Panretinal cryotherapy in neovascular disease

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SUMMARY Panretinal cryotherapy (PRC) was used to treat 15 eyes with rubeosis, nine of which had established neovascular glaucoma, and seven eyes with proliferative diabetic retinopathy. The rubeosis regressed, with preservation of vision and return to normal of intraocular pressure, in all but one eye. With one exception all eyes with proliferative retinopathy also showed new vessel regression after treatment. PRC may be considered an effective alternative to retinal photocoagulation in the treatment of advanced rubeosis, early rubeotic glaucoma, and in certain circumstances proliferative diabetic retinopathy.

Iris and retinal neovascularisation occurring secondary to an ischaemic retinopathy may cause loss of vision by a number of mechanisms. These include vitreous haemorrhage, traction retinal detachment, and neovascular glaucoma. For many years selective retinal ablation has been shown to induce regression of both retinal and iris neovascularisation in a significant number of cases. The first successful application of retinal ablation in the treatment of rubeotic glaucoma was in 1960, when 360° ablation of the retina anterior to the equator was performed with surface diathermy. In 1964 cryotherapy was substituted, but when it was limited to the anterior retina many eyes lost light perception. Panretinal cryotherapy (PRC) applied to the retina posterior to the equator has been advocated as a method of retinal ablation, but reports to date have concluded that PRC should be withheld until rubeotic glaucoma is present because of the risk of serious complications, or the PRC has been combined with cyclotherapy.

Our study presents the outcome of 22 eyes treated with PRC in the last six years at the Oxford Eye Hospital. The study includes nine eyes with neovascular glaucoma, six with advancing rubeosis, and seven with proliferative diabetic retinopathy.

Materials and methods

All eyes receiving PRC from one clinic between January 1979 and December 1985 were included in this study. This method of retinal ablation was adopted if poor media clarity, poor pupillary dilatation, extensive retinal oedema, or patient intolerance prevented adequate photocoagulation.

Prior to PRC 10 eyes had received laser or xenon panretinal photocoagulation which had not produced neovascular regression.

Where previous photocoagulation to the posterior retina was not considered to be sufficient, or no treatment had been given in the past, xenon photocoagulation was applied around the vessel arcades and temporal to the macula immediately before PRC, with the same retrobulbar anaesthetic. In five eyes PRC was used alone (eyes 5 and 6, Table 1 and eyes 1, 2, and 3 Table 2). One eye early in the series had cyclotherapy performed with the PRC (eye 1 Table 1).

PRC can be delivered under local or general anaesthesia. A 360° peritomy is performed, and 4/0 silk traction sutures are placed beneath the four rectus muscles to aid exposure. A total of 40 freeze-thaw applications with the 2.5 mm retinal cryoprobe are delivered under indirect ophthalmoscopic view where possible. Each quadrant receives 10 applications, a row of four centred on the equator followed by two circumferential rows of three posteriorly. Each application produces an area of retinal ablation of approximately 12 mm², and applications should be just confluent. No applications are performed within 5 mm of the macula or 3 mm of the disc. The time taken to produce the desired iceball is measured during initial application and varies from 5 to 10 seconds. It is important to measure the time for posterior applications, as these will be slightly longer than for anterior. This is due to the increased scleral...
and choroidal thickness encountered posteriorly and a greater tendency for heat to be absorbed from surrounding orbital tissue. If posterior applications are not delivered under direct vision, then a longer application time may be required to achieve the desired reaction.

When photocoagulation is to be given, it should be done before PRC, as there will be too much chemosis or corneal epithelial changes to allow effective light coagulation for some days. This is due to either difficulty in applying a contact lens or a reduction in the clarity of the cornea.

The area of retinal ablation produced by the above method of PRC has been determined with the following mathematical model:

If the area of retina posterior to the equator is assumed to be one half of a sphere with radius 12 mm, then the area of retina available for treatment = \( \frac{1}{2} \pi r^2 \times 1357 \text{ mm}^2 \) (where \( r \) is the radius).

It is not desirable to treat within 5 mm of the macula or 3 mm of the disc. Therefore the effective area for treatment reduces to 1357–75–44 mm\(^2\) = 1238 mm\(^2\).

If one cryo application produces 12 mm\(^2\) of retinal ablation, 40 applications produce 480 mm\(^2\). Therefore the percentage of available retina treated = \( \frac{480}{1238} \times 100 = 39\% \).

This percentage will increase to between 45 and 50\% of the retina posterior to the equator if xenon applications are delivered immediately prior to PRC.

**Results**

**Rubeotic Glaucoma**

Of the nine eyes with rubeotic glaucoma five were secondary to diabetic retinopathy (one eye had coexisting disc new vessels), three were secondary to central retinal vein occlusion (CRVO), and one followed central retinal artery occlusion (eye 9). So far all eyes have remained pain free, all showed regression of iris neovascularisation, and all but one eye had an intraocular pressure within the accepted normal range on no medication. This was the only eye to lose all light perception in this group during the follow-up period, which ranged from four months to three years. The visual acuity improved in two eyes, remained unchanged in four, and deteriorated in three (Table 1).

