

XANTHOMA CORNEAE AS HEREDITARY DYSTROPHY*

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A PATIENT presented herself in 1944 at the Kivelä Hospital Polyclinic for Eye Diseases with central opacities of both corneae formed by small crystals. This finding led to the discovery of the cases described in this paper, and, although continuous observation has been possible in one case only, they are probably of sufficient interest to merit publication.

Case Reports

Case 1. K. A., the wife of an artisan, born October 13, 1909. Her father died of pulmonary tuberculosis at the age of 46, her mother at an advanced age

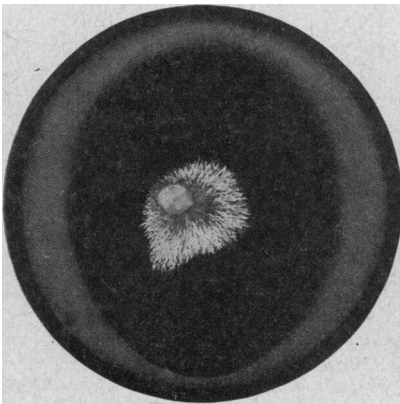


FIG. 1.—Case 1. Right eye.

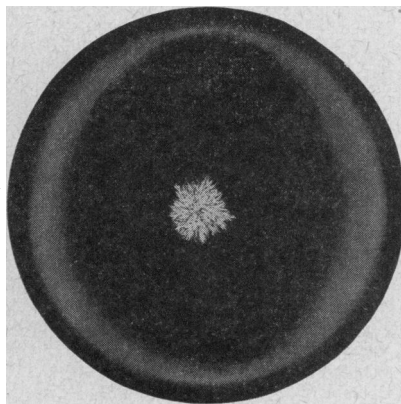


FIG. 2.—Case 1. Left eye.

of some unknown disease. According to the history, her parents and grandparents had normal eyes and good vision. The patient herself had always been healthy. She had been married 10 years, had no children, and no miscarriages. Menses regular, rather scanty. The patient's eyes had always been healthy. As a child she had noticed on both corneae small spots which had not changed in any way. Her vision had always been good.

Medical examination at the Department for Internal Diseases revealed nothing abnormal. Blood picture normal; blood uric acid 3.9 mg. per cent.; blood cholesterol 437 mg. per cent. X-ray examination showed no signs of gout. Hypoplasia uteri was noted in the gynaecological examination carried out at the Women's Clinic of Helsinki University.

Ophthalmological examination: R.V.=6/7.5, L.V.=6/5. The eyes were free from congestion. In the centre of both corneae were yellowish patches 2.5 mm. in diameter in the right eye, and 2×1 mm. in the left. At the edge of the

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cornea, about 1 mm. from the limbus was an opaque ring, 2 mm. broad, dense in the periphery and becoming less so towards the centre of the cornea. The slit-lamp showed that the yellowish patches consisted of glittering needle-like crystals situated just under the corneal epithelium and extending to the inner third of the cornea. The opacity at the edge was a structureless mass with no discoverable crystals. No blood vessels or vascular remnants were seen. The inner eye was normal on both sides.

The patient was seen periodically to date. She was given folliculin orally and dionin locally for 8 months, when this treatment was discontinued because the condition seemed to remain unchanged. The patient presented herself approximately every second month, and in the Autumn of 1947 the central opacity was found to be markedly smaller in both corneae; in the left it seemed to have very nearly disappeared and only a small number of isolated crystals could be seen by the slit lamp. The blood cholesterol was 243 mg. per cent. The patient said that in the preceding summer she had changed her diet and had

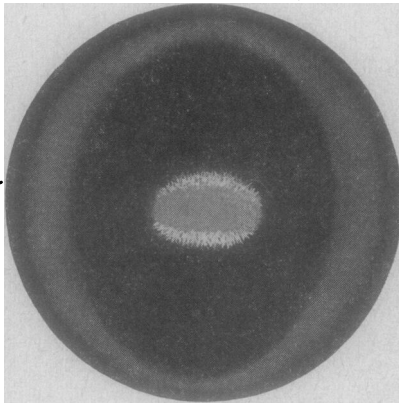


FIG. 3. Case 2. Right eye.

