Rubeotic glaucoma

REDMOND J. H. SMITH

From the Western Ophthalmic Hospital and Moorfields Eye Hospital, City Road, London EC

SUMMARY The literature of theories of causation of rubeosis and thrombotic glaucoma is briefly reviewed and attention is drawn to the fact that the causative role of anoxia of the retina, leading secondarily to rubeosis of the iris and subsequent glaucoma, was first described in 1954. After that attempts were made to prevent the rubeosis by means of destruction of large areas of retina, initially by surface diathermy, but subsequently by cryotherapy. Although the visual results of this treatment have proved to be extremely poor, nevertheless none of the 18 eyes involved has had to be enucleated. It is hoped that in the future a judicious combination of better prediction and better treatment should make thrombotic glaucoma a preventable disease.

Glaucoma associated with rubeosis of the iris is one of the most lethal forms of the disease. It usually leads to complete loss of vision and intractable pain, accompanied by bleeding into the anterior chamber. The most common variety is that following occlusion of the central retinal vein, variously called haemorrhagic or thrombotic glaucoma. An identical picture can also follow rubeosis in diabetic retinopathy and in certain cases of long-standing retinal detachment, either simple or secondary to choroidal neoplasia. The condition can also occasionally occur after occlusion of the central retinal artery.

Before 1954, although the relationship between glaucoma and occlusion of the central vein of the retina was recognised, the mechanisms involved were not. Nor had the sequence of events leading to the glaucoma been observed and recorded. Rubeosis itself, in which apparently new vessels ramify on the anterior surface of the iris and in which ectropion of the pigmented pupillary border eventually occurs, had been observed by many workers in 'thrombotic glaucoma' and had been seen in diabetes by Salus¹ and Kurz,² though François³ thought the condition of the iris in diabetes was different from that in central retinal vein occlusion. Rubeosis was also seen in 'cyanosis retinae',⁴ in Eales's⁵ disease and long-standing retinal detachment,⁵ and in retrolental fibroplasia.⁶ Wagener⁷ described rubeotic glaucoma occasionally occurring after retinal arterial ischaemia and thought it had a similar origin in retinal hypoxia to that of venous rubeosis.

The pathology of central retinal vein occlusion had been studied extensively by Verhoeff,⁸ Coats,⁹ and many others. The association of primary glaucoma with central vein occlusion had been pointed out by Foster Moore,¹⁰ Sugar,¹¹ and others, and the formation of new blood vessels on the iris and in the filtration angles had been described.¹²⁻¹⁴ There was, however, no agreement among the various authors about the timing or the role of the neovascularisation, some believing it preceded and others that it followed the glaucoma.

Ashton *et al.*,¹⁵ clearly showed that retinal ischaemia induced by oxygen overdosage triggering retinal blood vessel closure in the premature eye preceded and probably caused neovascular and fibrous proliferation in the anterior retina and iris. In view of this work Smith¹⁶⁻¹⁸ carried out a prospective study of cases of central vein occlusion with the object of observing the onset and progress of rubeosis iridis. As a result of this study it was proposed that retinal ischaemia caused the release of a hypothetical metabolite which acted incidentally on the iris, to which it was carried by the circulation of the intra-ocular fluids, producing neovascularisation on the iris in exactly the same way that it is produced on the retinal surface or on the optic disc in branch vein occlusion or diabetes or in the anterior vitreous as rete mirabile in anterior retinal ischaemic disease or in Eales's disease. (Indeed it is possible that the same principle may extend to the pathology of disciform degeneration of the retina, so that the preliminary detachment of the central retina with or without the pigment epithelium may produce enough hypoxia in

Correspondence to Mr Redmond Smith, 2 Harley Street, London WIN 1AA.

the detached receptors to invoke a subretinal neovascular response from the underlying choroid—retroretinal rubeosis.)

The pathological principles involved in this sequence, which are of crucial importance, are thus as follows: first, chronic ischaemia and hypoxia of the retina leads to the release of a neovascularising factor; secondly, the factor, which is probably a diffusible chemical substance, can be transported to various sites in the eye by the intraocular fluids; thirdly, the resultant new vessels lie in a matrix which includes or induces fibrous tissue which eventually cause adhesions and contractions (peripheral synechiae and ectropion uveae in the iris and retinitis proliferans in the retina); and, fourthly, the new vessels may bleed.

