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Cavernous haemangioma of the retina and optic disc
A report of three cases and a review of the literature

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Cavernous haemangioma of the retina and of the optic disc is so rare that its existence as a separate entity has been challenged (Elwyn, 1940). Indeed, it has frequently been confused with Leber's miliary aneurysms, Coats's disease, and other retinal arteriovenous malformations. In this report three cases of cavernous haemangioma of the retina are described including a long-term re-examination of a previously reported patient.

Case reports

CASE I

A 63-year-old white man was referred in July 1974 for fluorescein angiography of a cavernous haemangioma of the retina of the right eye. He stated that an abnormality of the retina had first been noted during a routine examination in June 1940. His visual acuity at that time was 20/30 in the right eye and 20/15 in the left, and an absolute paracentral scotoma in the right visual field was identified. In the right fundus temporal to the macula was a well demarcated, slightly raised patch of whitish tissue covered with, and surrounded by, numerous small, frequently clustered, dark red globules of varying sizes. There were no haemorrhages and there was no enlargement of the nourishing blood vessels. Coats's disease had been the initial diagnosis and enucleation was advised. Subsequent consultation suggested that the lesion was probably nonprogressive but that it should be carefully observed. To facilitate this, several fundus paintings of the lesion were made between 1941 and 1944 (Fig. 1). Nonetheless, the patient was rejected from military service because of a potential visual handicap.

Our clinical records show there were no fundamental changes in the visual acuity or the ophthalmoscopic features of the haemangioma from 1956 to 1960. Since 1960 the patient has been followed-up by one of us (MHC) at yearly intervals with periodical fundus photography and no gross ophthalmoscopic alterations have been noted.

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* Deceased 31 July 1974

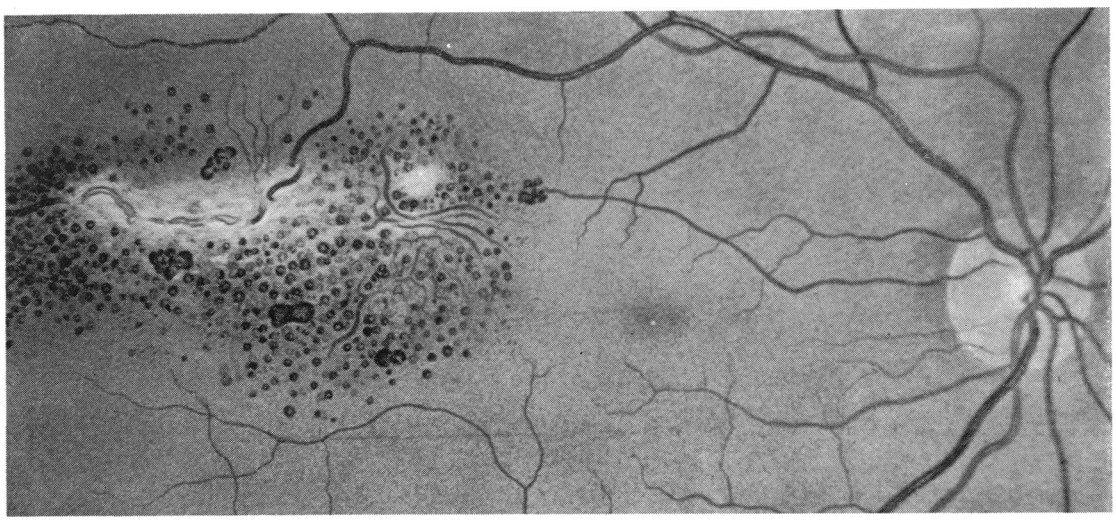


FIG. 1 *Case 1. Drawing of right fundus made shortly after discovery of cavernous haemangioma of retina superior and temporal to fovea.* (Reproduced by courtesy of Dr A. B. Rees)

When seen in 1974, the patient had no other contributory ocular history. He had a 13-year history of mild hypertension treated with reserpine and diuretics and a 4-year history of diabetes mellitus managed with weight reduction and an oral hypoglycaemic agent. After being in hospital briefly in 1961 for paroxysmal atrial fibrillation, he had been given long-term digoxin therapy. The patient's general physical and dermatological examinations were within normal limits. A serum protein electrophoresis was normal. Quantitation of immunoglobulins yielded IgG = 1050 mg per cent (normal 770–1130), IgA = 420 mg per cent (normal 80–200), and IgM = 125 mg per cent (normal 90–170).

The patient's father had died aged 75 years of a 'ruptured appendix'. His mother had had long-standing hypertension and severe arteriosclerotic vascular disease and, after two cerebrovascular accidents, had died of massive lower gastrointestinal bleeding, apparently as a result of intestinal infarction. No necropsy was performed. One sibling had died of epidemic influenza when in her thirties and an older sister had had a stroke when aged 50 years, and now at 71 years had diabetes mellitus and hypertension. Three other siblings were healthy. A niece had strabismus but otherwise her eyes were normal. The patient had two children, each without cutaneous hamartomas; the elder was in good health and the younger was mildly mentally retarded due to hypoxia at birth.

The patient's corrected visual acuity was 20/15 in each eye. An absolute paracentral oval scotoma extended from 10° to 35° nasal to fixation in the right visual field (Fig. 2). The visual field examination of the left eye was normal. With the exception of some peripheral lens opacities in each eye, the results of biomicroscopy were normal. Ophthalmoscopic examination of the right eye revealed a normal optic disc, macula, and posterior retinal vessels. Approximately one-half disc diameter temporal to the fovea was an irregularly raised, oval, retinal vascular malformation measuring about 3 by 1½ disc diameters (Fig. 3). The central grey-white portions of the localized mass were variably dense and contained some clearer cystic spaces. Several large, poorly delineated, slate-grey areas, possibly representing deep aneurysmal malformations or haemorrhage, appeared under the cicatrical mass. At its boundaries, the tented retina merged into the lesion. The superior temporal vein passed through the lesion and was normal, without sheathing, both proximal and peripheral to it. One moderately enlarged, U-shaped

