CHOROIDAL SCLEROSIS*

A POSSIBLE INTERMEDIATE SEX-LINKED FORM

BY

ARNOLD SORSBY AND MARY SAVORY

Royal College of Surgeons and Royal Eye Hospital

MARKED generalized choroidal sclerosis was observed in one member of each of two families (Figs 1 and 7), other members of which showed fundus lesions difficult to interpret. The present study poses two possibilities as to the significance of the choroidal sclerosis observed.

The H. Family (Pedigree Chart 1).—Four cases were observed: two brothers, a daughter of the younger brother, and their sister's son.

Case 1, Alfred H. (II, 6), aged 45, proband. There was no antecedent history of eye trouble in the family; the father, who died at 74, and the mother, who died at 75, were reputed to have been normal; they were not consanguineous. The patient had always had poor sight as long as he could remember but could see to read till the age of 31. His vision was hand movements, and the fundi showed generalized choroidal sclerosis with some pigment proliferation (Fig. 1, opposite). The disc and vessels did not suggest retinitis pigmentosa. This patient died from cerebral haemorrhage 3 months after the examination.

Case 2, Albert H. (II, 8), aged 41, younger brother of Case 1, had had poor sight since about the age of 6 years, and could see to read till about the age of 27; he was greatly troubled by the black-out during the war. Vision was hand movements in

FIG. 1.—Alfred H. (Case 1), aged 45, left eye. There is generalized exposure of the choroidal vessels with conversion of some of these vessels around the disc into white streaks. Pigment proliferation, somewhat reminiscent of retinitis pigmentosa is present, but the discs and vessels are not of the retinitis pigmentosa type. The right eye was similar.

each eye. His fundi (Fig. 2) showed exposure of the choroidal vessels with much atrophy. The characteristic conversion of choroidal vessels into white streaks seen in Case 1 was lacking. A certain amount of pigment, rather cruder than that seen in his brother, was present; as in his brother, the disc and vessels did not suggest retinitis pigmentosa. Re-examined 3 years later, there was no substantial change.

FIG. 2.—Albert H. (Case 2), aged 41, younger brother of Case 1, left eye. There is marked choroidal atrophy with relatively little suggestion of choroidal sclerosis. The atrophy is most marked where the choroidal sclerosis was most marked in Fig. 1. The right eye was essentially the same.

Case 3, Patricia H. (III, 22), aged 6, younger of the two children of Case 2 (the elder child, a boy, was normal). She was myopic and with -8 D sph. each eye read 6/36 and 6/24. She was normal on the Ishihara test. Her fundi (Fig. 3) were albinotic in background and the maculae stood out markedly, showing a number of white dots. A marked myopic crescent was present. The fundi, whilst not definitely pathological, were probably not altogether normal. Re-examined 3 years later the myopia had increased by about 2 D, and the visual acuity was 6/18 in each eye with full correction.

Case 4, Charles H—t (III, 18), aged 30, son of the proband's elder sister (II, 4). Vision with correction in the right eye -6 D sph., -3 D cyl., 10° , and in the left eye -9 D sph., -2 D cyl., 160° was hand movements. He had had trouble with his eyes ever since he could remember. The fundi, unlike those of his uncles, were reminiscent of retinitis pigmentosa, both in the type of pigment and in the form of the disc and vessels. In contrast to the classical form of retinitis pigmentosa, there was considerable choroidal exposure centrally with a definite macular lesion (Fig. 4). His mother (II, 4), who died at the age of 22 at his birth, is reputed normal.

FIG. 3.—Patricia H. (Case 3), aged 6, daughter of Case 2, left eye. The fundus is albinotic in type. There is a marked circular crescent around the disc. The macular area is not albinotic and shows a number of white glistening dots. The right eye was similar.

FIG. 4.—Charles H—t (Case 4), aged 30, nephew of Case 1, right eye. There is exposure of the choroidal vessels throughout the fundus background with some suggestion of choroidal sclerosis around the disc and mottling at the macula. The disc and vessels are consistent with the retinitis pigmentosa reaction which is seen towards the periphery. The left eye was the same.

Taking the family as it stands, the possibility of sex-linkage arises, but the evidence is not conclusive; apart from Case 3, five women in this family (II, 2; II, 3; III, 10; III, 16; IV, 1) were examined and found to have normal fundi, so that the only suggestion of a carrier state centres in Case 3. It is unlikely that a simple recessive is at issue, for Cases 1, 2, and 4 belong to two generations. A dominant mode of inheritance is possible, but against it is the fact that the parents of the proband and the mother of Case 4 were reputed normal.

A not unreasonable reading of these four cases is therefore that Cases 1 and 2 represent choroidal sclerosis at two different stages, Case 4 the relatively uncommon retinitis pigmentosa type of this affection recorded elsewhere (Sorsby and Davey, 1955), and Case 3 the carrier state of the affection in the daughter of an affected man. For two reasons it is difficult to regard this group as illustrating different stages of

choroideremia: the marked choroidal sclerosis shown by Case 1 and the retinitis pigmentosa type of reaction shown by Case 4 fit ill with any such reading.

The K. Family (Pedigree Chart 2).—Four cases (Cases 5-8) were observed here: a boy, his mother, her brother, and his daughter.

PEDIGREE CHART 2.—The K. Family.

