Medical Memoranda

"Sunflower Cataract" in Wilson's Disease

[WITH COLOUR PLATE FACING PAGE 97]

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Copper deposition in the cornea giving rise to the classical Kayser-Fleischer ring is one of the few diagnostic signs in clinical medicine, and it is always found in patients with Wilson's disease once the nervous system is involved. In the early hepatic stage of the illness, when pigmentation is relatively light, it may be difficult to see the copper granules, but these can probably be detected in most if not all cases by slit-lamp examination and gonioscopy. A much less common ocular manifestation of Wilson's disease is the so-called "sunflower cataract," and although this has been relatively well documented in the German literature it has received little attention in English-language journals (see Cumings, 1959). The sunflower cataract was first described by Siemerling and Oloff (1922), who pointed out the similarities between the lens changes they observed in a patient with Wilson's disease and those produced by an intraocular foreign body containing copper. Boudin and Pépin (1959) described the cataract as a rare and late manifestation of Wilson's disease associated particularly with the "pseudosclerotic" form of the illness.

During the past six years we have been able to study the case of a girl who presented with emotional instability and loss of control of fine movements of only three months' duration. After admission to hospital she was found to have green opacities in her lenses, and this led directly to the correct diagnosis of Wilson's disease. These lens abnormalities are described in detail below, together with the changes which were observed during the course of treatment with penicillamine.

CASE REPORT

The patient was born on 4 May 1950 of unrelated parents. Her early development was uneventful and she had an excellent school record, always being near the top of her class. In December 1962 it was noticed, both at home and at school, that she was becoming emotional, that she was finding her school work increasingly difficult, and that her handwriting was deteriorating. It was also noticed that her speech had become slurred, and there appeared to be increasing difficulty in the execution of fine movements, such as writing, doing up buttons, and feeding herself. The patient complained, "My fingers curl inwards and my toes turn under." She also admitted that her gait was "peculiar" because she dragged her right leg. She tired easily and had to be taken to school by car.

She was sent to a child guidance clinic, where she was found to have an I.Q. (Stanford-Binet) of 122. She was then referred to the paediatric outpatient clinic at the Coventry and Warwickshire Hospital, where she was admitted under the care of one of us (H. P. W.).

There was one sibling, a brother aged 18, who was clinically normal. Examination showed her to be an attractive left-handed girl of normal height and weight for her age. At times she had a vacant look, with open mouth and drooling; at other times she was tearful and upset. She had one prominent vascular spider on her neck and one on her left hand. Her heart and lungs were normal, and in the abdomen the liver and spleen could not be felt.

Her eyes showed bilateral Kayser-Fleischer rings, bilateral sunflower cataracts, and deposits of copper on the posterior surface of the cornea, on the anterior and posterior lens surfaces, and in the vitreous (Colour Plate, Fig. 1).

In the central nervous system the cranial nerves were normal, apart from a spastic tongue with slurred speech, and there was a fine tremor of both hands at rest which became more marked on movement, so that she had great difficulty in doing up buttons and

tying shoelaces, and this was associated with considerable emotional upset. She could not walk without support. Her tendon reflexes were brisk and the plantar responses flexor. Preliminary investigations showed a depressed level of serum copper, a raised urine copper excretion, a mild generalized amino-aciduria, but normal liver-function tests. At this stage she was started on treatment with penicillamine HCl, the dose being rapidly built up to 300 mg. three times a day, and on this the urine copper excretion rose to 3,400 $\mu\text{g.}/24$ hours. Within three weeks of starting treatment her tremor was greatly diminished and she was able to uncurl the fingers of her left hand for the first time in weeks; drooling also decreased and she was able to walk without support, though she tired easily.