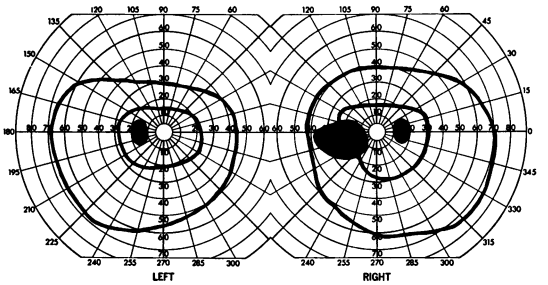


FIG. 2 *Case* 1. *Visual field examination with Goldmann perimeter* (111–2, 1–2) *shows absolute paracentral scotoma* (*even to V-4 isoptre*) *in right eye corresponding to retinal hamartoma*

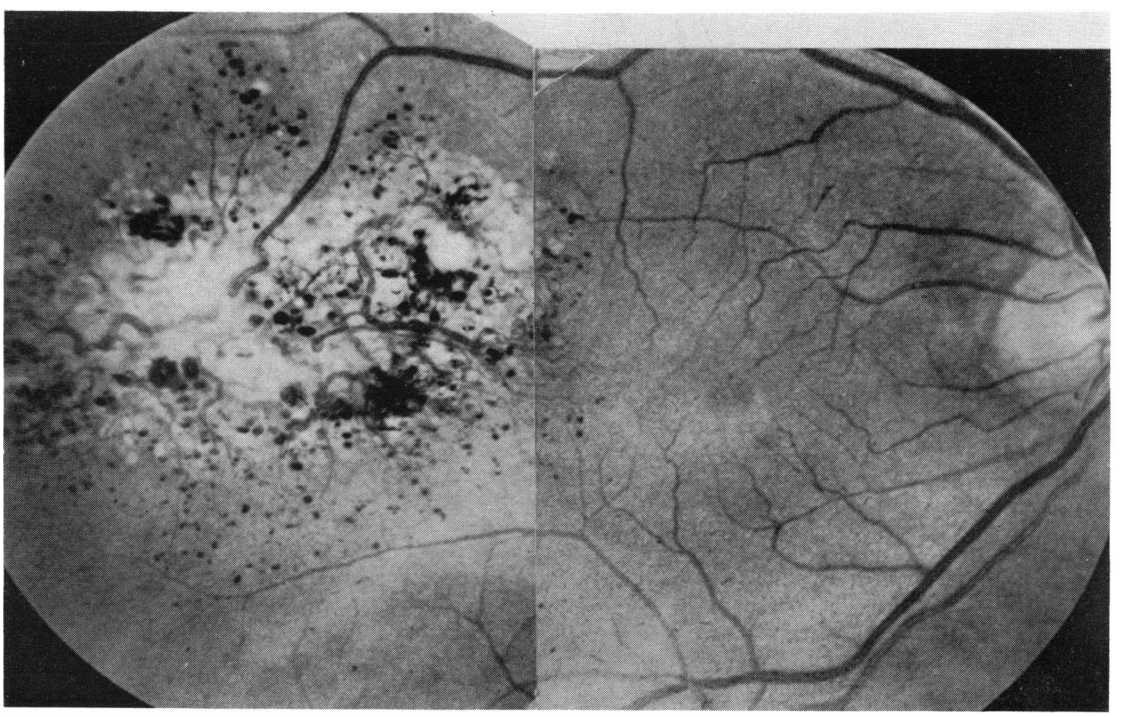
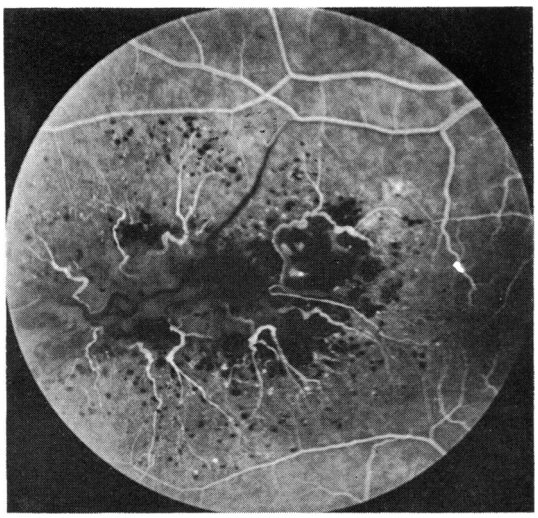


FIG. 3 *Case* 1. *Posterior pole of right eye in* 1974 *shows that cavernous haemangioma of retina is drained by branch of superior temporal vein. Several small branch arteries of normal calibre approach tumour. Compare Fig.* 1, *made* 34 *years earlier*

vein within the lesion did not appear to be connected to other retinal vessels but its course could not be clearly defined amidst the scar tissue. The tumour was peppered with numerous dark red spherules varying from dot-like to about twice the diameter of the major retinal vessels. Some of these demonstrated plasma/erythrocyte sedimentation with the interface shifting with changes in head position. In the adjacent retina, cherry-like bunches of these globules appeared to drain towards the main mass through tiny venules. The several afferent arterioles were normal. Biomicroscopy showed no retinal oedema, fatty exudates, or haemorrhages. Digital compressions of the globe and Valsalva's manoeuvre did not affect the morphology. The peripheral retina was normal and no evidence of diabetic microangiopathy was found. The left fundus was normal.

Fluorescein angiography revealed patchy screening of choroidal fluorescence in the area of the mass but normal arterial filling of the adjacent retina (Fig. 4*a*). Perfusion of the branches of the superior temporal vein comprising the tumour was markedly delayed. The saccules began to fill in the late venous and recirculation phases, some filling homogeneously and some not at all (Figs 4*b* and *c*). Plasma/erythrocyte sedimentation was apparent even 1 hr