Case 5, Brian K. (III, 4), aged 7, proband, was brought for examination by his mother as his eyes tended to water at the cinema. His vision was found normal but the fundi showed extensive mottling (Fig. 5). There was no nightblindness. A tentative diagnosis of early choroideremia was made. The Ishihara test was normal.

Case 6, Alice K. (II, 12), aged 42, mother of Case 5, had normal vision and no subjective symptoms. The fundi showed a marked mottled and white reaction, not inconsistent with an extreme degree of the carrier state of choroideremia (Fig. 6). The Ishihara test was normal.

FIG. 5.—Brian K. (Case 5), aged 7, left eye. There is heavy mottling centrally and an exaggerated pepper-and-salt reaction towards the periphery. The disc and vessels are normal. The right eye was similar.

FIG. 6.—Alice K. (Case 6), aged 42, mother of Case 5, left eye. There is an extensive mottled and white reaction throughout the fundus. The disc and vessels are normal. The right eye was similar.

Case 7, George K. (11, 2), aged 58, a brother of Case 6. Visual acuity 6/9 in the right eye, 6/18 in the left eye, fields contracted to about 10°. The fundi (Fig. 7) showed exposure of the choroidal vessels and a reddened central area. Some peripheral pigmentation was also present. There was no suggestion of retinitis pigmentosa at the disc or vessels.

Case 8, Violet E. (III, 1), aged 30, daughter of Case 7, had full vision and no subjective symptoms. The fundi showed peripheral mottling consistent with the carrier reaction of choroideremia (Fig. 8).

FIG. 7.—George K. (Case 7), aged 58, brother of Case 6, left eye. With a normal disc and vessels there is exposure of the choroidal pattern everywhere except centrally. There is conversion of some of the vessels to white streaks and considerable choroidal atrophy in the upper nasal sector. Some pigmentation, not definitely of the retinitis pigmentosa type, is present. The right eye was essentially similar.

FIG. 8.—Violet E. (Case 8), daughter of Case 7, aged 30, right eye. The periphery shows extensive mottling. The left eye was similar.

The family history was clear and there was no consanguinity. The findings, as far as they go, are reasonably suggestive of choroideremia in Cases 5 and 7, and of the carrier state in Cases 6 and 8. The point of interest here is that considerable choroidal sclerosis was seen in the proband's uncle, and that there is, as yet, no conclusive evidence that the family is indeed affected by choroideremia.

Discussion

The first family shows four different pictures in the four members seen. Case 1 shows a fairly typical generalized choroidal sclerosis, whilst in Case 2 choroidal atrophy predominates. Case 3 is only doubtfully pathological, and if the child does indeed represent a carrier state, the difficulty arises that there is no recognized carrier state to fit the picture. Case 4 agrees fairly well with the retinitis pigmentosa type of reaction seen occasionally in generalized choroidal sclerosis. If the family is interpreted as affected by choroidal sclerosis, the history fits ill with the established dominant mode of inheritance, for neither the parents of Cases 1 and 2, nor those of Case 4 are known to have been affected. There is therefore some justification for

regarding the group as affected by generalized choroidal sclerosis, possibly inherited in a sex-linked manner.

In the second family, the evidence for intermediate sex-linkage is good, for two carrier women were seen, and these four cases would fit fairly readily into the diagnosis of choroideremia, except for the facts that Case 7 shows more marked choroidal sclerosis than is recognized as occurring in choroideremia, and that the final stage of choroideremia was not observed here. If this family is indeed an instance of choroidal sclerosis rather than of choroideremia, the evidence for an intermediate sex-linked form of generalized choroidal sclerosis becomes fairly convincing.

Intermediate sex-linkage is well established in choroideremia and in retinitis pigmentosa, and there is nothing inherently improbable in an intermediate sex-linked form of choroidal sclerosis. It would thus be possible to regard choroideremia, intermediate sex-linked retinitis pigmentosa, and intermediate sex-linked choroidal sclerosis as determined by a series of allelomorphs of the same gene in the X-chromosome (as is assumed for the different grades of colour vision deficiency). Such a reading would help to explain the family likeness of these three affections.

Summary

(1) A family in whom the proband showed generalized choroidal sclerosis revealed two other affected men, one of whom showed extensive choroidal atrophy and the other a retinitis pigmentosa reaction with a macular lesion and exposure of the choroidal vessels centrally. A daughter of one of the affected men showed an anomalous central fundus appearance, possibly indicative of a carrier state.

(2) In another family generalized choroidal sclerosis was seen in a man whose daughter, as also his sister and her young son, showed fundus reactions suggestive of choroideremia.

(3) If the first family is regarded as one of generalized choroidal sclerosis, the history would suggest that the affection may be inherited in an irregularly dominant manner in addition to the established dominant mode of inheritance. Likewise, if the second family is regarded as one of choroideremia, well marked choroidal sclerosis must be accepted as an intermediate stage of the affection.

(4) As against the possibility that these two families represent different affections—irregularly dominant choroidal sclerosis and sex-linked choroideremia—the possibility is indicated that there exists an intermediate sex-linked form of choroidal sclerosis.

Our thanks are due to Mr. Arthur Lister for information and facilities to examine Case 4.

REFERENCE

SORSBY, A., and DAVEY, J. B. (1955). *British Journal of Ophthalmology*, **39**, 257.