Glaucoma in the Hallermann-Streiff syndrome

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The Hallermann-Streiff syndrome is a complex association of developmental anomalies principally involving structures of ectodermal origin. The constant expressions of the syndrome are dyscephaly with mandibulo-facial malformation, bilateral congenital cataracts, and dental anomalies, while hypotrichosis, cutaneous atrophy, microphthalmos, and proportionate dwarfism are frequently present (Table I) (Ponte, 1962). Numerous inconstant ocular features have been described, including anti-mongoloid palpebral fissures, blue sclerae, keratoglobus, malformation of the drainage angles, peripheral anterior synechiae, iris atrophy, persistent pupillary membrane, posterior synechiae, membranous cataract, amorphous retrolenticular membrane, vitreous opacities, pale optic discs, colobomata at the optic nerve entrance, retinal folds, various atrophic chorio-retinal changes and glaucoma (Table II) (Ludwig and Korting, 1950; François, 1958; Falls and Schull, 1960; Wolter and Jones, 1965; Ide and Webb, 1969).

Table I *Main features of the Hallermann-Streiff syndrome.*

A. Constant	B. Frequently present
1. Dyscephaly with mandibulo-facial malformation	4. Hypotrichosis
2. Bilateral congenital cataracts	5. Cutaneous atrophy
3. Dental anomalies	6. Microphthalmos
	7. Proportionate dwarfism

Table II *Inconstant ocular features of the Hallermann-Streiff syndrome.*

1. Anti-mongoloid palpebral fissures	5. Peripheral anterior synechiae	9. Membranous cataract	13. Colobomata at optic nerve entrance
2. Blue sclerae	6. Iris atrophy	10. Amorphous retrolenticular membrane	14. Retinal folds
3. Keratoglobus	7. Persistent pupillary membrane	11. Vitreous opacities	15. Atrophic chorio-retinal changes
4. Malformation of the drainage angles	8. Posterior synechiae	12. Pale optic discs	16. Glaucoma

It is the purpose of this communication to describe two patients who have the classical manifestations of the Hallermann-Streiff syndrome with glaucoma, and to discuss the aetiology, prevention, and therapeutic problems of this complication.

Case Reports

Case 1. A Caucasian male born at term in June, 1967, after a normal pregnancy, weighed 4 lb. 10 oz. at birth. There was no family history of hereditary disorder and the unrelated parents, who were born in 1936, are both healthy. There was one previous stillbirth in 1961, of which no details

are available. There are no siblings. The infant was first seen in the Eye Department at the age of 5½ months, when he was found to have the characteristic features of the Hallermann-Streiff syndrome (Table I). Dense bilateral cataracts obscured all view of the ocular fundi. A discission operation was carried out on the right eye at the age of 7 months and a red reflex was reported in this eye 2 weeks later. The left cataract absorbed spontaneously between the ages of 8 and 13 months. No ocular inflammation was observed.

The infant was kept under frequent observation and was re-admitted for further assessment at the age of 17 months. At this time his height was 24.5 in., and he weighed 12 lb. 11 oz., both measurements below the third percentile for his age. There was fronto-parietal bossing, hypoplasia of the mandible and maxilla, and a small beak-like nose. The teeth were delayed and irregular in eruption and the ears showed a vestigial antitragus. There was cutaneous atrophy, especially evident on the face at the bridge of the nose where the subcutaneous veins were particularly prominent. The hair on the scalp was fair and rather sparse. Optokinetic responses were elicited in each eye and the peripheral fields were full to large fixation targets. The eyelashes and brows were absent. There was pendular nystagmus and a marked alternating squint with limited abduction of each eye. The paralimbal sclera was greyish-blue and the corneae were bright and clear (see Figs 1 and 2).

FIG. 1 Case 1, full face

FIG. 2 Case 1, profile

Examination under anaesthesia revealed that the right horizontal corneal diameter measured 9.0 mm. and the left 9.5 mm. The intraocular pressures were 26 mm. Hg in the right eye and 36 mm. Hg in the left (Schiötz tonometer 7.5 g. wt). The anterior chambers were clear and deep centrally, but gonioscopic examination revealed that the drainage angles were closed in all meridians of both eyes by peripheral anterior synechiae. The irides were greyish-blue and atrophic and there was a small degree of iris *bombé* in each eye. Both pupils were irregular and dilated only slightly with cyclopentolate 1 per cent. Fine strands of persistent pupillary membrane extended from the collarettes to lenticular capsule remnants, and there were multiple posterior synechiae in both eyes. There were good red reflexes in each eye, and ophthalmoscopic examination revealed coarse granular mottling in the equatorial regions. There was a retinal fold projecting from the lower temporal quadrant to the paramacular area of the right eye.