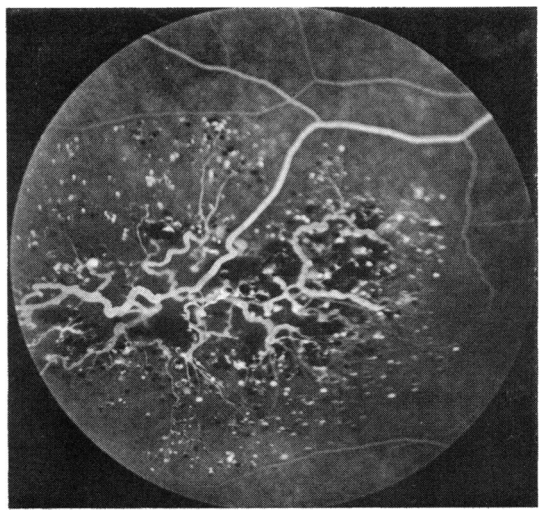
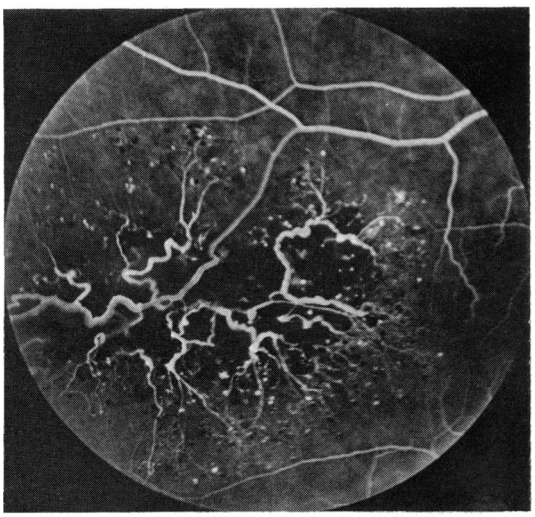
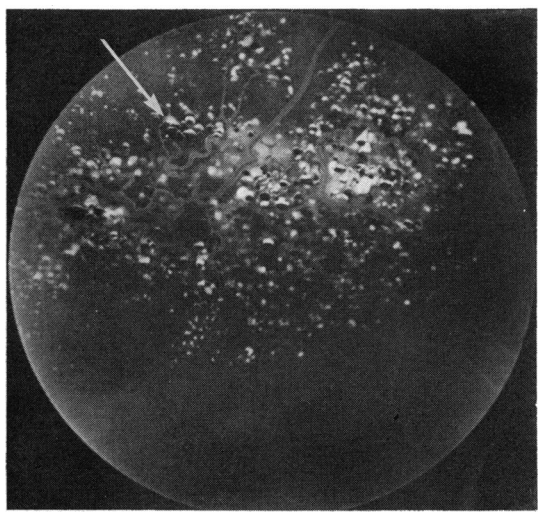


FIG. 4 *Case* 1. (*a*) *Fluorescein angiography reveals that perfusion of adjacent retinal circulation is normal but that venous drainage of peripheral clusters of aneurysms is markedly slowed*

(*c*) *After several minutes, adjacent retinal vascular fluorescence begins to fade, but haemangioma is still intensely fluorescent*





(*b*) *Slowly, more globules fill with dye and most smaller venous branches within lesion connect with main superior temporal branch vein*

(*d*) 45 *min after dye injection, most but not all aneurysms have evidence of dye perfusion and most show plasma/erythrocyte sedimentation (arrow)*

after dye injection, long after the background and retinal vascular fluorescence had faded (Fig. 4*d*). Minimal staining of the malformation was present but no specific sites of vascular leakage of dye were found.

Attempts to review the patient's early ophthalmological examinations were frustrated by the destruction of the 'outdated' medical records of the several earlier consultants, but comparison of current photographs with a previous fundus drawing showed only minor changes in the appearance of the lesion over a period of 34 years.

CASE 2

A 35-year-old black man was seen in an emergency room on 18 June 1971, after he had received a blow to the left eye in a fight. A diagnosis of traumatic uveitis of the left eye was made and the patient was treated with a mydriatic collyrium. When he returned for examination 7 days later, a large white lesion with multiple aneurysms in the inferior temporal quadrant of his right eye was noted, and a consultation was requested. His only other ophthalmological examination had been in 1957 when he had briefly been in hospital for facial cuts also received in a fight. The patient had then been informed that evaluation was normal and he was unaware of any other ocular problems. His previous medical history was otherwise unremarkable except for a short time in hospital for an adverse reaction to penicillin. He had no cutaneous hamartomas.

The patient's father had died of 'stomach cancer' when 59 years old. His mother had died in middle age of unknown causes. A sister and a half-brother were living and reportedly well, but were not available for examination. No family history of brain tumours, convulsive disorders, haemorrhagic diseases, diabetes mellitus, sicklaemia, or ocular disease was elicited.

His visual acuity without correction was 20/20 in each eye and the intraocular pressures by applanation were 14 mm Hg. Examination of the anterior segment of the right eye showed no abnormalities. The optic disc of the right eye was normal and the arterioles were slightly burnished with mild arterio-venous nicking. Distal to the junction of the branch venule draining the inferior meridians of the fovea, the inferior temporal vein became tortuous and included a corkscrew loop as it extended towards the peripheral lesion in the lower temporal quadrant. At the equator, there were large clusters of aneurysm-like globules mingled with a reasonably demarcated, raised white mass of tissue, approximately 3 by 2 disc diameters in size. Many of the globules seemed to be partially hyalinized with white thickened walls. Digital massage of the globe and Valsalva's manoeuvre did not alter the appearance of the lesion. Only one venous branch seemed to run through the lesion which appeared to be normal in calibre where its course could be observed amid the fibrous-like material. No venous sheathing and no major arterial supply could be identified. Inferior and slightly nasal to the main configuration were two round chorio-retinal scars with pigmented borders, each approximately one-half disc diameter in size. Peripheral to the lesion, there was no cystic change in the retina and around the lesion there was no evidence of intraretinal or subretinal fluid, haemorrhage, or fatty exudates. The macula and the entire retinal periphery were normal.