Thus this fundamental pathological process, first clearly identified in retinopathy of prematurity by Ashton *et al.*,¹⁵ lies at the basis of at least 3 major ophthalmic diseases, namely, retrolental fibroplasia, diabetic retinopathy, and thrombotic glaucoma, with disciform macular degeneration (retroretinal rubeosis) as a possible fourth.

Where the understanding of a pathological sequence is attained, the next step is for some form of treatment to be devised to try to modify or prevent it. In the case of retrolental fibroplasia the initial avascularity of the retina caused by oxygen over-dosage was prevented by suitable modifications of oxygen therapy in premature infants. In the case of rubeotic glaucoma due to central vein occlusion no action was taken for some years after the publications

of 1954, but in January 1960 an attempt at fundamental treatment was started.¹⁹

Materials and methods

Between January 1960 and September 1966 9 eyes (of 8 patients) were treated by anterior retinal diathermy. The technique involved applications of surface diathermy in a band 14 to 16 mm from the limbus at 70 milliamps for 5 seconds. Subsequent monitoring was carried out where visibility allowed and adequate retinal destruction was seen.

Results

The results are summarised in Table 1. It can be seen that only 1 patient retained good vision, the first patient, and another retained 6/36. Otherwise, visual results were very poor, but rubeosis was inhibited or abolished in 5 of the 9 eyes, and the final intraocular pressures were normal in 5 eyes. Persistent uveitis occurred in all the eyes with flare and cells in the aqueous humour.

With the advent of cryotherapy it was decided to abandon surface diathermy in favour of cryoablation of the retina in the hope that the lesser uveal and virtually absent surface damage would reduce post-operative uveitis. From May 1966 until April 1979 a further 9 eyes of 9 patients were treated by cryoablation. The earlier cases were treated by cryoablation by choice, but in some other later cases cryoablation was used as an alternative to panphoto-

Table 1 Anterior retinal diathermy

Date first seen	Hosp. no. File no.	Sex/Age	Eye	Brief history	Follow-up	Final state			
						Rubeosis	Pain	IOP	VA
1 June 59	595739 21	M/53	L R	Bilateral CRVO with rubeosis and corneal oedema. ARD 360° both eyes L-Jan 60, R-Mar 60	18 mo 18 mo	Reduced Not improved	0	15	6/9
31 Dec. 59	002237 23	M/72	L	CRVO plus open angle glaucoma. Rubeosis began after 4 mo. ARD 360°. Had diabetic coma aged 93. Still alive 1980	21 yr	Abolished	0	20	CF
3 Aug. 60	607031 24	M/80	R	CRVO with pupillary and trabecular rubeosis. ARD 360°	8 mo	'almost nil'	0	23	6/36
1960	Private patient 22	M/70	—	Established thrombotic glaucoma. 360° ARD		Not improved			
22 Aug. 60	556825 25	M/54	L	Thrombotic glaucoma with trabecular rubeosis, but no PAS. ARD 360°	6 mo	Nil	0	18	4/60
Feb. 63	D51138 58	F/67	L	CRVO—glaucoma after 3 mo with trabecular rubeosis. ARD 360°	2½ yr	Nil	0	9	CF
1965	D53882 84	F/73	L	Diabetic rubeosis. IOP 53. ARD 360°	6 mo	Still present		60	No PL
1966	C56699 88	M/37	R	Diabetic with rubeosis. ARD 360° plus 3×cyclo-diathermies	9 mo	Improved	0	26	PL

CRVO=central retinal vein occlusion. ARD=anterior retinal diathermy. IOP=intraocular pressure. CF=counting fingers. PL=perception of light. NPL=no perception of light.