After 2 weeks' administration of acetazolamide (Diamox) 10 mg./kg. body weight /24hrs a further examination under anaesthesia was carried out. The intraocular pressures were 23 mm. Hg in the right eye and 26 mm. Hg in the left (Möller hand-held applanation tonometer). Since that time the intraocular pressures have remained around this slightly elevated level.

Case 2. A Caucasian female born at term in May, 1936, after a normal pregnancy. There was no family history of any hereditary disorder and the unrelated parents are both healthy. The mother was born in 1909, and the father in 1905. There was a stillbirth in 1938, of which no details are available. There are no siblings. The patient was first seen in the Eye Department at the age of 3 months, and exhibited the characteristic features of the Hallermann-Streiff syndrome (Table I). Discission operations were carried out on each eye at the age of 5 years. Postoperatively the corrected vision was recorded as 5/50 ('E' test) in each eye. At the age of 22 years the patient returned to the hospital complaining of deterioration in the vision of the right eye. The corrected vision was then hand movements in the right eye, and 4/60 in the left. The intraocular pressures were 41 mm. Hg in the right eye and 31 mm. Hg in the left (Schiötz tonometer 10 g. wt.). Miotic therapy failed to reduce the pressures, and a right trephine operation was carried out and repeated without success 4 months later. This was followed by a right cyclodiathermy operation in a further 9 months, but the visual acuity in the right eye deteriorated to bare perception of light while in the left eye the visual acuity was maintained at 4/60, with a full peripheral field to confrontation, in spite of poor control of the intraocular pressure which ranged between 25 and 45 mm. Hg (Schiötz tonometer 10 g. wt.). The left optic disc was reported to be pale and cupped. At the age of 28 years the patient developed a granulomatous anterior uveitis in the left eye and the pressure became still higher, ranging between 40 and 70 mm. Hg (Goldmann applanation tonometer). The uveitis settled, but the intraocular pressure failed to respond to treatment with local miotics and systemic acetazolamide (Diamox). A left trephine operation was carried out, and repeated without success 10 months later. This was followed by a left upper nasal quadrantic cyclodialysis in a further 2 months. The medical therapy was continued but the pressure still remained high, between 20 and 40 mm. Hg (Goldmann applanation tonometer).

The patient was examined in this department at the age of 32 years. She was of normal intelligence and small proportionate stature. Her height was 53 in. and she weighed 91 lb. There was marked brachycephaly with frontal bossing and hypoplasia of the mandible. The nose was beak-like and the antitragus of both ears was very small. The dentition was irregular and there were several persisting deciduous teeth. The skin was thin and atrophic and the hair on the scalp was sparse (see Figs 3 and 4).

FIG. 3 Case 2, full face

FIG. 4 Case 2, profile

The patient's corrected vision was perception of light in the right eye and counting fingers at 1 ft. in the left. The projection of light in the right eye was poor and the left peripheral field showed gross constriction to confrontation. The eyebrows and lashes were scanty. There was pendular nystagmus and a marked right convergent squint. There were extensive bilateral ciliary staphylomata. The right cornea was ectatic and oedematous with large epithelial bullae. The left cornea was less oedematous with fine epithelial bullae and there were crenated keratic precipitates. The right and left transverse corneal diameters measured 9.5 mm. The intraocular pressures were 45 mm. Hg in the right eye, and 25 mm. Hg in the left (Goldmann applanation tonometer). The state of the right cornea precluded any further assessment of the eye.

The left anterior chamber was deep centrally and showed a mild flare with occasional cells. Gonioscopic examination revealed that the drainage angle was closed off by peripheral anterior synechiae in all but the upper nasal quadrant, where the cyclodialysis had been carried out. Here the angle appeared open with multiple coarse strands of iris tissue extending across to the region of Schwalbe's line. The iris was greyish-blue and atrophic. The collarette was ill-defined and strands of persistent pupillary membrane extended to lenticular capsule remnants. There were multiple posterior synechiae. A red reflex was present, but fundus detail was poorly defined.