In July 1963 she was transferred to Addenbrooke's Hospital, Cambridge, for additional studies of her copper metabolism. Penicillamine was stopped during the course of these investigations. The serum ceruloplasmin was 1 mg./100 ml. and the serum copper 33 $\mu\text{g.}/100$ ml. The urine copper excretion varied between 344 and 503 $\mu\text{g.}/24$ hours. After a test dose of penicillamine HCl 600 mg. the serum copper concentration fell to 24 $\mu\text{g.}/100$ ml. and the copper clearance rose from 0.6 to a maximum of 19.5 ml./minute, and in six hours she excreted 875 $\mu\text{g.}$ of copper. Studies with radiocopper showed no incorporation of copper into ceruloplasmin, the 24/2-hour ratio was 0.21 (normal greater than 0.8). Less than 2% of the plasma radiocopper passed through a semipermeable membrane, but after the addition of penicillamine to the plasma (3 mg./ml.) 100% of the copper became available for filtration at both 2 and 24 hours after administration of the radiocopper. Normally not more than 25% can be mobilized by this technique. At this point she was able to return home, taking D-penicillamine HCl 450 mg. three times a day.

About six months after starting treatment she had improved greatly, and though still tiring easily she was able to return to school. After 18 months of treatment she was virtually free of signs in her nervous system, but the Kayser-Fleischer rings and sunflower cataracts were unchanged. Her penicillamine dose was reduced slightly to 600 mg. twice a day. Three years after the start of treatment she was extremely well and hoping to learn shorthand-typing after leaving school. She was free of abnormal physical signs, the Kayser-Fleischer rings were fading, and the chalcosis of the lens was decreasing. It was at this stage that the lens changes were painted by Mr. T. R. Tarrant at the Institute of Ophthalmology in London (Colour Plate, Fig. 2). At this time also there was a marked reduction in the serum copper, the urine copper, and the amount of copper excreted after a test dose of penicillamine. By the summer of 1968, five years after treatment was started, she had developed into a tall good-looking self-possessed girl, with no signs of her disease. She was trained as a shorthand-typist, though she admitted she could not quite achieve the normal speed of shorthand—but this is always difficult for left-handed individuals. Her serum copper and urine copper had reached extremely low levels. There was no evidence of penicillamine toxicity, but the xanthurenic acid excretion after a tryptophan load had risen to the upper limit of normal, suggesting borderline pyridoxine deficiency. Her Kayser-Fleischer rings were reduced to top crescents only and the lenses were virtually normal. She was seen again in December 1968 for slit-lamp photography of her eyes (Colour Plate, Fig. 3), which showed the complete clearance of the copper deposits from the lenses. Details of the relevant laboratory tests are given in the Table.

Biochemical and Clinical Changes During Treatment with D-penicillamine HCl

Date	Serum Ceruloplasmin (mg./100 ml.)	Serum Cu ($\mu\text{g.}/100$ ml.)	Urine Cu ($\mu\text{g.}/\text{day}$)	Urine Cu (on Penicillamine) ($\mu\text{g.}/6$ Hours)	C.N.S. Disability	Lens Changes	Penicillamine Dose (mg./day)
7/63	1	33	503	875	3+	3+	450 x 3
12/64	0	19	47	579	±	3+	600 x 2
4/66	0	16	27	362	0	2+	600 x 2
8/67	0	10	7	295	0	1+	600 x 2
7/68	0	6	39	333	0	0	600 x 2
Normal	> 27	> 90	< 50	< 400			

COMMENT

This case provides several features of unusual interest in the understanding of the lenticular changes due to copper deposition.

Rarity of Copper Deposition in the Lens in Wilson's Disease.—The factors governing the deposition of the copper are not known. This case appears to show that the deposition is not necessarily a late manifestation of the disease, as claimed by Boudin and Pépin (1959). Although rare, sunflower cataracts in Wilson's disease have been reported by Fleischer (1922), Siemerling and Oloff (1922), Vogt (1926, 1929a, 1929b), Jess (1929), Rohrschneider (1934), and Thiel (1934).

