreated. The diagnosis of Wilson disease is based on the results of several clinical and biochemical tests.[10, 11, 12] Each of the diagnostic tests has its limitations, and only the combination of clinical, biochemical and genetic tests provides a powerful and reliable tool for the diagnosis of Wilson disease.The diagnosis is easily overlooked but if discovered early, effective treatments are available that will prevent or reverse many manifestations of this disorder.The available treatments are chelating agents (D-penicillamine and trientine) and zinc salts[13]. In general, the approach for treatment is dependent on whether the patient is asymptomatic or has symptoms, and on the predominant manifestation of the symptoms.

Case Report:

An eight-year old, Male Child, born by a non-consanguineous marriage, presented to our hospital with history of abdominal distension since 1 week with past history of yellowish discoloration of skin and sclera 6 months back, not associated with fever, for which the child received Ayurvedic medications(unknown) after which icterus apparently resolved. His parents were healthy, with no similar family history or medical history. General physical examination suggestive of pallor and icterus. Vitals were normal except Blood Pressure measuring more than 99th and 95th percentile systolic and diastolic readings respectively. Systemic examination revealed hepatomegaly (Liver span 13 cm), moderate grade ascites with shifting dullness and absent fluid thrill. Abdominal Girth was 68 cm on the day of presentation. Provisional diagnosis of hepatitis was assigned.

Ophthalmic examination revealed greenish brown ring at descemet's membrane level on slit lamp suggestive of Kayser-Fleischer ring which was not associated with oscillations, gaze paresis, or accommodative insufficiency. There was no history of night blindness. The patient had not given any history of trauma and there was no sign of any intraocular copper foreign body seen.

Laboratory findings revealed decreased Serum Albumin, A/G ratio < 1, Normal-to-slightly increased serum transaminases, slightly raised Total serum bilirubin and Direct bilirubin >50%, deranged Prothrombin time(PT) and activated partial thromboplastin time(aPTT). Normal kidney function tests observed. Urine Routine was within normal limits. Hemogram showed low haemoglobin, low platelet count, normal total leukocyte count, increased mean corpuscular volume (MCV) with peripheral smear suggestive of macrocytic anemia. Serum B12 levels were decreased.

Serum ceruloplasmin and 24-hour urinary copper levels were sent in view of Wilsons Disease (WD). Serum ceruloplasmin was 16 mg/dL and 24-hour urinary copper level was 800 microgram/L.

USG revealed coarse echotexture of Liver, Hepatomegaly, with normal PV and IVC calibre.

The patient was started on Zinc sulphate 75mg/day. Taking into consideration the cost-effectiveness and financial status of the parents, child was started on D- Penicillamine initially with 10mg/kg/day, empty stomach with 6hrs time interval between zinc and the chelator, along with Pyridoxine 25mg/day. Repeat CBC trend observed to see for any markers of Bone Marrow depression associated with D-Penicillamine.

Child improved over the course of the hospital stay. Icterus resolved clinically. Abdominal distension reduced with abdominal Girth measuring 60 cm on day of discharge. Vitals were within normal limits. The child did not show any signs of bleeding over the complete hospital stay.

Further plan is to monitor Hemogram, look for any adverse drug reactions and improvement over follow up with regular ophthalmic examinations for K-F rings, S. Ceruloplasmin and 24-hour urinary Copper levels at regular intervals of 3,6, and 12 months initially.

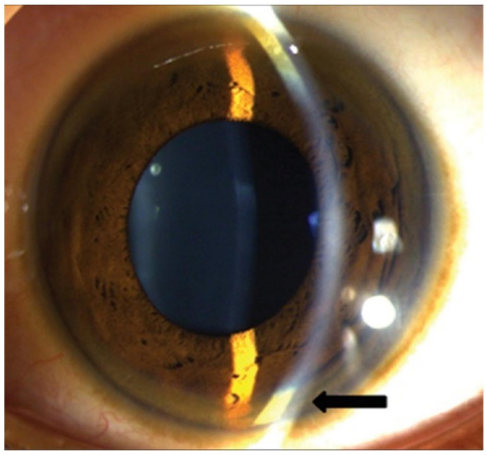

Fig 1: K-F ring demonstrable on Slit-Lamp examination

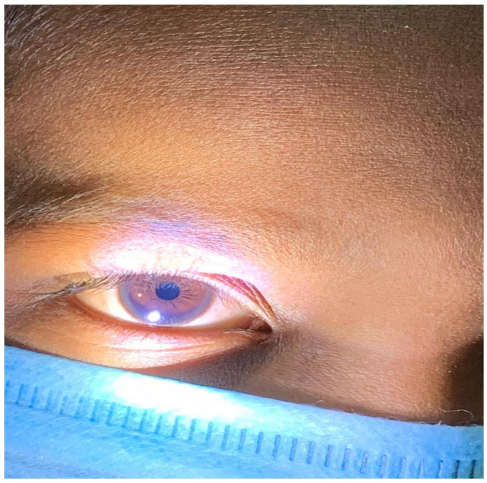

Fig 2: shows KF rings on bed-side torch examination

Discussion:

The patients with Wilson disease usually present with the liver disease in the first decade and develop neurological manifestations later on in 2nd decade of life, hence early diagnosis and starting of treatment for Wilson Disease is very essential in preventing the child from developing neuropsychiatric symptoms and liver cirrhosis.