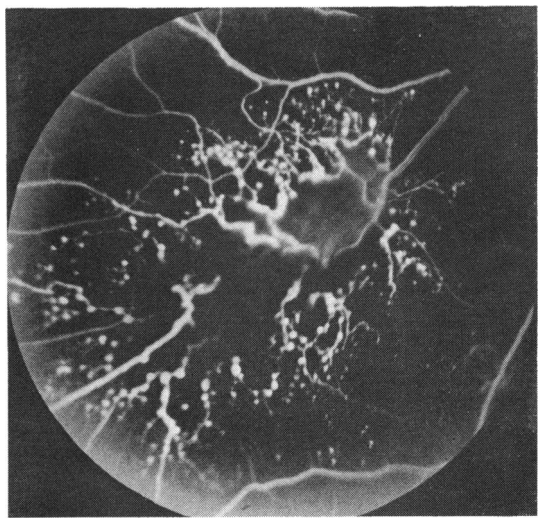
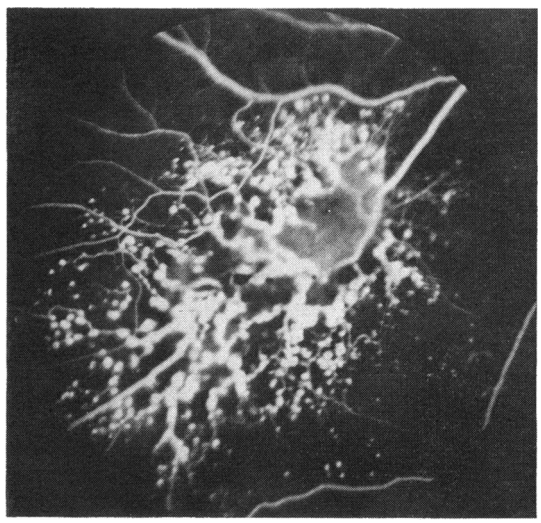


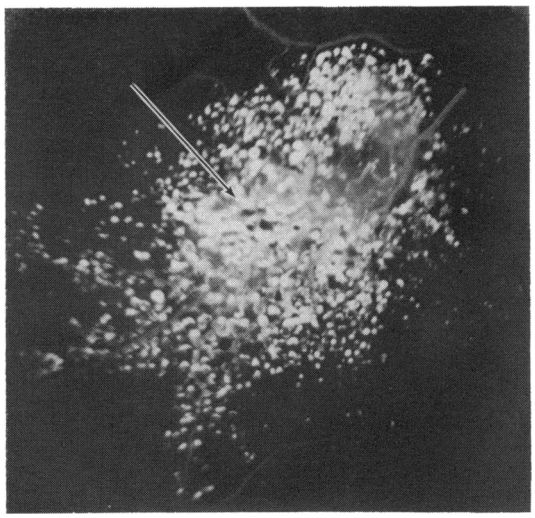
FIG. 5 *Case 2. (a) During early venous phase of fluorescein angiogram, aneurysms at periphery of haemangioma have begun to fill with dye and many small venules drain towards its less well perfused centre*



(b) Slowly, middle of malformation begins to perfuse and aneurysms of various sizes appear

The left eye showed a minimal burnished reflex from the arterioles as in the right eye but was otherwise unremarkable.

A fluorescein angiogram of the right eye showed that the anomalous vessels perfused much more slowly than the adjacent normal retinal vasculature (Figs 5*a* and *b*). Even 45 min after injection, most of the aneurysms were incompletely filled with fluorescein and demonstrated plasma/erythrocyte sedimentation well after the dye had left the remainder of the retinal vessels. There was no evidence of staining of the lesion or vascular extravasation of dye (Fig. 5*c*, overleaf).



(c) 45 min after injection, most of saccules show fluorescein-plasma/erythrocyte sedimentation (arrow) without extravasation into adjacent tissues. Normal retinal vascular fluorescence has virtually disappeared

The diagnosis of cavernous haemangioma of the retina was made. Although photocoagulation was considered, nothing about the lesion suggested activity, bleeding, or a threat to macular vision.

The patient was last examined in September 1974. During the intervening 38 months, diabetes of adult onset had been diagnosed and this was well controlled by diet. A visual field evaluation showed a relative scotoma in the right eye corresponding to the retinal lesion (Fig. 6). Serum protein electrophoresis was normal and quantitative immunoglobulins included IgG=1150 mg per cent (normal 770–1130), IgA=230 mg per cent (normal 80–200), and IgM=280 mg per cent (normal 90–170). Ophthalmoscopically the lesion in the right eye was unchanged. The cherry-like saccules at the borders appeared to be redder and more thin-walled than those towards its centre (Fig. 7). Plasma/erythrocyte sedimentation with shifting of the interface with changes of head position was apparent in some of them. Many of the peripheral

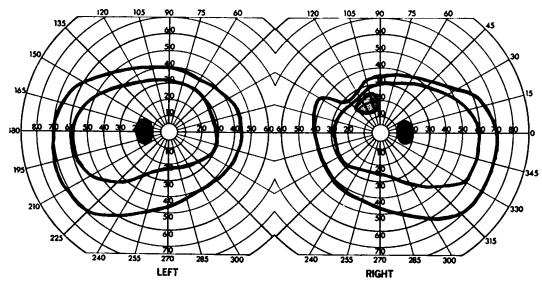


FIG. 6 *Case 2. Appearance of cavernous haemangioma of retina in September 1974, is unchanged from 1971. Note, congenital venous loop in inferior temporal vein (white arrow) and the inactive chorio-retinal scars (striped arrows)*

globules appeared to drain towards the lesion through tiny venules. A short fibrous tuft extended from the centre of the mass into the vitreous but no retinal break was identified. At least three branches of the inferior temporal artery fed the lesion, but no arterial or venous enlargement was noted. There was no evidence of recent or old vitreous haemorrhage and no suggestion of diabetic microangiopathy in either eye. Careful photographic comparison failed to show any changes in the haemangioma between the initial and the most recent evaluation.

CASE 3

A 45-year-old healthy white woman was found at a routine ophthalmological examination to have a vascular lesion nasal to the optic disc of the right eye. She denied having had any previous difficulty with her sight. Although she had a few dermal naevi and many sebaceous cysts, she had no cutaneous vascular lesions. The uncorrected visual acuity in each eye was 20/15. The left eye was normal, as were the results of the external and biomicroscopical examinations of the right eye. Ophthalmoscopy of the optic disc and macular area of the right eye was normal. Along and underlying the distribution of the superior nasal vein was a whitish mass resembling fibrous tissue, approximately 4 by 1½ disc diameters in extent, beginning about 3 disc diameters from the margin of the optic nerve head (Fig. 8). Multiple dark red saccular aneurysms, clustered in some areas, covered the surface and the margins of the lesion. A few spots of mottled depigmentation were present along the superior margin of the major lesion and a scattering of pigment clumps within and at its borders. No retinal haemorrhages or exudates were seen. The course of the vein through the lesion was somewhat irregular. The vein was minimally engorged for a short distance at the nasal end of the malformation but emerged beyond it on to normal appearing retina. Several secondary and tertiary branches of the superior nasal arteriolar tree approached the margins of the anomalous area, but these normal vessels did not demonstrate beading or sheathing. The adjacent retina was cystic and slightly tented. The vessels at the disc manifested minimal traction towards the lesion and a few tension lines were visible below the disc. The remainder of the retinal periphery to the ora serrata was normal. Fluorescein angiography was not performed and the patient was unavailable for subsequent examination.

