

Kayser-Fleischer Ring as the Initial Presentation of Wilson Disease - A Case Report and Review of Literature

Dr. P. Rajasekhar MS¹, Dr. M. Parnikumar MS², Dr. J. Sahithi³

¹Assistant Professor, Department of Ophthalmology, Guntur Medical College, Guntur, A. P., India

²Professor of Ophthalmology, Guntur Medical College, Guntur, A. P., India

³Post Graduate in Ophthalmology, Guntur Medical College, Guntur, A. P., India

Abstract: An 18 year old female presented with bilateral Kayser Fleischer ring and bilateral sunflower cataract. There were coexisting hepatic symptoms. Her serology was positive for hepatitis B. Her ceruloplasmin levels were abnormal and ultrasound abdomen showed altered hepatic echogenicity. We report the interesting case of Wilson disease with characteristic ophthalmic manifestations where diagnosis of this condition plays a crucial role in the management and follow up.

Keywords: Kayser Fleischer Ring, Sunflower Cataract, Wilson Disease, Ceruloplasmin, Serum Copper

1. Case Report

An eighteen year old young female had been experiencing fatigue, anorexia, melena and mass per abdomen over the last several months developed fever, shortness of breath and puffiness of face over last 3 days. The patient was admitted for treatment and work up of undiagnosed condition in medical ward and referred to ophthalmology OPD for the evaluation of Kayser Fleischer ring. On examination she had pallor, icterus and oedema of face. She also had basal crepitations on auscultation, hepatomegaly and splenomegaly on palpation of abdomen. Slit lamp examination revealed the presence of bilateral pronounced greenish brown Kayser Fleischer ring and bilateral sunflower cataracts. Visual acuity in both eyes was 6/6 and extraocular movements were normal. Gonioscopy also showed the greenish brown pigmentation on trabecular meshwork extending upto schwalbe's line.



Figure 1: Showing Kayser-Fleischer ring

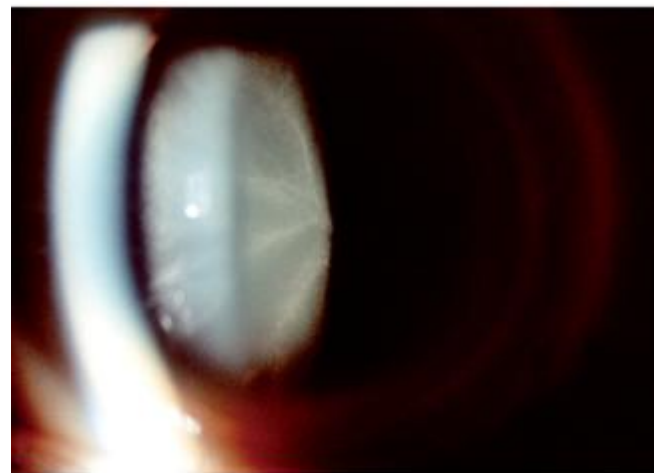


Figure 2: Showing Sunflower cataract

Routine investigations showed haemoglobin level as 9.8g% and E.S.R. was 120 mm/1st hr. Liver function tests revealed Serum Bilirubin I .4mg% with all other tests being normal. Serology was positive for Hepatitis B. Free Serum Copper was 122 mcg/dL. Serum ceruloplasmin was 5 mg/dL. Ultrasound abdomen showed reduced hepatic echogenicity, peri Gall bladder oedema, prominent portal vein and massive splenomegaly.

2. Discussion

Pathophysiology

Wilson Disease is caused by mutation in the copper-transporting gene ATP7B on chromosome 13, which facilitates the transfer of copper into the Golgi apparatus where it combines with ceruloplasmin or other proteins like cytochrome oxidase. Failure of this process leads to instability and decreased half life of ceruloplasmin and paradoxical ceruloplasmin deficiency. The free circulating copper (which is toxic as it inhibits enzymatic processes) accumulates in liver cytosol resulting in hepatocyte

degeneration and cirrhosis. When the sites for copper binding in the liver are saturated, free copper is released into the circulation and accumulates in other tissues like the eye, brain (basal ganglia) and kidneys amongst others leading to morphological changes, functional derangements and clinical manifestations. Wilson disease has variable presentations with hepatic or neuropsychiatric manifestations or sometimes presymptomatic patients present with Kayser Fleischer ring. Wilson disease has incidence of 1 in 30,000.