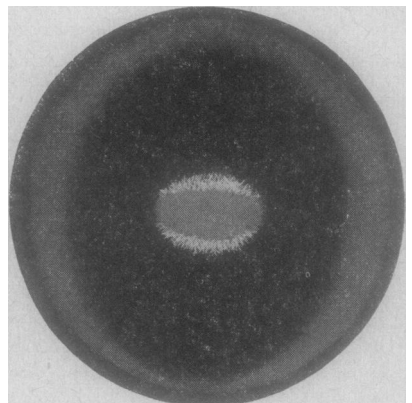


FIG. 4—Case 2. Left eye.

taken fat only in the form of butter. Otherwise she had lived mainly on vegetables. Her food had thus been poor in cholesterol.

After this the patient's condition changed comparatively little until early summer, 1948, when the opaque patches began to enlarge and the crystals in them increase. In the right cornea the crystals in the centre coalesced into a diffuse mass forming an irregular plate with holes. Crystals were also seen in the periphery. The blood cholesterol had again increased and was now 328 mg. per cent. In spite of the enlarging opaque patches and their increasing density the patient's vision deteriorated very slightly. She had gradually returned to her former liberal diet, because she found the restricted diet too expensive.

Case 2. P. A., brother of Case 1, born March 3, 1897. He had had various infectious diseases, and had been suffering from dyspepsia for a considerable time. His eyes had always been healthy, but of late he had noticed some dimness when reading. He did not admit to having noted anything abnormal in his corneae.

Medical examination at the Department for Internal Diseases at the Kivelä Hospital revealed achylia gastrica; pulmonary emphysema; normal renal function. Blood picture normal; blood calcium 11.3 per cent.; blood uric acid 4.0 mg. per cent.; blood cholesterol 274 mg. per cent.

Ophthalmological examination: R.V.=6/7.5 c+2.0 D.S. L.V.=6/10 c+1.5 D.cyl. axis 150°. Both eyes were quiet and free from congestion. In the centre of both corneae opaque patches about 3×4 mm. in extent. Ring-like opaque patches at the margins of the corneae, resembling those noted in the former patient. When examined by the slit-lamp the marginal opacity was found to be diffuse.

The central opaque patches were diffuse in the middle, greyish-yellow in colour, and occupied two-thirds of the thickness of the cornea. In the upper and lower margins of this diffuse centre, vertical, glittering, yellowish, needle-shaped crystals were seen superficially as in Case 1. No open or obliterated blood vessels were present. The deeper parts of the eyes were normal.

Case 3. P. K., brother of Cases 1 and 2, artisan, born January 6, 1914. He had been treated for nephritis several times and had once suffered from polyarthritis. He had also been hospitalized for gastric ulcer. At 13-14 years the patient had noticed that there was something the matter with his eyes but could not remember what. There had been no subjective symptoms in the eyes and he had always seen well.

Medical examination at the Department for Internal Diseases revealed duodenal ulcer and chronic nephritis. Blood picture normal; blood uric acid 3.5 mg. per cent.; blood cholesterol 257 mg. per cent.

Ophthalmological examination: R. and L.V.=6/5. The eyes were quiet, no congestion. In the centre of both corneae semi-circular opaque patches with a

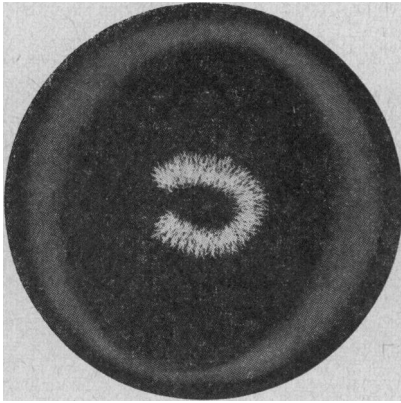


FIG. 5.—Case 3. Right eye.