Discussion

In the first edition of his textbook, Reese (1951) describes a group of patients with 'capillary haemangioma of the retina'. Characteristically, these angiomatous neoplasms of the retinal capillaries occupy a circumscribed zone of glial proliferation slightly raised, overlying which are numerous small superficial dark red vascular globules nourished by normal retinal vessels. These angiomas are probably congenital and do not progress. They tend to be prevalent in females. Subsequently Reese (1956a) attempted to integrate the lesion in some of these

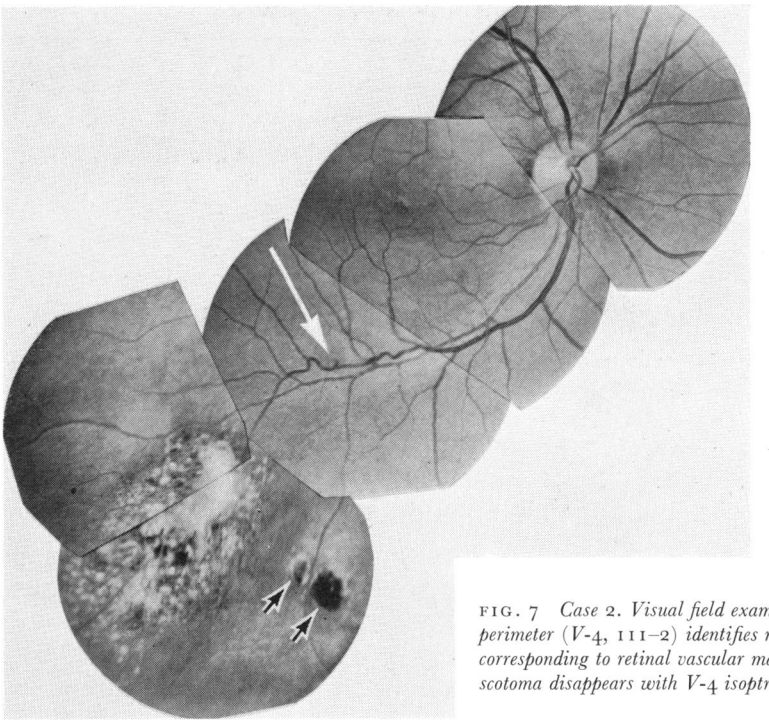


FIG. 7 *Case 2. Visual field examination with Goldmann perimeter (V-4, 111–2) identifies relative scotoma in right eye corresponding to retinal vascular malformation. Note that scotoma disappears with V-4 isoptre. Left visual field is normal*

patients with his concept of telangiectasis of the retina as a precursor of Coats's disease. He acknowledged (Reese, 1956b) that he had not examined the histopathology of a so-called capillary haemangioma. Later he deleted mention of the entity entirely (Reese, 1963), incorporating it into his discussion of Coats's disease. Thus, confusion has arisen about the true nature of this malformation and its appropriate classification among the blood vessel growths of the central nervous system, including the retina. Recently, the term 'cavernous haemangioma' has been used to distinguish this entity from other angiomatous malformations, including Leber's multiple miliary aneurysms, Coats's disease, hereditary haemorrhagic telangiectasia, von Hippel's disease, and other arteriovenous communications of the retina.

FIG. 8 *Case 3. Along the superior nasal vein near equator is cavernous haemangioma of retina with dense fibrous tissue at centre and clusters of aneurysms around its margin.*
(Monochrome reproduction from colour transparency)

The description of each of our patients agrees with the original criteria of Reese and the recent summary of Gass (1971) that cavernous haemangioma of the retina is typically a localized, sessile, vascular tumour consisting of numerous, closely clustered, thin-walled globules sprouting from a retinal vein. Grape-like bunches of these aneurysms may be adjacent to the main lesion and appear to drain towards it by tiny venules. Plasma/erythrocyte sedimentation in some of the saccules implies a markedly slow rate of perfusion. A grey-white veil interpreted variously as glial or fibrous tissue composes the body of the malformation, causes minimal elevation on an irregular surface, and blankets the involved vein. The white membrane is not a conspicuous feature of the lesions involving the optic disc. The calibre and the course of both afferent and efferent vessels are undisturbed.

The essential features of cases of cavernous haemangioma of the retina and of the optic disc in the available literature are summarized in the Table (overleaf).

Altogether 37 cases of this rare malformation, including those in this report, have been sufficiently

Table 1 *Summary of cases of cavernous haemangioma of the retina and of the optic nerve reported in the literature*

Date	*Author*	*Age* (yrs)*	*Sex*	*Race*	*Eye*		*Vision*	*Presenting symptoms*
					Right	*Left*		
1934	Niccol and Moore	32	M		X		R 20/120	Scotoma Metamorphopsia
1937	Scheyhing	21	M		X	X	R 15/400, L —	Headaches Scintillations Loss of vision
1940	Weskamp and Cotlier	17	F		—		—	Convulsions since age 12 years
1948	Neame	7	F			X	L 20/20	—
1949	Appelmans and others	54	M			X	L 20/20	Fleeting retrobulbar pain
1954	Piper	11	F		X		R 20/140	Loss of vision
		4	M			X	L 3/200	Esotropia Amblyopia
1955	Wallner and Moorman	26	F	W		X	L 20/20	Routine refraction
1956	Davies and Thumin	34	M	W	X		R 20/70	Blurred vision
1956	Reese	29	F		X		R 20/15	Occipital headaches
		24	F		X	X	R 20/15 L 20/40	Poor vision left eye
		15	M			X	—	Headaches
		14 (5)	M			X	L 20/20	None
1962	Kogan and Boniuk Hogan and Zimmerman	2	F	W	—		—	—
1963	Thiel	—	—			X	—	—
		—	—		—		—	—
1964	Larsen	12 (4)	F		X		R HM	Esotropia Amblyopia
1967	Frenkel and Russe	13	M	W	X	X	R 20/20 L 20/20	Herpetic keratitis
		10	F	W	X		R 20/20	Routine examination
1968	Amalric and Biau	6	M			X	—	Viral meningoencephalitis
1968	Witmer and others	47	F			X	L 20/20	Recurrent vitreous haemorrhages
1969	Larsen	21 (20)	F		X		R 20/20	Muscae volitantes
1969	Wessing	57	F			X	—	—
1970	Blodi, Allen, and Frazier	13	F	W		X	L 20/20	Routine examination
1971	Krause	37 (24)	F			X	L 20/200	Exotropia Amblyopia
1971	Gass	2½ (6 mths)	F	W	X		R Unsteady fixation	Esotropia

