INHERITED RETINAL DETACHMENT*

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THE majority of familial cases of retinal detachment have occurred in myopes, and appear to show autosomal recessive or dominant inheritance. The literature has been extensively reviewed by Richner (1936) and Rieger (1941). Two pedigrees consistent with X-chromosomal inheritance and not associated with myopia are here presented, and similar cases are discussed.

Pedigree I

In the first pedigree (Fig. 1) all seven cases occurred in males, and transmission was through unaffected females. Most of the family live in two neighbouring villages in Ayrshire, where the chief occupations are agriculture and mining.

Affected Members

Case 1 (II, 5), James W., aged 72, is bed-ridden with cardiac disease, and does not give a reliable history. Two years ago his Wassermann reaction was negative.

Right eye divergent, no perception of light, no red reflex, presumably because of a total detachment of the retina. Immature amber cataract, no signs of iritis.

Left eye immature central cataract, good projection of light. Fundus visible, with exception of macular area, with pupil dilated. Below there is a dark-grey, snail-shaped membrane projecting into the vitreous, with its tail attached to the retina. Temporal to it are white dendritic lines in the retina. The more temporal group are very white and have sharply defined edges, exactly like those in Case 2. The more nasal group, which have a yellowish tint and branch less, may be an earlier stage. There are two round central vitreous opacities.

Case 2 (III, 25), John He., aged 41, known to have defective vision before the age of 1 year, sight has changed little for as long as he remembers, attended school for the blind at age 12, has occasional fine nystagmus.

Right eye divergent, as can be seen in a snapshot taken 30 years ago, with limited adduction. Abduction of the left eye slightly limited. Visual acuity in both eyes 3/60, c. + 5.0 D.S. Pupils dilate poorly and both lenses have a small posterior polar opacity. Disks are partly atrophic and vessels narrow, especially in right eye. Macular area in each eye occupied by a slightly raised, white-speckled plaque, with a few bright cholesterol crystals and small clumps of pigment. In the right macula there is a small crater; its base is formed of a spongy red tissue, and from its upper border a white strand passes downwards, on the surface of the retina. An area of retina, temporal to the macula and extending to the periphery along a branch of the superior temporal artery, is

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FIG. 1.—Pedigree I.

shallowly detached. In the supero-temporal region in each eye there is a cystic detachment, with a sharply defined curving edge and a very tenuous transparent inner layer. There are corresponding defects in the visual fields. There are numerous white dots and dendritic lines in groups, especially below and temporally. Where the retina is detached they lie in the deeper layer. The right fundus is illustrated in Fig. 2. The patient has eccentric recognition of colours. There is not an absolute central scotoma.

FIG. 2.—Right fundus of Case 2, Pedigree I.

Case 3 (IV, 28), Robert N., aged 22, was down-graded in army because of poor eyesight.

Visual Acuity: Right eye c. +1.0 D.S. +1.5 D.C. axis $180^\circ = 6/24$.

Left eye c. +0.75 D.S. +0.75 D.C. axis $180^\circ = 6/12$ less one letter.

Both maculae show a circumscribed mottled area, with indistinct white dots on a red background, over about one disk diameter.

Case 4 (IV, 32), Henry M., aged 20, at present serving in B.A.O.R., was examined when on leave. He is emmetropic, and the visual acuity in each eye is 6/5. Both fundi show pseudo-neuritis; there is marked glial sheathing of the vessels on the disks, which appear blurred and swollen. The veins are full and tortuous. There is a little fine white and red mottling of both maculae. A small cystic detachment can be seen in the extreme lower temporal periphery of the right eye, with a corresponding defect in the visual field. He reads the Ishihara colour plates normally.

Case 5 (IV, 45), Robert Ho., aged 10, propositus, known by his mother to have poor vision for over 4 years, has a right convergent strabismus, with poor abduction, especially of the right eye, which has nystagmoid movements on abduction.

Visual acuity: Right eye c. $+1.0$ D.S. $+1.0$ D.C. axis $90^\circ = 6/60$.