During the past 6 months the patient has been instilling adrenaline bitartrate 1 per cent. (Eppy) twice daily into the left eye, in addition to miotics and systemic acetazolamide (Diamox). The left intraocular pressure has fallen to within normal limits, ranging from 12 to 17 mm. Hg (Goldmann applanation tonometer). The epithelial bullae have cleared, and the anterior chamber remains quiet. The vision has improved slightly to counting fingers at 2 ft.

Discussion

In view of the findings in these two patients it was interesting to discover that only a small minority of the patients with the Hallermann-Streiff syndrome reported in the literature were found to have glaucoma. A short review of some of these patients is therefore relevant.

The most fully documented patient with the Hallermann-Streiff syndrome and glaucoma has been reported by several authors over the past 23 years (Moehlig, 1946; Falls and Schull, 1960; Wolter and Jones, 1965).

This male patient was born 2 months prematurely in July, 1938, and weighed 3 lb. 2 oz. The mother noticed what appeared to have been a spontaneous rupture of the cataractous left lens at the age of 18 months. He was first reported at the age of 3 years, when he was found to have nystagmus, a left divergent squint, a right congenital cataract, and left aphakia. A right discission operation was carried out under general anaesthesia at this age, and the lens matter was said to have dissolved satisfactorily in a quiet eye. At the age of 8 years, he was reported to have a left divergent squint, bilateral microphthalmos and aphakia, normal anterior chambers, round central pupils, clear media, and normal fundi.

Iridocyclitis with intermittent glaucoma developed in the left eye at the age of 20 years. This failed to respond to local atropine and steroids, and the blind painful left eye was enucleated in 1964. Histological examination revealed a closed anterior chamber angle with newly formed Descemet's membrane extending around the false angle onto the anterior iris surface. The empty lens capsule was attached to the iris pigment epithelium, and was ruptured in its anterior aspect. Granulomatous inflammatory reaction with epithelioid and giant cells extended from the ciliary body and iris to the anterior rupture in the rolled-up lens capsule. There was extensive retinitis proliferans, a retinal detachment, and marked atrophy of the optic disc and optic nerve.

Wolter and Jones (1965) commented that the granulomatous reaction around the remaining lens capsule suggested that the chronic iridocyclitis may have been due to hypersensitivity to the cataractous lens substance.

The first patient described by Hallermann (1948) had total bilateral congenital cataracts.

At the age of 7 months a discission operation with anterior chamber wash-out was performed on the left eye, and at 3 years of age the cataract in the right eye absorbed spontaneously. After this the right eye was apparently quiet, but the patient was later found to have posterior synechiae and secondary glaucoma. A superior iridectomy operation was performed to relieve the secondary glaucoma. When reviewed at the age of 22 years the right eye was blind and the intraocular pressure considerably raised. The corrected visual acuity of the left eye was 5/35 and the intraocular pressure was normal.

Streiff (1950) described a female patient who was born 2 months prematurely and according to the parents could not see as a child.

At the age of 18 years the patient was seen by Professor Streiff's father, who found bilateral microphthalmos and total congenital cataracts and performed a discission operation on each eye. The visual acuity in the right eye improved to counting fingers, but after a year secondary glaucoma occurred in each eye and vision was lost. When this case was reviewed 12 years later the patient, now aged 31, had raised intraocular pressure in each eye and there was glaucomatous cupping of the right optic disc, but vitreous opacification obscured the view of the left fundus. No evidence of active intraocular inflammation or sequelae of intraocular inflammation had been observed in the anterior segments of the eyes (personal communication).

Ullrich and Fremerey-Dohna (1953) reviewed a 2½-year-old girl with the syndrome who had bilateral microphthalmos, cataract, and posterior synechiae.

The intraocular pressures were recorded as 30 mm. Hg in the right eye and 40 mm. Hg in the left. Multiple discission operations were performed on both eyes, and a good view of the fundus was obtained. Aphakic spectacles were fitted and the child could see, but no accurate estimate of visual acuity was possible. No further mention was made of the intraocular pressures.