Haemorrhage	*Exudate*	*Associated systemic conditions*	*Progress*
Superficial	Shallow retinal detachment	Healthy	Enucleated after 45 days
No	Retinal striae	Negative general, neurological, and dermatological examination Negative skull *x* rays	None in 7 mths
—	—	Intracranial calcifications Cutaneous angiomas Cavernous haemangioma of brain Father had epilepsy	Death (necropsy)
—	—	—	—
No	No	Many cutaneous birthmarks	Enucleated for possible melanoma
No	No	Negative skull *x* rays	—
Superficial	Flat retinal detachment	Normal paediatric examination	—
—	—	Multiple cutaneous angiomas Negative skull *x* rays	None in 18 mths
Histologically subretinal	No	Alcoholism Seizures Negative skull *x* rays	Enucleated for possible melanoma
—	—	Negative neurological examination	None in 6 yrs**
—	—	Negative general examination	None in 6 yrs***
—	—	Negative neurological examination, skull *x* rays, pneumoencephalogram, electroencephalogram	None in 2 yrs
Several into vitreous	—	—	Slight increase in size over 20 yrs***
Only histologically	No	—	Enucleated for possible retinoblastoma
—	—	—	—
—	—	—	—
Superficial	—	Negative general and neurological examinations	Nearly unaltered for 8 yrs
No	No	No dermal or conjunctival lesions Hypogammaglobulinaemia	Slow, generalized increase over 2 yrs
No	No	Sister of Case 1 Defect in delayed hypersensitivity	—
—	—	—	Photocoagulated with success
Yes	No	—	Photocoagulation arrested growth and caused macular traction and visual loss
Superficial	—	Negative general examination	Unaltered for 1 yr
—	No	—	—
No	—	—	None in 4 yrs
Large preretinal haemorrhage	Shallow retinal detachment	Schizophrenia No facial angiomas Negative skull and orbital *x* rays	None in 8 mths Suicide with necropsy Globes not examined
Old vitreous and pigment epithelial haemorrhage	Macular traction	Prematurity Cutaneous angiomas Twin sister has cutaneous angiomas	Vitreous haemorrhage and regression after photocoagulation

(continued overleaf)

Table I (*continued*)

Date	*Author*	*Age* (yrs)*	*Sex*	*Race*	*Eye*		*Vision*	*Presenting symptoms*
					Right	*Left*		
1971	Gass	33 (27)	F		X		'Normal'	Convulsions
		51 (45)	F	W	X		R 20/15	Routine examination
1971	Gautier-Smith and others	41 (21)	F	W	X		R 20/30	Loss of vision
1971	Mildner	14 (13)	F			X	L 20/15	Routine refraction
1972	Stucchi, Bianchi, Cometta, and Faggione	12 (11)	M		X		R 20/30	Esotropia Posterior uveitis both eyes
1974	Robinson and Gitter	29	M	W		X	—	None
		60	M	W	—		—	—
1974	Gass	54 ('20s')	M		—		—	Routine examination
Present series		63 (29)	M	W	X		R 20/15	None
		38 (35)	M	B	X		R 20/20	None
		45	F	W	X		R 20/15	None

* Age at initial diagnosis in parentheses

described to allow some generalizations about its clinical features. The average age at presentation is 23 years. Approximately one-quarter of the lesions were identified during the first 30 years of life. About 60 per cent of cases (20 of 35 cases in the table) for whom the sex is recorded occurred in women, confirming the sexual predilection suggested by Reese. All patients for whom race is specified are white except for Case 2; this appears to be the first extensively reported occurrence in a black individual.

Among the cases in which only one eye is involved, the right eye (15 of 29 cases) is not affected more often than the left eye. No preferred laterality is noted among instances of optic disc involvement. There have been three reports of bilateral involvement (Reese, 1951; Scheyhing, 1937; Frenkel and Russe, 1967). In each of these, multiple foci are described in the right eye and minor involvement in the left. Conversely, only the report of Gautier-Smith, Sanders, and Sanderson (1971) clearly describes multiple tumour sites in one eye without a focus in the other eye. Unfortunately, Mildner (1971) relates the tumour in his patients to the adjacent artery, thus clouding an understanding of its topography. Although Larsen (1969) felt that the lower nasal quadrant was the usual site of the lesion, no preference for location is noted for either the retinal or the optic disc tumours if this whole series is reviewed.

Generally the visual acuity of the affected eye is good, unless the macula is involved directly (Gass, 1971; Piper, 1954; Krause, 1971) or with traction from the lesion (Scheyhing, 1937; Piper, 1954). On only one occasion (Larsen, 1964, 1969) was there profound unexplained loss of sight when the optic nerve, papillomacular bundle, and macula were apparently normal.

The visual field examination usually reveals enlargement of the blind spot in optic nerve lesions and scotomas corresponding to retinal malformations. In our Case 1, the scotoma was absolute and, according to verbal description, unchanged during his

Haemorrhage	*Exudate*	*Associated systemic conditions*	*Progress*
Subretinal	No	Cutaneous angiomas of face and leg Skull *x* ray and carotid angiogram normal Father died of cavernous haemangioma of brain Niece had seizures	Minor changes over 5 yrs
No	No	Bouts of orbital pain and lid ecchymosis	Minor changes over 4 yrs
—	—	Extensive cutaneous and probable cerebral and cervical angiomas Normal serum globulins Negative family history	Progression over 20 yrs
—	—	Biopsy proven cutaneous haemangioma Normal general and neurological examinations Normal skull *x* ray and electroencephalogram No family history	Regression after photocoagulation
Superficial	No	Negative paediatric and dermatological examinations Positive toxoplasma dye test	None in 8 mths
No	No	No systemic, dermal, or neurological disease	Obliteration after photocoagulation
No	—	—	—
—	—	Cutaneous angioma Convulsions One child had cutaneous angiomas and convulsions and died after excision of cerebral cavernous haemangioma	None in over 20 yrs
No	No	None	No change in 34 yrs****
No	No	None	None in 3 yrs
No	No	None	—

** Also reported in Reese (1951). *** Also reported in Reese (1951 and 1963). **** Also reported in Reese (1951 and 1956a)

extended period of observation although the earlier records had been destroyed. In Case 2, the defect was relative.