Left eye c. $+0.25$ D.S. -1.75 D.C. axis $180^\circ = 6/18$ full, one letter of $6/12$.

The right fundus shows a detachment of most of the lower half of the retina (Fig. 3). At 8 o'clock and 5 o'clock what may be holes are crossed by retinal vessels (the second hole is not so definite as it appears in the Figure). A thin transparent veil is present in the temporal part of the vitreous. Like the other vitreous veils in this family, I have not seen it undulate with slight movements of the eye. To appreciate it, one must first focus with a $+6$ D. lens on its inner edge which curves upwards and nasally to fade above. No temporal edge can be seen. The macula is raised, with a fine white mottling. The individual spots are blurred, with indefinite edges. The detachment was operated on, a diathermy barrage being applied from 5 to 8 o'clock without effect.

The left macula is similar to the right, although the appearance is slightly less marked. Radiating reflexes are seen around it, especially through the undilated pupil. Infero-temporally there is a vitreous veil, whose edges can be followed all round, and indistinct white markings in the extreme periphery (Fig. 4).

FIG. 3.—Right fundus of Case 5, Pedigree I. FIG. 4.—Left fundus of Case 5, Pedigree I.

Both fields show a supero-nasal constriction, and the right also shows a temporal constriction. The defect in the right field corresponds to the detachment but not to the vitreous veil, while that in the left roughly corresponds to the veil. There is, in both eyes, a relative central scotoma for red and green, extending for 5° from the fixation point for the $5/1000$ object, and 1° for the $10/1000$. He reads the Ishihara colour plates normally.

Case 6 (V, 10), Robert E., aged 9, noted to have poor vision at the school clinic 2 years ago. I have been able to examine both this patient and Case 7 in their home only, and am indebted to Dr. Inglis of Kilmarnock for information on their visual acuity and refraction. In January, 1951, the visual acuity in the right eye was c. ± 0.5 D.S. $+1.0$ D.C. axis $105^\circ = 6/18$, and in the left eye c. $+1.5$ D.S. ± 1.0 D.C. axis $75^\circ = 6/24$.

Both maculae are raised, with a fine white mottling and a red central spot. There is a triangular vitreous veil below in the right eye, and white markings round the periphery of both eyes.

Case 7 (V, 11), Peter E., aged 8, has had a left convergent strabismus since infancy.

Visual Acuity: Right eye c. +2.0 D.S. +1.0 D.C. axis $90^\circ = 6/18$.

Left eye c. +1.5 D.S. +0.5 D.C. axis $75^\circ = 6/36$.

The maculae of both eyes are raised and show a fine red and white mottling. In addition there is a detachment of about two-thirds of the lower half of the right retina. This seems to be overlaid by a fine sheet, resembling a vitreous veil, deficient at one part where a sharp, highly curved edge can be seen. Supero-temporally an infolded trumpet-shaped vitreous veil is present.

Other Ocular Abnormalities in the Family

V, 19, male infant, aged 20 months. He was seen while on a visit with his mother from London, and examination under a general anaesthetic could not be arranged then. As far as could be seen, the macular reflexes were abnormal and of a greyish colour. I hope to be able to examine him again soon.

II, 6, female, aged 69, has colloid-like bodies at both maculae.

III, 23, male, aged 46, eldest son of II, 6, and the brother of Case 2, has less well-marked colloid bodies at the left macula. His right eye has a largely absorbed traumatic cataract due to a penetrating injury, a red reflex through it but no fundus details can be observed.

III, 10, female, aged 50, has finely pigmented granular maculae, not resembling those previously described, and normal vision.

III, 20, female, aged 39, mother of Case 5, has haemorrhages and exudates, much more marked in the right eye, and resembling an arterio-sclerotic retinopathy. Her vision is good and her fields full. Her blood pressure is normal, and her subcutaneous arteries not palpably hardened. Her blood picture is normal, her Wassermann and Kahn reactions are negative, and other clinical examinations show no abnormality other than moderate obesity.

