Fading Kayser–Fleischer ring revisited

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Abstract:
Kayser-Fleischer (KF) ring, caused by deposition of excess copper in the Descemet membrane, is a characteristic ocular manifestation of Wilson disease (WD). Disappearance of KF rings following successful treatment of Wilson disease is typically a slow process that occurs over years. Herein, we describe a 19-year-old girl who presented with neuropsychiatric manifestations and was found to have KF rings on slit lamp examination. Subsequent evaluation (brain imaging, liver function tests, serum ceruloplasmin and urinary copper studies) confirmed a diagnosis of Wilson disease with neurological and hepatic involvement. She was treated with d-penicillamine. She had remarkable fading of KF rings within a span of 6 months of copper-chelating therapy, which was also associated with significant improvement in her neurological symptoms. Though KF rings are a harbinger of neurological Wilson’s, their disappearance does not always correlate with systemic improvement – an interesting finding in this case.

Keywords: KF ring, Wilson disease

Introduction
Wilson disease (WD) is an autosomal recessive disorder caused by the mutations of ATP7B gene that brings the binding of copper to ceruloplasmin and eliminates excess copper into bile. The clinical features of WD occur due to impaired biliary excretion and the resultant accumulation of copper in the liver and extrahepatic sites such as brain, kidney, cornea, and heart. The manifestations include neurological symptoms (such as dystonia, coarse tremors, dysarthria, and behavior disturbances), hemolytic anemia, chronic liver failure, and cardiomyopathy. In the Descemet’s membrane, free copper from the aqueous humor loosely binds to albumin and is deposited in the form of Kayser–Fleischer (KF) rings. They are observed in a significant proportion of WD patients with systemic involvement – ranging from 59% in presymptomatic cases to 100% in those with neurological manifestations. Following successful treatment with penicillamine and after liver-transplant, the KF-rings may resolve partially or completely in the reverse order of their appearance – a process that typically takes several years. We report the case of a 19-year-old girl diagnosed with WD with frank psychiatric manifestations and KF rings which dramatically faded in a short span of 6 months following medical treatment.

Case Report
A 19-year-old girl with no known past medical history was brought to the psychiatry department by her mother for complaints of aggressive behavior and poor scholastic performance with difficulty in concentration for the last 2 years. She also had intermittent intention tremors of the hands since the age of 15 years and involuntary movements suggesting typical batwing tremors. Her systemic evaluation including neurological examination was within the normal limits. Slit-lamp examination revealed bilateral heavily pigmented KF rings in the Descemet’s membrane of both eyes [Figures 1a, b and 2a, b]. Her complete blood count was normal. Serum biochemistry workup revealed total bilirubin of 9.2 mg/dL (reference range: 0.2–1.0 mg/dL); aspartate aminotransferase of 107 U/L (reference range: 15–37 U/L); alanine aminotransferase of 72 U/L (reference range, 12–78 U/L); alkaline phosphatase of 150 U/L (reference range: 40–140 U/L); serum ceruloplasmin of 73 mg/dL (reference range: 90–160 mg/dL); and urinary copper of 188 mcg (reference range: 0–50 mcg).

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phosphatase of 30 U/L (reference range, 50–136 U/L); as well as low serum levels of ceruloplasmin (0.02 g/L; reference range, 0.2–0.5 g/L). Her 24-h urinary copper excretion was elevated at 85.6 μg/day (reference range, 3–50 μg/day). Abdominal ultrasound study depicted chronic liver parenchymal disease with small, shrunken liver with coarse echotexture and nodular surface with splenomegaly. Magnetic resonance imaging of the patient’s brain revealed nearly symmetrical T2/FLAIR hyperintensities involving bilateral basal ganglia, thalami and midbrain, especially posterior pontine region (Figure 3). A diagnosis of WD was made, and she was started on copper-chelating treatment with oral d-penicillamine. After 6 months of therapy, the pigmentation of Kayser–Fleischer rings has faded considerably (Figures 5 and 6) with concomitant improvement in behavioral abnormality and tremors. The patient is continuing the d-penicillamine treatment.

**DISCUSSION**

WD, a rare but major metabolic disorder involving copper metabolism, is found worldwide, with an estimated prevalence of 1 case/30,000 live births in most populations,[5] Hepato-lenticular degeneration is usually detected during adolescence; half of the patients have onset before 16 years of age and gradual copper accumulation in the liver eventually leads to the development of cirrhosis. Among patients with neurologic involvement, the disease may progress until the patient becomes severely dystonic, akinetic, and mute. A retrospective analysis of 282 patients by Taly et al. found that manifestations in WD include neurologic deficits (69.1%), hepatic abnormalities (14.9%), pure psychiatric symptoms (2.4%), and osseo-muscular dysfunction (2.1%), whereas 5.3% patients were presymptomatic.[5]

The classical ophthalmological finding is the presence of the Kayser–Fleischer ring, which is considered pathognomonic of WD. In the Descemet’s membrane, free copper from the aqueous humor loosely binds to albumin and is deposited in the form of KF rings, evaluated on slit-lamp examination.
On anterior segment-optical coherence tomography, KF ring is visualized as intense hyperreflectivity at the level of Descemet’s membrane in the peripheral cornea.[6]

In the case discussed here, medical treatment of an adolescent female with oral d-penicillamine resulted in quick reversal of KF ring in a short span of 6 months along with significant improvement in neurological features and cognitive abilities. Although gradual regression of KF ring has been reported in the literature, the process is unrelated to improvement of systemic manifestations. Treatment with d-penicillamine causes the ring to disappear, in the reverse order of its formation.[6] Very slow regression of KF ring over 12 years was noted in a case reported by Heckmann et al. on the treatment with oral penicillamine.[7] In another case series of 4 WD patients who underwent liver transplantation, disappearance of KF ring was noted in variable duration of time over years.[9] To the best of our knowledge, this expeditious fading of KF ring with simultaneous improvement of systemic symptoms has not been reported.

Medical treatment options for WD are drugs that chelate copper and those that prevent gastrointestinal copper absorption. In the order of their introduction into clinical practice, available copper chelators are dimercaprol, penicillamine, dimercaptopropane sulfonate, and trientine. It runs an invariably fatal course if not adequately treated by decoppering therapy.[9] Progression is usually gradual, but sudden deterioration may also occur. Most patients will die from liver disease (cirrhosis or acute liver failure), while a significant proportion die due to complications from progressive neurologic disease.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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