Table 2 *Cryoablation*

Date first seen	Hosp. no. File no.	Sex/Age	Eye	Brief history	Follow-up	Final state			
						Rubeosis	Pain	IOP	VA
4 May 66	664008 90	M/50	L	CRVO with early rubeosis of iris. Cryoablation and repeat cyclodiathermy	7 yr	Not abolished	0	30	NPL
3 Mar. 64 (photo)	000348 101	M/56	R	CRVO in open angle glaucoma rubeosis of iris and angle 1971. Retinal cryoablation	9 yr	Not abolished	0	31	NPL
27 Mar. 72 (iris photo)	D63402 108	F/47	L	CRVO with thrombotic glaucoma. IOP 70 mmHg and corneal oedema. 360° retinal cryoablation	7½ yr	Abolished	0	18	CF
16 Nov. 72	D64206 108	F/60	L	CRVO with thrombotic glaucoma. IOP 80 mmHg. 360° cryoablation	5 yr	Abolished	0	16	NPL
23 Aug. 73	D65165 108	M/68	L	CRVO with chronic open angle glaucoma. Rubeosis developing. Iris angiography. 360° cryoablation	9 yr	No change	0	20	NPL
20 Aug. 74	D66461 108	M/75	L	CRVO with thrombotic glaucoma. Extensive angle closure and rubeosis. 360° cryoablation	3 yr	Cured	0	20	PL
3 Mar. 75	D67008 108	F/71	L	Old CRVO—disc vessels and rubeosis. IOP 50 mmHg. Peripheral anterior synechiae: 40%. 10.3.75: 'peripheral retinal cryoablation'	5 yr	Nil	0	20	NPL
7 July 78	054355 108	M/53	L	Established thrombotic glaucoma. IOP 40 mmHg. Laser followed by 360° retinal cryotherapy plus cyclo cryotherapy	1 yr	Regression	0	26	NPL
17 Apr. 79	058177 108	M/75	R	Diabetic with thrombotic glaucoma. IOP 60 mmHg. Angle flush plus small hyphaema. 360° cryoablation. Later repeated	1 yr	Failure	+	28	NPL

Abbreviations as in Table 1.

coagulation because of opacities in the media. One case was treated by both laser therapy and cryoablation. The technique consisted in applying cryotherapy to the entire pre-equatorial retina, and retinal destruction was monitored by ophthalmoscopy where possible.

The visual results in this series were rather worse than in the previous group, 7 of the 9 eyes ending with no perception of light, 1 with only hand movements, and another with counting fingers. Intraocular pressures were improved in most; however, rubeosis was reduced in 1 and abolished in 4, and only 1 eye remained painful.

Discussion

One hopes that the poor visual results in these 2 groups of eyes can be attributed to the retinal vascular disease. Although it is possible that the retinal ablation did enough damage to contribute to the poor visual prognosis, without cryoablation a proportion of the eyes would have progressed to the gross form of rubeotic glaucoma with intractable pain, necessitating enucleation. Indeed in Laatikinen and Kohner's 1976 series²⁰ 17.7% of such eyes developed thrombotic glaucoma.

It is claimed, therefore, that the diathermy or the cryoablation of extensive areas of retina reduced the extent of the ischaemic retina to such a degree that

the production of the neovascularising factor fell below the threshold for iris neovascularisation and that this resulted in regression of the rubeosis.

These early attempts at treatment must, however, be considered crude and somewhat indiscriminate. Rather than waiting for rubeosis to start, by which time extensive vasoformative membranes would have been formed, far more extensive than the visible rubeosis, it would be preferable to be able to select accurately those cases which were likely to suffer from rubeosis and treat them only.

Laatikinen and Kohner²⁰ showed that fluorescein angiographic evidence of extensive capillary closure following retinal vein occlusion was always followed by rubeotic glaucoma. Laatikinen²¹ in a preliminary report of 8 cases of vein occlusion, 1 of arterial occlusion with rubeosis, and 1 of diabetes with rubeosis, carried out panphotocoagulation and found virtually identical results to those presented in this paper. Her results are confirmed in a larger study²² in which a randomised clinical trial was carried out with controls, and similar results have been reported in retinal cryoablation by May and others.²³

In summary, therefore, the position at this stage appears to be as follows. The available evidence supports the theory that retinal hypoxia induces rubeosis iridis by means of a diffusible substance, as first proposed in 1954. The ability to predict rubeosis has been enormously improved by the fluorescein

angiographic techniques which have become available. Early attempts at treatment by diathermy or cryotherapy saved vision in only a very few eyes, but the eyes themselves were saved. Later, photocoagulation with the benefit of fluorescein angiographic knowledge produced approximately similar results clinically, namely, very little visual salvage but no loss of eyes.

The next stage in these studies therefore appears to be to consolidate the earlier work and to confirm the absolute necessity of early panretinal ablation where fluorescein studies suggest the likelihood of rubeotic glaucoma.

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