Non-affected Members

Convergent strabismus or the history of one in childhood appears in IV 1, and in IV, 24 and her husband, and also in their children V, 13 and 14.

One eye of IV, 11 is myopic; this being the only myopic eye noted in the family.

Pedigree II

The members of the second family, whose pedigree is illustrated in Fig. 5, live in Glasgow. Here the evidence for X-chromosomal inheritance is much less strong than in the first family.

Affected Members

Case 1 (II, 1), Thomas He., aged 51, did some boxing in his youth, and remembers a particular blow in 1926 on the right eye, which had always been convergent, and in which the vision then became misty. In 1930 a cataract was removed from it at another hospital and a detached retina found.

At present the right eye is convergent and has no perception of light. The cornea is partly opaque, perhaps due to old cyclitis. The iris has a surgical

FIG. 5.—Pedigree II.

coloboma above and the pupil is occupied by a dark grey mass. No red reflex is obtained.

In the left eye the visual acuity is c. +4.0 D.S. +0.5 D.C. axis $105^\circ = 6/5$ part. There are pigmentary changes at the macula and in the periphery below. The visual field is full. The patient reads the Ishihara plates normally.

Case 2 (II, 5), Francis He., aged 39, propositus, had poor vision in the left eye since childhood. He also did some boxing but does not recall a blow on the left eye. He attended hospital in 1947, and diathermy was unsuccessfully applied for a detachment of the lower part of the left retina, with an infero-temporal anterior dialysis. It was noted then that the right vision could not be improved beyond 6/12.

Visual Acuity: Right eye c. +0.75 D.S. = 6/12.

Left eye c. +0.75 D.S. = 6/36.

The pupils dilate poorly, especially the left. There is no sign of previous irido-cyclitis. No foveal reflex can be seen in the right macula. The rest of the fundus is normal and the visual field full.

There are pigmentary changes at the left macula. The lower half of the retina is detached, and appears white and opaque. Diathermy scars can be seen infero-temporally, but no hole. There is a field defect corresponding to the detachment. Colour vision tested on the Ishihara plates is normal.

Case 3 (III, 16), David Ha., aged 17. He is unaware of any defect.

Visual Acuity: Both eyes c. +2.5 D.S. +0.5 D.C. axis $105^\circ = 6/6$.

There is a detachment in the lower temporal quadrant of the right eye, extending about half-way to the disk, with a white demarcating zone round part of it (Fig. 6). There is a large anterior dialysis, extending from 6 to 9 o'clock. The macula has a water-silk reflex and is slightly granular. Glia extends over the disk margins. The left macula is normal. There is a small disinsertion in the left eye from 4.30 to 5 o'clock, with no detachment. There is an upper nasal defect in the right field; the left field shows a slight flattening of the upper nasal periphery.

FIG. 6.—Right fundus of Case 3, Pedigree II.

detachment of the retina, vitreous veils, and dendritic white lines. The majority are hypermetropic, but Case 4 is emmetropic, and Case 5 has mixed astigmatism, mainly myopic, in one eye. Two have convergent and two divergent strabismus.

The following more or less similar cases appear in the literature:

Thomson (1932) described four brothers, first seen in a school clinic in 1920, all with a bilateral macular lesion, and one with bilateral retinal detachment. All were slightly hypermetropic, and in none was the corrected vision better than

Other Members

Several of III, 16's nine brothers and sisters have convergent squints and are hypermetropic. No myopic eyes were found in the family.

Discussion

Pedigree I.—The outstanding features of the affected members of the first family are the macular lesion, cystic

6/12 partly. The vision appeared to deteriorate over the period of observation. White spots and figures were also present in the fundi. Relative central colour scotomata were found, similar to those in Case 5. The Wassermann reaction, tested in two, was negative. The description and illustration of the maculae correspond closely to my Cases 5, 6, and 7. Four sisters and the parents were reported normal.