There has been concern about the threat of spontaneous haemorrhage from these vascular malformations. Many authors have noted a few tiny haemorrhages on the surfaces of the lesions or in the subretinal space. Reese (1951, 1956a, 1963) recorded one case of optic disc involvement in which recurrent small vitreous haemorrhages always resolved to leave good vision. Witmer, Verrey, and Speiser (1968) observed a woman with a history of recurrent vitreous haemorrhages for 10 years and visual acuity of 20/20 in the affected eye. Krause (1971) reported a large inferior vitreous haemorrhage which was not apparently visually significant, because the tumour itself involved the macular area. One of the cases related by Gass (1971) had evidence of old subretinal and intravitreal blood when first evaluated. We have detected no overt haemorrhages throughout the periods of observation of any of our patients. We have not found a report of the discovery of a cavernous haemangioma of the retina in an eye enucleated because of total vitreous haemorrhage or secondary glaucoma. The response of such an haemangioma to direct global trauma is moot. However, we feel that the relative risk of massive, spontaneous haemorrhage from these angiomas is low.

Intraretinal or subretinal fatty exudates do not occur. Grey-white retinal or epiretinal tissue may be a prominent component of these malformations and may be associated with slight traction on the adjacent retina as noted in our Cases 1 and 3. The cellular origin of this tissue is unexplained. The significance of the chorio-retinal scars which accompany the lesions in our Case 2 is unknown. No other signs of recent or old inflammation were manifest.

The findings of fluorescein angiography have been stated several times but are sufficiently characteristic to merit a summary. The choroidal blush and arterial filling of adjacent retina are normal. There may be patchy screening of underlying choroidal fluorescence

by the grey-white membrane of the main tumour and by the dense, blood-filled saccules. The peripheral saccules begin to fill at the early to mid-venous phase but perfusion of the anomalous veins in the central portions of the tumour mass and of the central clusters of aneurysms is significantly delayed, usually until after the peak of the full retinal venous phase. Although some of the spherules ultimately fill completely with dye, others appear nonperfused, and most show fluorescein-plasma/erythrocyte sedimentation, consistent with stagnation of blood flow. In late phases, there is pooling and layering of flourescent plasma in the saccules, giving further evidence of incomplete or sluggish circulation. The tumours may stain faintly, but extravascular leakage of dye does not ensue, intimating that both the retinal pigment epithelium and the blood-retina barrier are undisturbed.

Apart from minor changes in morphology, no progression of size or extent has been noted in the majority of these haemangiomas. Indeed, no significant alterations have appeared in our Case 1 over a period of 34 years. Reese (1956a) reported that in one of his cases the haemangioma had increased slightly in size over a period of 20 years. Frenkel and Russe (1967) detected a gradual and generalized increase in the number of retinal aneurysms over 2 years in their index patient. However, only Gautier-Smith and others (1971) recognized progressive diffuse angiomatous involvement related to all the major veins in one eye of a truly unusual patient.

The coexistence of vascular hamartomas in several organ systems including retina has been mentioned by several authors. Weskamp and Cotlier (1940) first identified a neurocutaneous syndrome associated with cavernous haemangioma of the retina. Their patient, a 17-year-old girl, had two 'dime-sized' red-violet capillary malformations of the occipital scalp and convulsions at the age of 12 years. After radiological evidence of intracranial calcification, a cavernous haemangioma was removed from the pre-Rolandic region. Interestingly, her father had had epilepsy and had died of undetermined causes, but no mention of skin changes was made.

Appelmans, Decock, and Van Opstal (1949) noted a great number of birthmarks (*taches naeviques*) on the skin of the trunk of their patient, but they did not clearly state that these were vascular lesions.

Wallner and Moorman (1955) reported a 26-year-old white woman with cavernous haemangioma of the optic disc and numerous reddish-purple vascular lesions on the trunk. She was asymptomatic and radiological studies of the skull were normal.

Gass (1971, 1974) has supported the association of retinal, dermal, and cerebral angiomas. Both Case 1 of his earlier paper and her identical twin sister who was ophthalmologically normal had cutaneous vascular hamartomas. The family history was apparently unremarkable. Gass's second case had seizures, multiple cutaneous angiomas, and a cavernous haemangioma of the retina. Her father had had epilepsy and had died of intracranial haemorrhage. Cavernous haemangiomas of the midbrain, pons, and cerebellum were found at his necropsy. A niece also had 'seizures'.

As mentioned above, Gautier-Smith, Sanders, and Sanderson (1971) detailed the involvement by venous angiomas in the skin, brain stem, spinal cord, and the retina in a young woman. The histology and the clinical course of the cutaneous angioma, the progression of motor and sensory deficits, and the appearance, of the retinal lesions strongly suggested that the vascular anomaly was the same in the several sites. However, the authors were unable to identify specifically the cranial and spinal malformations by myelography and extensive angiography. There was no family history of neurological disease or cutaneous naevi.

Mildner (1971) described a 14-year-old girl with a cavernous haemangioma of the retina who had had a cavernous haemangioma removed from her chest wall within her first year of life. Her general physical and neurological examinations, roentgenograms of the skull, and electroencephalogram were normal. She had no family history of ocular, dermatological, or neurological disorders.

Krause (1971) reported a cavernous haemangioma of the retina in a 37-year-old female with schizophrenia. She had no facial angiomas. Skull and orbital *x* rays revealed no intracranial calcifications. A necropsy after her suicide identified no intracranial abnormalities. The eyes were not included.

Recently, Gass (1974) reported another pedigree in which the father had a cutaneous angioma on one arm and a cavernous haemangioma of the retina in one eye, and generalized convulsions. One of his children, who had multiple cutaneous angiomas, developed seizures and died following the excision of a cavernous haemangioma of the cerebral ventricular system.