K-F rings are absent in young patients with hepatic Wilson disease up to 50% of the time but are present in 95% of patients with neurologic symptoms. In the case reported above child presented with K-F rings without any neurologic symptoms which is seen on very rare occasions. Wilson Disease is one of the few liver diseases which can be treated and cured medically with only rare instances of surgical interventions when complications arise. Hence early Diagnosis and Management is the mainstay in the treatment of WD.WD requires lifelong medical therapy. Zinc therapy, Metal (Cu) Chelators have been found to have good results in the management of WD[14, 15] are regarded as standard care therapy in treatment of Wilson Disease. D-penicillamine and trientine

produce comparable outcomes, although D-penicillamine had a slightly higher rate of adverse events[15]. Keeping in mind the financial constraints of the parents, child was started on D- Penicillamine at our centre. However we could not rule out other causes of thrombocytopenia.

Conclusion:

As Wilson disease is a rare disease the diagnosis is likely to be missed. There should be a high index of suspicion in all cases of liver diseases when no clear cut etiology is being ascertained. Our patient was a defaulter as he didn't come for follow-up despite repeated telephonic communications.

Patient/Parents consent taken.

Compliance with Ethical Standards.

Conflict of Interest None

References :

1. Scheinberg I H. Wilson disease. J RheumatolSuppl 1981790–93. [PubMed] [Google Scholar]

2. Wiebers DO, Hollenhorst RW, Goldstein NP. The ophthalmologic manifestations of Wilson disease. Mayo ClinProc 1977; 52: 409–16.

3. Bull P C, Thomas G R, Rommens J M.et al The Wilson disease gene is a putative copper transporting P-type ATPase similar to the Menkes gene. Nat Genet 19935327–337. [PubMed] [Google Scholar]

4. Tanzi R E, Petrukhin K, Chernov I.et al The Wilson disease gene is a copper transporting ATPase with homology to the Menkes disease gene. Nat Genet 19935344–350. [PubMed] [Google Scholar]

5. Stremmel W, Meyerrose K W, Niederau C.et al Wilson disease: clinical presentation, treatment, and survival. Ann Intern Med 1991115720–726. [PubMed] [Google Scholar]

6. Gitlin J D. Wilson disease. Gastroenterology 20031251868–1877. [PubMed] [Google Scholar]

7. Roberts E A, Schilsky M L. A practice guideline on Wilson disease. Hepatology 2003371475–1492. [PubMed] [Google Scholar]

8. Cairns JE, Williams HP, Walshe JM. "Sunflower cataract" in Wilson disease. BMJ 1969; 3: 95–96

9.Richard JM, Friendly DS. Ocular fi ndings in pediatric systemic disease. PediatrClin North Am 1983; 30: 1123–44.

10.Schilsky M L. Wilson disease: genetic basis of copper toxicity and natural history. Semin Liver Dis 19961683–95. [PubMed] [Google Scholar]

11. Brewer G J. Recognition, diagnosis, and management of Wilson disease. ProcSocExpBiol Med 200022339–46. [PubMed] [Google Scholar]

12. Ferenci P, Caca K, Loudianos G.et al Diagnosis and phenotypic classification of Wilson disease. Liver Int 200323139–142. [PubMed] [Google Scholar]

13. Wiggelinkhuizen M, Tilanus ME, Bollen CW, Houwen RH. Systematic review: clinical efficacy of chelator agents and zinc in the initial treatment of Wilson disease. Aliment PharmacolTher. 2009 May 1;29(9):947-58. doi: 10.1111/j.1365-2036.2009.03959.x. PMID: 19210288.

14. Rodríguez B, Burguera J, Berenguer M. Response to different therapeutic approaches in Wilson disease. A long-term follow up study. Ann Hepatol. 2012 Nov-Dec;11(6):907-14. PMID: 23109455.

15. Weiss, K. H., Thurik, F., Gotthardt, D. N., Schäfer, M., Teufel, U., Wiegand, F., … Stremmel, W. (2013). Efficacy and Safety of Oral Chelators in Treatment of Patients With Wilson Disease. Clinical Gastroenterology and Hepatology, 11(8), 1028–1035.e2. doi:10.1016/j.cgh.2013.03.012

Indian Journal of Basic and Applied Medical Research; March 2021: Vol.-10, Issue- 2, P. 28 - 32
DOI: 10.36848/IJBAMR/2020/26215.55562

Date of Publishing: 05 March 2021
Author Declaration: Source of support: Nil, Conflict of interest: Nil
Ethics Committee Approval obtained for this study? NA
Was informed consent obtained from the subjects involved in the study? YES
For any images presented appropriate consent has been obtained from the subjects: NA
Plagiarism Checked: Urkund Software

DOI: 10.36848/IJBAMR/2020/26215.55562