Anderson (1932), discussing anterior dialysis, described (p. 705) and illustrated what resembles a band-shaped vitreous veil associated with such a tear, in a young man whose other eye had a complete detachment.

Mann and Macrae (1938) first recognized vitreous veils in two brothers and a third unrelated young man; their ages ranged from 17 to 21, and all were hypermetropic. One eye in each of the brothers had a retinal detachment. Branches of retinal vessels extended on to the veils, and whitish markings were present in the periphery. Though the corrected vision varied from 6/12 partly to counting fingers, no macular lesion was described or illustrated, and the poor central vision was ascribed to retinal amblyopia. No field defects corresponding to the veils were present.

Cibis (1940) described bilateral retinal detachment in male hypermetropic uniovular twins aged 13. All four detachments lay in the infero-temporal quadrant, and were strikingly alike. They were associated with optic atrophy and cystic macular degeneration.

Juler (1947) described three unrelated boys, aged from 5½ to 8 at their first visit and observed for from 4 to 8 years. All had bilateral inferior detachment with corresponding visual field defects and poor central vision, the best being 6/9 partly. Macular lesions were described in two cases. In one the macula showed a shallow detachment and slight fibrosis in the one eye and thin scarring in the other, and in the other the macula showed a slight granularity. The detachments were cystic, the thin inner layer showing holes crossed by retinal vessels, some of which appeared to have sunk back to the level of the non-detached portion. The right eye of the second case was remarkably similar to that of my Case 5. The refraction varied from slight myopia to slight hypermetropia, and one had a convergent strabismus. The periphery of the fundi were tessellated and mottled. The detachments appeared to be stationary or slightly progressive. Two had vitreous haemorrhages which cleared. All were normal physically and mentally, and tests for syphilis were negative.

In the discussion which followed Juler's paper Miss Mann stated that since 1939 she had seen two more such cases: in a boy aged 10 and in his uncle aged 44. The latter believed his visual acuity and fields had not altered since childhood.

Trevor-Roper (1950) described a man aged 28, known to have had poor vision for 12 years, as having "a sheet of retina with fine tortuous blood vessels in front of the normal retina in the lower quadrant of the left eye" (illustrated). A curving peripheral "bite" was absent from the inner sheet. He remarked that it would have resembled a shallow detachment had it not been for the presence of subjacent retinal vessels. There was a corresponding constriction of the visual field. Though the eyes appeared otherwise normal, the vision in each was only 6/24 after correction of moderate hypermetropic astigmatism. This seems to me to be a case of splitting of the retina, the cleavage being such as to separate the infero-temporal retinal artery and vein. The small scattered foci of intense choroidal sclerosis noted may resemble the white lines in my cases.

Pedigree II.—The cases in the second family do not differ from the usual detachment with disinsertion, which shows many points of difference from detachment in general.

Most of the cases (63 to 70 per cent.) recorded in the literature occur in males, the maximum incidence being between 20 and 30 years (with a similar age curve for cases apparently due to trauma), they have a marked predilection for the infero-temporal quadrant, are often associated with cysts (23 per cent.), are often bilateral and symmetrical (14 per cent.), have a range of refraction similar to the general population, and may remain stationary and unnoticed for years (Gonin, 1930; Anderson, 1932; Shapland, 1932, 1933, 1949; vom Hofe, 1934; Arruga, 1951; Leffertstra, 1950). Corresponding figures for detachments in general are 60 to 65 per cent. in males, maximum age incidence 20 years older, predilection for the upper quadrants, often bilateral but not symmetrical, and 70 per cent. in myopes (Arruga, 1933; Gonin, 1934; de Rötth, 1939; Shipman, 1950).

Retinoschisis, a splitting of the retina in a disinsertion, was first described by Bartels (1933) who found it in two patients, both moderate myopes, one being male and one female. Each had a disinsertion above in one eye, with a thin grey membrane remaining on the choroid in the tear. In the male, retinal vessels crossed the margin of the tear on to the membrane. The choroid could be clearly seen through small oval holes in the membrane. Bartels ascribes this appearance to a splitting of the inner layers of the retina.