Kayser Fleischer Ring

The ring is reported more frequent in H1069Q (most frequent mutation in Wilson Disease in Hungary) homozygous patients, with higher mean age at diagnosis than patients heterozygous or negative for H1069Q. This may suggest a genetic predisposition. Kayser–Fleischer ring was first described by Bernhard Kayser [1902] and Bruno Fleischer [1903]. It is present in 95% of patients with neurologic symptoms. It is seen in only 40% of pre symptomatic patients, and in 65-70% of patients with hepatic manifestations. In children presenting with liver disease, Kayser–Fleischer rings are usually absent.

The K-F ring is believed to be formed by the copper particles which infiltrate into Descemet's membrane through the endothelial cells from the aqueous humor. The smaller particles coalesce over a period of time to give rise to larger deposits, granules which may or may not be in zones. This 'corneal chelate' accounts for the K-F ring. It is seen simultaneously in both eyes, when associated with systemic disorders. However, Innes *et al.* have reported a case of unilateral K-F ring in a patient with Wilson Disease. This patient had a scarred eye (with low intraocular pressure and reduced aqueous production) which did not show the K-F ring. Hence they postulated that the copper deposition is through the aqueous (which was markedly reduced in the scarred eye), rather than limbal circulation (which was normal in the scarred eye). Moreover, it may not be just due to passive diffusion but may be attributed to cellular activity, the copper granule production being related to formation of the basement membrane by endothelial cells.

The density of Kayser Fleischer ring correlates with the severity of disease. They are not entirely specific for Wilson's disease, since they may be found in patients with chronic cholestatic diseases. K F ring could fade or disappear with chelation [80-90%] or liver transplantation. The ring tends to disappear in the reverse order of its formation. But it is not a good predictor of clinical improvement. Its reappearance while on therapy indicates noncompliance.

3. Sunflower Cataract

Other rare characteristic feature with prevalence of 17% in Wilson's disease, which is caused by deposits of copper in the capsule and subcapsular cortex of the lens. Sunflower cataract in Wilson disease was first described by Siemerling and Oloff [1922].

4. Importance of Kayser Fleischer Ring

Identification of the K-F ring in any patient with unexplained central nervous system disease, poorly categorized psychiatric disorder, abnormal liver function tests, chronic active hepatitis, cirrhosis of liver, rickets, renal tubular acidosis, unexplained Coomb's negative hemolytic anaemia, especially if there is a relation with WD or any of the conditions mentioned above should prompt the physician to undertake diagnostic workup for WD. At times, the K-F ring could be the first detectable manifestation of WD and in such rare instances, ophthalmologists play a critical role in the early recognition of WD. Larger K-F ring size may correlate with the severity of the disease, but not necessarily with the magnitude of urinary copper excretion. It is one of the clinical parameters used in monitoring patients on therapy although its reduction is not necessarily a good predictor of clinical improvement. Its reappearance while on therapy may indicate non-compliance. Kayser-Fleischer ring detection is one of the screening tests for first-degree relatives of a WD index case. Early detection and treatment of WD may prevent the associated morbidity and mortality of the disease.

5. Conclusion

Wilson disease is a rare condition caused by deficiency of ceruloplasmin resulting in widespread deposition of copper in tissues. The characteristic pigmentation of cornea in the form of Kayser-Fleischer ring and pigment deposition in the lens as sunflower cataract which were present in this case are pathognomonic signs of Wilson disease.

References

- [1] Kim HB, Kim JC, Byan YJ. Kayser Fleischer ring in Wilson's disease. *J Korean Ophthal Soc* 1979;20:129-31.
- [2] Innes JR, Strachan IM, Triger DR. Unilateral Kayser-Fleischer ring. *Br J Ophthalmol* 1986;70:469-70.
- [3] Belkin M, Zeimer R, Chajek T, Friedman G, Melamed E. Non-invasive quantitation of corneal copper in hepatolenticular degeneration (Wilson's disease). *Lancet* 1976;1:391-4.
- [4] Gotto J, Williams R. Wilson's disease: Diagnosis and current treatment options. *Prescriber* 2005;16:25-30.
- [5] Folhoffer A, Ferenci P, Csak T, Hovarth A, Hegedus D, Firneisz G, et al. Novel mutations of the ATP7B gene among 109 Hungarian patients with Wilson's disease. *Eur J Gastroenterol Hepatol* 2007;19:97-9.
- [6] Bajart AM, Pavilack MA. Conjunctiva, cornea and sclera. In: Albert DM, Jakobiec FA, Robinson NL, editors. *Principles and practices of ophthalmology*. 1st ed. Philadelphia: WB Saunders; 1994. p. 294-319.
- [7] Lossner A, Lossner J, Bachmann H, Zotter J. The Kayser Fleischer ring during long-term treatment in Wilson's disease (hepatolenticular degeneration): A follow-up study. *Graefes Arch ClinExp Ophthalmol* 1986;24:152-5.