Clinical picture

The eye in Wilson disease

Although the distinctive and diagnostically valuable signs present in the eyes of patients with symptomatic Wilson disease have been described in specialist journals and in monographs\(^1,2\) on this disease, they have received little attention in the general literature. Furthermore, they have not been definitively illustrated. These are the Kayser-Fleischer (KF) rings (Figure 1) and the sunflower cataracts. As a result, many physicians, although they know of such signs, have never seen them or as a result may have missed them when present, as did Wilson\(^3\) himself in his original description of the disease which now bears his name. Indeed, for many years he denied that they were related to this condition. The rings were first described by Kayser in 1902 and then by Fleischer in 1909.\(^4,5\)

The fact that the rings are composed of copper was finally established by Gerlach and Rohrschneider as late as 1949,\(^6\) shortly after Cumings\(^7\) had demonstrated that excess copper was deposited in the brains and livers of patients dying of this disease. That the corneal rings were indeed due to copper deposition was confirmed by Sternlieb.\(^8\) Originally, it was believed that the presence of such copper containing rings were diagnostic of Wilson disease but in 1975 Fleming and his associates\(^9\) were able to show that such copper deposits in the cornea could also be found in patients with primary biliary cirrhosis and in 1977 they also recorded the presence of such rings in other forms of chronic liver disease especially those associated with long-term cholestasis.\(^10\)

The sunflower cataract was first described by Seimerling and Oloff in 1922\(^11\) and they noted the similarities between the cataract seen in their patient with Wilson disease to that produced by an intraocular foreign body containing copper. This was not, in fact a true cataract as the changes were in the lens capsule and did not affect vision. When viewed with the naked eye, the appearance was of a greenish disc in the centre of the pupil (Figure 2), and when the pupil kept dilated the disc was said to increase proportionally in size.\(^12\)

Viewed with a slit lamp, the appearance in the anterior capsule of the lens, according to Duke Elder,\(^13\) was of radiating fronds said to correspond to folds in the iris while in the posterior capsule it was uniform and without pattern. Cairns \textit{et al.}\(^14\) on the other hand demonstrated that it was the anterior capsule that had the uniform disc and the petal-like fronds were on the posterior capsule and that they had no relationship to the folds in the iris was also noted. They were also able to show that, unlike the claim of Boudin and Pepein,\(^1\) the cataract was only a late manifestation of copper overload; in their patient and it was one of the presenting signs (Figure 3).

The rings have been described as brown or green in appearance though I have yet to see a green ring. However, when the rings were photographed with infrared film they did appear green (Figure 4). When viewed over a brown iris the rings may appear grey (Figure 5). The natural history of the KF ring is to appear first as a top crescent in the top arc of the cornea from 10 to 2 O’clock, then correspondingly in the inferior crescent eventually joining laterally to form the complete ring. The pigment deposition first appears peripherally, where it is densest, and extending centrally seldom exceeding 5-mm in depth.\(^13\) The microscopic appearances were described by Uzman and Jakus.\(^16\)

They reported two zones of pigmentation at 2 and 0.6 U from the endothelial surface of Descemet’s membrane; some of the pigment granules being as large as 0.35 U. On the other hand, Scheinberg and Sternlieb,\(^2\) using electron microscopy, found three discrete layers of copper containing granules in the same zone as reported by Uzman and Jakus. This was not in keeping with the appearance of the cornea when photographed using a slit lamp and gonioscope (Figure 6). The reason for the deposition of copper first in the superior and then the inferior crescents, as was suggested by Cairns and Walshe,\(^15\) was due to the vertical flow of aqueous fluid in the anterior
chamber of the eye leaving these crescents more freely irrigated by the metal.

Once decoppering treatment was started, copper was removed from both the lens capsule and the corneal rings. The first description of clearing of a cataract was by Cairns et al.\textsuperscript{14} and in their patient the cataract was resolved before the corneal rings. Removal of copper from the rings starts in reverse order to deposition. First the rings are thinned and then broken laterally after which the top and bottom crescents thin and, in most cases disappear completely (Figure 7) but this may take several years. They also showed that as copper is removed from the cornea it leaves pits or scars with the appearance of beaten metal, a valuable sign that a ring is resolving. False KF rings have been described by Scheinberg and Sternlieb\textsuperscript{2} and also by Cairns and Walshe.\textsuperscript{15} They also showed that in their patient, the
rings, though on superficial inspection were identical to true copper rings, on slit lamp examination were in a different layer of the cornea and were homogeneous and not granular. Careful regular inspection of the status of the rings during treatment is a valuable index of the copper status of the patient and of the efficacy of therapy (Walshe JM, submitted for publication).

In the experience of Scheinberg and Sternlieb,2 corneal rings are always present in neurological Wilson disease but not necessarily so in pre-symptomatic and hepatic stages of the disease. This is also my experience in over 300 cases. However, there have been some reports of rings being absent in neurological cases. There are two possible explanations of this: early, lightly pigmented rings may have been missed by inexperienced observers not using a slit lamp and gonioscope; or the diagnosis may have been incorrect. A known phenomenon for this disease.17

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Conflict of interest: None declared.

References


Figure 7. The eye from Figure 2, after treatment with penicillamine. The KF ring and cataract have been resolved.