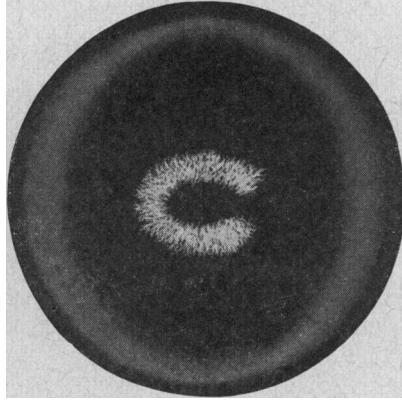


FIG. 6.—Case 3.—Left eye.

radius of 3 mm., the thickness of the arc being 1.5-2 mm. The arcs were open temporally. In the marginal parts of the corneae there were opacities similar to those noted in cases 1 and 2. The central opaque patches were of crystals similar to those in the cases described above and the crystals were present in the same corneal layers. In this case it could be seen very clearly that the crystals had settled mainly in radial formation. No coalescence was noted. The deeper parts of the eyes were normal.

One week after the examination at the hospital the patient developed anuria at home and was re-admitted to the Department for Internal Diseases. His condition became rapidly worse, but he himself and his relatives wanted him discharged from hospital. He died after a couple of days. Permission for autopsy was withheld.

Case 4. Son of Case 3, born August 15, 1941. When three weeks old the patient had been treated at the Children's Department of Maria Hospital for some eruption of the skin. Opacities in the corneae had been noted at that time, but he had never been examined by an eye specialist. The patient had been otherwise healthy.

Medical examination at the Kivela Hospital Department for Internal Diseases: general health good, nothing pathological noted. Blood picture normal; blood uric acid 4 mg. per cent.; blood cholesterol 285 mg. per cent.

Ophthalmological examination: R. and L.V.=6/4. The eyes were quiet, uncongested. Elliptical opaque patches were noted in the centre of the corneae, the clear centres of the opaque patches were 2×3 mm., the thickness of the arc

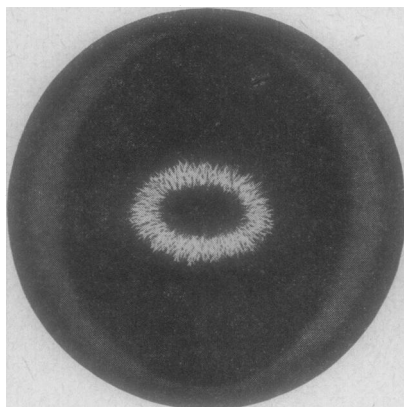


FIG. 7.—Case 4. Right eye.

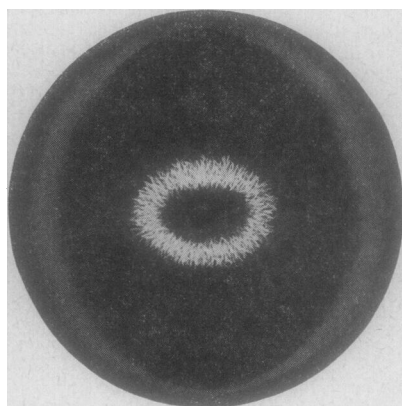


FIG. 8.—Case 4. Left eye.

about 2 mm. Examination by the slit lamp showed the opacity to be formed of similar crystals in the same junction as in the former cases. No coalescence was noted. In the marginal parts of the corneae the opaque rings were rather indistinct. The deeper parts of the eyes were normal.

Discussion

We have thus three siblings and the child of one with similar changes in the corneae. Although only two generations were observed, we are obviously dealing with a hereditary phenomenon. The disease is characterized by slow development, lack of irritation and lack of corneal blood vessels, and according to the histories begins in early childhood. Although we have been able to follow only one patient to date, yet a composite picture of the disease and its course can be built from the symptoms and signs in this and the other cases.

Although the disease is hereditary, other factors contribute to its development. Diet evidently plays an important role in the genesis of the disease. These patients showed a marked tendency to increased blood cholesterol, which in one case was controlled by restricted intake.