From these few instances, it is reasonable to suggest that the syndrome of cavernous haemangioma of the retina and of the optic nerve, cutaneous angioma, and the cavernoma of the cerebrum and brain stem could be included among the hereditary hamartomatoses. After reviewing his pedigrees, Gass concluded that the condition was inherited as an autosomal dominant. It is probable that its penetrance and expressivity are highly variable. Indeed, others, such as Collier (1967), have reported an association of venous angiomatous malformations of the retina and of the optic disc with cutaneous angiomas. While ultimately these reports may merit consideration within this syndrome, its full definition must await further clinical reports and careful retrospective

analysis of similar vascular lesions in the organs involved.

Frenkel and Russe observed cavernous haemangiomas of the retina in a sibship. Their first patient had hypoimmunoglobulinaemia and bilateral retinal tumours. However, his dermatological and neurological examinations and skull roentgenograms were normal. His sister had a uniocular lesion and a defect in delayed hypersensitivity. In two of our patients, the results of protein electrophoresis were normal and the quantitation of immunoglobulins showed only nonspecific increases in several fractions. The only other published report (Gautier-Smith and others, 1971) of serum globulins in a patient with cavernous haemangioma of the retina was normal. Therefore, we cannot substantiate the possible connexion between these vascular malformations and hypogammaglobulinaemia.

The appropriate management of these tumours has been a subject of some discussion. Four eyes have been enucleated, one for suspected malignancy (Niccol and Moore, 1934), two for possible malignant melanoma (Appelmans and others, 1949; Davies and Thumin, 1956), and one for a clinical diagnosis of retinoblastoma (Kogan and Boniuk, 1962; Hogan and Zimmerman, 1962). More conservative intervention appears to have been described first by Amalric and Biau (1968), who reported the successful photocoagulation of a retinal tumour, although they did not give details. Witmer and others (1968) repeatedly photocoagulated a haemangioma which had been the source of recurrent vitreous haemorrhages and were able to arrest its growth. However, they failed to destroy it and secondary macular traction caused a loss of visual acuity to 20/100 (P. Speiser, personal communication).

Gass (1971) placed a single row of xenon photocoagulation around the margin of the tumour in one of his cases. Unfortunately a catastrophic vitreous haemorrhage ensued. With its resolution 16 months later, considerable regression of the tumour and its replacement by fibrous tissue were noted, unfortunately with traction on the macula.

Mildner (1971) described direct photocoagulation of the microvascular components of the tumour in his patient. He documented a prompt partial regression, but with striking scarring and traction on adjacent retinal vessels.

Recently, Robinson and Gitter (1974) recounted their experience with argon laser coagulation of a cavernous haemangioma of the retina. Treatment was undertaken because of the possibility of spontaneous haemorrhage. The authors successfully obliterated the lesion without complications, carefully avoiding main venous channels.

In reviewing these five cases, we note both the absence of massive subretinal exudation after treatment, quite contrary to the usual experience with the angioma of von Hippel's disease, and the possibility of extensive haemorrhage and scarring with traction. However, considering the absence of retinal oedema or exudate during its natural evolution, the rarity of significant spontaneous vitreous haemorrhage, and the infrequency of detectable progression, the malformation probably does not require therapy. If extensive vitreous or subretinal haemorrhage does occur in a particular instance, both cryopexy and photocoagulation should be capable of eliminating the process. More experience is needed to define the specific treatment method which will minimize its hazards. The cavernous haemangioma of the optic disc probably bears a higher risk because of its vital location, more extensive vascularity, dramatic elevation, and the relative paucity of stromal elements in its structure.

Most retinal vascular malformations do not present material confusion in the diagnosis of cavernous haemangioma of the retina and of the optic nerve. No direct anastomoses of arteries and veins can be identified and therefore the entire group of retinal arterio-venous communications recently reviewed by Archer, Deutman, Ernest, and Krill (1973) can be dismissed. The intraocular involvement of hereditary haemorrhagic telangiectasia (Davis and Smith, 1971), tuberous sclerosis, and the Sturge-Weber syndrome may be considered but can be eliminated on morphological grounds. Von Hippel's disease can be differentiated by the appearance of multifocal, discrete, isolated nodules, the frequently enlarged, nondescript afferent and efferent channels, and associated intraretinal and subretinal exudation. Although the feeding vessels usually do not leak fluorescein, the haemangioblastoma of von Hippel demonstrates profuse transudation of the dye and no evidence of aneurysmal dilation of the small vessels within the neoplasm (Haining and Zweifach, 1967).

Coats's disease and Leber's multiple miliary aneurysms offer the greatest challenge in the differential diagnosis. We agree with recent authors (Archer and Krill, 1971; Egerer, Tasman, and Tomer, 1974) that these two diseases may be closely related. Certainly, fluorescein angiography identifies many common features. In the arterial phase, major vessels of irregular calibre perfuse a dilated capillary bed with patches of non-perfusion or dropout. A few saccular microaneurysms are strung along the precapillary arterioles and border the zones of capillary loss. The areas of retinal capillary bed closure are bridged by arterio-venous shunts with relatively rapid circulation (Henkind and Wise, 1974). Fluorescein stains the vessel walls and the aneurysms and both dye and serous fluid leak profusely into the retina. Fatty exudates form haloes along capillaries and other vessels and the macula may be involved if the disorder occurs in the temporal retina. Cavernous haemangioma of the retina has

few of these features, being primarily a venous malformation without vascular decompensation (Wessing and Meyer-Schwickerath, 1971)

Summary

We report characteristics of three cases of cavernous haemangioma of the retina, bringing to 37 the number now reported in the available literature. This rare, benign, congenital malformation is non-progressive, usually unilateral, somewhat more frequent in women, and rarely a source of intraocular haemorrhage. The fluorescein angiographic features include a normal arterial and venous supply, extraordinarily slowed venous drainage, no arterio-venous shunting, no disturbances of vascular permeability, and no secondary retinal exudation. Almost always, isolated clusters of vascular globules with plasma/erythrocyte sedimentation surround the main body of the malformation. These findings differentiate the anomaly from other retinal vascular diseases. Therapeutic intervention is seldom necessary.

Addendum

Since this paper was completed, we have identified a brief mention of an additional case of this hamartoma (Gass, 1972).

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