Leffertstra (1950), discussing 200 cases of disinsertion at the ora serrata operated on by Professor Weve, found retinoschisis noted in seven.

A few familial occurrences of disinsertion have been recorded. Schmelzer (1936) described two brothers with almost identical bilateral symmetrical detachments and disinsertions, who had had poor vision for several years, were practically emmetropic, and both had poor central vision. One eye of the younger brother was successfully operated on with some improvement in visual acuity. The Wassermann reactions and other general examinations were negative. The parents and four siblings were reported normal.

Leffertstra (1950) noted familial occurrence four times: twice in a brother and sister, once in a mother and daughter, and once in a father and son. The refraction of these cases is not given.

Sorsby and others (1951) found eight cases of detachment with disinsertion or choroidal sclerosis in three generations of a family, the pedigree being strongly suggestive of X-chromosomal inheritance. Their ages ranged from 13 to 66, and all except the youngest case had poor central vision, though in a few the maculae were apparently normal. Three of the older members aged over 50 had central or total choroidal sclerosis and no detachment, and the authors considered this the later stage to which the condition slowly progresses. Not one was myopic. The illustration of the left fundus of their Case 2 (Sorsby and others, 1951, Fig. 4) shows white dendritic lines like those in Cases 1 and 2 of my Pedigree I (see Fig. 2). They lie near the edge of a disinsertion, in the non-detached layer. The authors suggested a relationship with the cases of Mann and Macrae (1938) and Juler (1947), but investigation of the family of two of Juler's cases did not enable them either to prove or to disprove this idea.

The course in these cases is not exceptional in retinal detachment with disinsertion, for Leffertstra (1950) found that spontaneous reattachment sometimes

occurred in very long-standing cases, with atrophy of the retina and a picture resembling secondary retinitis pigmentosa.

A relationship with pseudoglioma (congenital retinal detachment), falciform folds of the retina, and retinal cysts is also suggested by Sorsby and others. As examples of the first condition they adduce families described by Clarke (1898), Pagenstecher (1913), Heine (1925), Wilson, R. (1936), Wilson, W. M. G. (1949), and Pajtás (1950), which appeared to show X-chromosomal inheritance.

To these families I would add one described by Arruga (1950), who saw in a boy aged 2 months a unilateral retinal detachment which in a few months became bilateral and total. General examination of the infant and his parents was negative, and syphilis was absent. In the three preceding generations seven males had similarly become blind, apparently with X-chromosomal inheritance.

Congenital falciform folds are usually considered to show autosomal recessive inheritance (Mann, 1935; Weve, 1938; Theodore and Ziporkes, 1940), and their relationship to those cases appears less likely.

Retinal cysts are most frequent in non-myopic males between 20 and 40, usually in the lower temporal quadrant (Neame, 1920; Ridley, 1936). Pathological studies by Neame (1920), Kapuscinski (1929), Custodis (1936), and Kornzweig (1940) all show that these cysts are due to a splitting in the outer molecular layer, and in some the internal limiting membrane is detached.

Weve (1936) believed retinal cysts to be responsible for 50 per cent. of his cases of detachment. Duke-Elder (1949) showed beyond doubt that a retinal cyst may become an anterior dialysis by observation of such a sequence in a man aged 44 while at rest in hospital prior to diathermy of the cyst.

In a doubtful category must be placed a family described by Hamilton (1946); two daughters and one son of a normal woman, and four sons of her normal sister, developed cystic detachment and cataract, with a probable infective element. One of the affected girls had congenital cystic disease of the lungs. There was no evidence of syphilis.

X-chromosomal inheritance of a macular lesion has, I believe, been only once previously described (Halbertsma, 1928). There was a pigmentary degeneration of the macula and neighbouring regions, associated with colour blindness.

X-chromosomal inheritance of retinal detachment, if shown to be sufficiently frequent, would account, at least partly, for the hitherto unexplained excess of male cases, especially with disinsertion.