Classical Appearance of Sunflower Cataract.—As described by Duke-Elder (1954), the appearance of sunflower cataract is that of a central green disc in the anterior capsule of the pupillary area, with radiating petals thought to correspond to the folds on the posterior surface of the iris. When posterior capsular deposition occurs, it is said by the same author to be uniform and without pattern. In support of his contention that the radiating petals are due to the folds on the posterior surface of the iris he cites the observations of Jess (1929, 1930), that if the pupil is kept dilated the central disc increases in size; of Hillemanns (1896), who showed that with a deformed pupil the central disc took the shape of the deformed pupil; and of Belz and Bonnet (1948), who observed a case with a hole in the iris in which a disc appeared behind the false pupil as well as behind the true pupil.

As seen in Fig. 2, the anterior lens capsule showed a simple disc of chalcosis, while the posterior lens capsule showed frond-like petals of deposition. This observation suggests strongly that the iris is not responsible for the characteristic sunflower pattern of discoloration, since, as in the above case, this may be present in the posterior lens capsule.

Clearing of Copper from the Lens.—The disappearance of copper from an avascular region like the lens following the recovery from the central nervous system lesion further shows the close relation of copper to the pathogenesis of the disease. This late disappearance of the metal from the lens suggests that after the body-stores of copper have been depleted by treatment with D-penicillamine the serum falls below a critical level, which then permits the relatively rapid resorption of the copper deposits in the lens.

The spontaneous clearance of copper deposition from the lens has been reported in chalcosis due to retained copper-containing foreign bodies by Zur Nedden (1903), Oloff (1926), Clausen (1930), Záhör (1930), Blake (1931), Müller (1931), Cordes and Harrington (1935), Marner (1945), and Belz (1952).

In all reported cases the process of clearing has been slow, and in some it has been incomplete. No case report has come to our notice recording the disappearance of copper from the lens in a case of Wilson's disease. The disappearance of Kayser-Fleischer rings is, however, well recognized. In the present case the rings survived the lens deposits, but were much attenuated.

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Appendicitis Presenting as Infection of Right Thigh

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CASE HISTORY

Ten days before his admission to hospital a 68-year-old man visited his doctor complaining of pain in the right flank. The pain had started four days previously and was described as like heart-burn. There was no vomiting or any urinary symptoms. Tenderness was present well out in the right iliac fossa, with some guarding. Rectal examination showed no abnormality. Four days later he developed anorexia and vomiting. His bowels were regular. After three further days he was visited at home on complaining of pain in the right femoral triangle. There was no pyrexia and the pulse

rate was not raised. Three days later he was admitted to hospital with an obvious infection of the right thigh with subcutaneous crepitus.

Examination showed an obese man who did not look particularly ill. His temperature was 98° F. (36.7° C.), pulse rate 96, and blood pressure 120/80. The abdomen was soft with no localized tenderness. The right thigh was swollen, red, and tender, and there was diffuse palpable crepitus. All movements of the right hip-joint were limited and painful.

He was given 8 ml. of anti-gas-gangrene serum, and penicillin 500,000 units six-hourly and streptomycin 1 g. twice daily were started. Under general anaesthesia multiple incisions made into the right thigh produced only a little foul-smelling pus from the region of the adductor muscles. Aerobic and anaerobic culture resulted in a growth of non-haemolytic streptococcus.

The patient recovered well from the anaesthetic, and the following day his condition was entirely satisfactory. On the second day

J. E. CAIRNS *ET AL.*: "SUNFLOWER CATARACT" IN WILSON'S DISEASE

FIG. 1.—1963. Copper deposits in lens before treatment with penicillamine.

FIG. 3.—December 1968. Lens, photographed as in Fig. 1, showing total clearing of copper deposits after treatment with penicillamine.

Anterior lens surface.

Posterior lens surface.

FIG. 2.—1966. Copper deposits in lens. Painting (Mr. T. R. Tarrant) of anterior and posterior lens surfaces and optical section of lens (arrowed).