A patient with a particularly interesting ocular history who represents a *forme fruste* of the syndrome, having all the features listed in Table I but congenital cataracts, was reported by Schondel (1943) and Gregersen (1956).

The patient's visual acuity was recorded as counting fingers at 0.5 m. at the age of 5 years, and the pupils dilated poorly with atropine. At the age of 12 years there was nystagmus, a convergent squint, and marked microphthalmos. The corneal diameters measured only 8 mm. Fine keratic precipitates were present, and the irides were funnel-shaped, reminiscent of iris *bombé*. The pupils contained cicatricial remnants of exudate adherent to the anterior lens surface. Red reflexes were present, but no accurate fundus detail could be seen because of the nystagmus. Between the ages of 15 and 25 years, spontaneous membranous conversion of the lenses occurred. At the age of 30 years glaucoma developed in the right eye. This was tolerably controlled by the administration of acetazolamide (Diamox) and pilocarpine. The corrected visual acuity was recorded as 1/18 and 1/24.

The abnormalities which are likely to cause an elevation of intraocular pressure in the Hallermann-Streiff syndrome have two possible origins. They may be developmental anomalies or complications and sequelae of intraocular inflammation. Duke-Elder (1964) stated that, in microphthalmos, the development of glaucoma is a relatively common occurrence, depending presumably upon the smallness of the cornea, the relatively great size of the lens, and the presence of persistent embryonic tissue in the angle of the anterior chamber. In the patients with the Hallermann-Streiff syndrome, microcornea is one of the salient features, but glaucoma usually occurs in most patients after the lens has been needled or undergone spontaneous rupture. The only description of malformation of the anterior chamber angle appears in the report of Ludwig and Korting (1950), but they did not specify the type of malformation. However, the evidence of intraocular inflammation

in the syndrome is strong and where glaucoma has occurred there have almost invariably been signs of uveitis or its sequelae. Our second patient had particularly uncontrollable glaucoma when the anterior uveitis was active and both patients had posterior and peripheral anterior synechiae. Of the five patients with glaucoma reviewed from the literature, the case described by Streiff (1950) was exceptional in that there was no evidence of intraocular inflammation or its sequelae. The inflammation is typically a granulomatous anterior uveitis, and occurs in the majority of patients where there has been surgical or spontaneous release of the lens matter into the anterior chamber. This is compatible with the suggestion of Wolter and Jones (1965) that the uveitis may represent a hypersensitivity reaction to cataractous lens substance.

There is clearly a better prognosis with surgical discission than with spontaneous cataract absorption. This is apparent in the patient described by Moehlig (1946), Falls and Schull (1960), and Wolter and Jones (1965), and in the patient described by Hallermann (1948). These two patients had a discission operation performed on one eye with a fair result, but spontaneous cataract absorption occurred in the other eye, which became glaucomatous and blind. The reports from Gregory (1955) and van Balen (1961), each describing two patients who had bilateral discission operations with satisfactory results, support this observation. However, the patient who underwent bilateral discissions at 18 years of age (Streiff, 1950) and our second patient show that cataract surgery does not eliminate the hazard of glaucoma.

Therefore it appears preferable to operate on the cataracts of both eyes of these patients as soon as possible, thus avoiding spontaneous cataract absorption and suppression amblyopia. Postoperative reviews must be frequent and regular to ensure that if intraocular inflammation occurs it is diagnosed and treated promptly. The ophthalmic surgeon should not delay intervention in the hope that spontaneous cataract absorption will occur in a difficult microphthalmic eye, as the prognosis is worse and he has no control over the timing of the event.

The onset of glaucoma in patients with the Hallermann-Streiff syndrome presents a most difficult therapeutic problem. Our limited experience indicates that medical treatment with local miotics and systemic carbonic anhydrase inhibitors is the most advantageous. Gregersen (1956) used this combination with some success. The addition of adrenaline bitartrate 1 per cent. (Eppy) appears to have been particularly useful in our second patient. Surgical treatment has been unsuccessful. Hallermann (1958) performed a superior iridectomy to reduce intraocular pressure without success, and our second patient had numerous surgical procedures which failed to reduce the intraocular pressure.

Summary

Two patients with the Hallermann-Streiff syndrome who developed glaucoma are reported. Five similar patients are reviewed from the literature, and the aetiology, prevention, and therapeutic problems of the complication are discussed.

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