By giving cholesterol to laboratory animals, this substance appears even in a healthy cornea and artificial gerontoxon is produced. The condition, in fact, seems to be an intermediary between the physiological corneal changes of old age and the pathological changes of dystrophy. Kohashi (1929) fed animals on lanolin and produced an opacity in the centre of the cornea, and further found that the severing of the seminal duct caused clearing of the corneal opacities in some cases, although the lanolin diet was continued without interruption. This proves that an excess of

cholesterol is not the only factor causing storage of the substance in the cornea.

Looking for similar cases in the literature, we first examined the descriptions of hereditary corneal dystrophies given in most textbooks classified after Bücklers (1938). Our cases, however, do not fit into these groups, although they undoubtedly belong to the hereditary primary corneal dystrophies. Axenfeld (1930) defines the condition as a change in the transparency of the cornea, not due to any external cause such as injury, infection, inflammation, or physical or chemical effect.

We also found in the literature a few cases of hereditary crystalline degeneration of the cornea, first described by Schnyder (1939). Both Cavara (1940) and Pandolfi (1941) published similar reports. Their descriptions of the disease and the pictures published correspond exactly with our cases in regard to both the hereditary character and the ophthalmological picture.

Schnyder did not give the blood cholesterol values of his patients, but in Cavara's and Pandolfi's cases these were within normal limits, while in each of our own cases the blood showed an evident increase of cholesterol.

In the literature there are no cases of hereditary corneal dystrophy with elevated blood cholesterol. Among the non-hereditary corneal dystrophias, on the other hand, corneal xanthoma with lipid changes is mentioned. This disease and our cases are both characterized by lack of irritation, the presence of crystals, and a diffuse opacity in the cornea, with increase in the blood cholesterol.

The fact that Axenfeld noted clearing of the opacity in one case of xanthoma corneae is a very important feature. Zeeman and Groen (1947) succeeded in producing complete clearing of the cornea with a strictly vegetarian diet. Their treatment was based on Schoenheimer's statement that man is unable to absorb sterols from vegetables. This is in agreement with the corneal clearing and decrease of crystals noted in our first case as a result of the patient's adopting a vegetarian diet of her own accord.

These facts suggest that in our cases the opaque patches were due to cholesterol crystals. It is true that crystals were of unusual shape, but Schoenheimer (1923) has shown that the cornea is the only place where cholesterol crystals are found, *intra vitam*, in the form of anisotropic needles.

Axenfeld assumed that in cases of xanthoma the cornea is capable of only partial consumption of certain substances, which are therefore stored. Animal tests, on the other hand, show that a healthy cornea has the capacity of storing cholesterol when there is a surplus. In our first case the blood cholesterol, still considerably above normal, had in fact decreased though when the conspicuous reduction in the amount of the corneal crystals was noted.

As our cases are similar to those of Schnyder (1939), Cavara (1940), and Pandolfi (1941) in hereditary character and ophthalmological picture, we assume that they are examples of the same dystrophy. In Cavara's and Pandolfi's cases the blood cholesterol was normal, but we may suppose that in their cases the incapacity of tissues to make use of cholesterol was so marked that storage took place even when the cholesterol value was normal.

On the other hand, our cases seem to have features in common with xanthoma corneae, including the increase in blood cholesterol, and the varying of corneal opacity with changes in the blood cholesterol content. These cases may be regarded as an intermediate form between corneal xanthoma and hereditary crystalline dystrophy of the cornea. In any case they are a hereditary form of corneal xanthoma.

Summary

One sister, two brothers, and a child had in the middle of their corneae opacities formed by needle-like crystals, and in the marginal parts ring-like opacities resembling gerontoxon. They all showed an increase of blood cholesterol. In one case the cholesterol content of the blood fell when the patient adopted a strict vegetarian diet, and at the same time the number of the corneal crystals was reduced and the opacity cleared. The crystals in the cornea increased along with an increase of the blood cholesterol. None of the patients had any symptoms of irritation. We are probably dealing with a hereditary form of xanthoma corneae, which connects this disease with hereditary crystalline dystrophy of the cornea as described by Schnyder, Cavara, and Pandolfi.

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