Pathogenesis

In the absence of pathological studies it is impossible to decide on the significance of certain unusual features, in Pedigree I especially. The macular defect, the most constant feature, has been very little described in the literature, although unexplained poor central vision is present in many of the cases discussed. In the younger patients (Cases 5, 6, and 7) the macula appears oedematous, with small white spots, possibly cystic in nature. In the older patients (Cases 3 and 4), the macula is flat, and may be interpreted as due to subsequent scarring. In Case 2, much more severely whittled from birth than the others, the whole macular area is thickened and affete, with a spongy red tissue underlying it.

Poor central vision, commonly associated with detachment and often remaining after surgical cure, is usually attributed to cystic degeneration of the macula (Reese, 1937). In disinsertion, unlike other detachments, it tends after surgical cure to worsen rather than to improve with time. It may be that it is sometimes due to an inborn retinal defect, which is also responsible for the detachment.

The cystic detachment in Cases 2, 4, 5, and 7 (Pedigree I) may be due to a splitting of the inner layers of the retina, perhaps, as in retinal cysts, in the outer plexiform layer, but possibly sometimes in a more internal layer (for example, the nerve fibre layer) separating the retinal vessels into two planes, as has apparently occurred in a case reported by Trevor-Roper (1950). Part of such a thin detached membrane may be separated off altogether and, being displaced forwards, appears as a vitreous veil, perhaps still connected to the rest of the inner layer by retinal vessels, the strongest and most resistant element in the retina (Arruga, 1933). Alternatively, as in Juler's cases, the vessels may remain across the holes thus left. Gonin (1934), describing pathological specimens, mentions such a splitting of the retina as forming the actual holes in detachments. On the other hand, as suggested by Mann and Macrae (1938), the veils may be formed by a vitreous condensation into which extensions of retinal vessels have grown, or may be related to the *membrana vasculosa retinae* of some animals.

Curious white dendritic lines, with a superficial resemblance to sclerosed choroidal vessels, are present in two of my cases and in one of Sorsby's, forming an important link between these two pedigrees. Salzmann (1912, Plate V, Fig. 5) depicts a surface view of the border portion of a retina with cystic degeneration, the cysts having for the most part coalesced into dendritic lines which in shape and size (allowing for the magnification) closely resemble these here described. The white colour may be due to exudate or to thickening of the walls, making the previously transparent cysts visible.

Prognosis and Treatment

One case in each of my two pedigrees was operated on, but without cure of the detachment. Schmelzer (1936) improved one case by operation. Disinsertions are usually regarded as favourable to operation (Weve, 1939). In the discussion of Juler's cases (1947) the consensus of opinion was against operation.

My cases, and the similar ones described, are stationary or very slowly progressive, but one eye (Case 1, Pedigree I) has probably gone on to total detachment. Most of the lesions which begin in very early life appear to become rapidly total (pseudogliomata).

Even if surgical cure of the detachment could be accomplished, it would presumably not improve central vision. Case 4, Pedigree I, and Case 3, Pedigree II, present a special problem, the patients having normal central vision and not being aware of any ocular abnormality. Should prophylactic

sealing off of the cyst in the former, and of the bilateral disinsertions in the latter, be attempted?

Summary

Two pedigrees are presented of families showing retinal detachment, consistent with X-chromosomal inheritance.

In one a macular abnormality, vitreous veils, and white dendritic lines were also present.

The literature of similar cases is reviewed and their relationship discussed. It is notable that poor central vision is present in most, although no clinically visible macular abnormality may be present. The cases in each family remain true to type, *i.e.*, pseudoglioma, cystic detachment with vitreous veils, or detachment with disinsertion, although the severity varies.

An attempt is made to explain some of the unusual features. It is suggested that an inherited macular defect associated with a tendency to retinal detachment is sometimes responsible for the poor central vision associated with detachment and following its surgical cure, and that X-chromosomal inheritance might partly explain the preponderance of male cases of detachment.

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