**Case 1.** This 69-year-old patient with diabetes mellitus for 12 years which had been controlled on oral hypoglycaemic agents. In December 1982 he had 255 laser burns to the posterior pole of his left eye (eye 7, Table 1) for maculopathy. No signs of neovascular disease were present at that time, the intraocular pressure was normal, and the acuity was measured at 6/9. Ten weeks later at a routine follow-up visit the eye was noted to have early rubeosis round the pupil margin, new vessels crossing the drainage angle temporally through 180°, and an intraocular pressure of 38 mmHg. Despite mild epithelial oedema of the cornea, the acuity remained at 6/9. PRC, incorporating 400 xenon burns to the posterior retina, was performed, and two weeks later the rubeosis had regressed and intraocular pressure returned to normal. The visual acuity fell to 6/36 postoperatively owing to macula oedema. This slowly improved, returning to 6/9 seven months later. Three years later the eye retained 6/9 acuity and has required only minimal laser therapy to control an area of peripheral retinal neovascularisation.

**Advancing Rubeosis**

Six eyes were treated for advancing rubeosis, three secondary to diabetes and three following CRVO. All six eyes showed regression of the rubeosis and none progressed to rubeotic glaucoma in the follow-up period, which ranged from two months to two years in this subgroup. Visual acuity either remained static or improved in all but one eye, which developed increased lens opacities (Table 3).

**Case 2.** A 62-year-old, mentally subnormal insulin-dependent diabetic of four years’ duration was first seen in May 1985. She was referred with corneal

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Rubeotic Glaucoma Eyes</th>
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</thead>
<tbody>
<tr>
<td><strong>Eye Age</strong></td>
<td><strong>Primary Disease</strong></td>
</tr>
<tr>
<td>1</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>68</td>
</tr>
<tr>
<td>3</td>
<td>74</td>
</tr>
<tr>
<td>4</td>
<td>74</td>
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<tr>
<td>5</td>
<td>87</td>
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<td>6</td>
<td>62</td>
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<td>7</td>
<td>69</td>
</tr>
<tr>
<td>8</td>
<td>60</td>
</tr>
<tr>
<td>9</td>
<td>60</td>
</tr>
</tbody>
</table>

**CRAO**=central retinal artery occlusion. CRVO=central retinal vein occlusion. CF=counting fingers. HM=hand movements. NPL=no perception of light.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Rubeosis with Normal IOP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eye Age</strong></td>
<td><strong>Primary Disease</strong></td>
</tr>
<tr>
<td>1</td>
<td>77</td>
</tr>
<tr>
<td>2</td>
<td>42</td>
</tr>
<tr>
<td>3</td>
<td>62</td>
</tr>
<tr>
<td>4</td>
<td>70</td>
</tr>
<tr>
<td>5</td>
<td>71</td>
</tr>
<tr>
<td>6</td>
<td>76</td>
</tr>
</tbody>
</table>

**AC**=arterial claudication. CRVO=central retinal vein occlusion. CF=hand movements.
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...continued.

Oedema from rubeotic glaucoma in her right eye (eye 6, Table 1) following intracapsular surgery performed 15 months earlier. This was successfully treated with PRC under general anaesthesia. The left eye (eye 3, Table 2) which had also received intracapsular surgery elsewhere, developed rapidly advancing rubeosis during August and September 1985. On 3 October PRC was performed on the left eye, again under general anaesthesia owing to the patient's mental state, and two weeks later the rubeosis had regressed completely.

Four months after the treatment of the left eye both eyes had normal intraocular pressures, and neither eye showed any evidence of rubeosis. The patient retained 6/60 acuity in each eye, the reduction being due to pre-existing diabetic maculopathy.

Retinal neovascularisation

Seven eyes were treated with PRC for disc or peripheral retinal neovascularisation. In 6 eyes this was secondary to diabetes and one eye had suffered a CRVO. Of the six diabetic eyes four were treated with PRC as vitreous haemorrhage prevented safe photoacoagulation and two PRC treatments were performed because the patients could not tolerate photoacoagulation. The eye with CRVO and disc new vessels had such extensive retinal oedema that adequate photoacoagulation was not possible.

In the four eyes with vitreous haemorrhage, visual acuity improved by 3 lines or more in 2 eyes and by one line in one eye (Table 3). Only one eye (eye 7, Table 3) lost vision, progressing via rubeotic glaucoma to no perception of light.

Case 3. A 47-year-old type 1 diabetic of 27 years duration presented in 1980 with disc new vessels in his right eye (eye 1, Table 3). Argon laser and xenon arc panretinal photoacoagulation failed to induce new vessel regression, and in December 1981 PRC was performed on this eye, when vitreous haemorrhage precluded further photoacoagulation. Xenon panretinal photoacoagulation to the left eye (eye 2, Table 3), performed in December 1981, was followed by a vitreous haemorrhage. At this time both eyes had significant vitreous haemorrhage, with increasing neovascularisation. PRC was performed on the left eye in February 1982. The vitreous haemorrhages in both eyes subsequently cleared, but the right eye suffered a further bleed in 1983 before clearing slowly. The left eye remained clear and maintained an acuity of 6/12 four years later. New vessels regressed in both eyes following PRC, but an epiretinal membrane causing macular traction had reduced visual acuity in the right eye.

Discussion

The natural course of rubeotic glaucoma often results in a blind and painful eye. Rubeosis has been stated to occur always at the pupil margin prior to its occurrence in the anterior chamber angle. Although all cases of early rubeosis do not necessarily progress to rubeotic glaucoma, progression may be rapid, particularly in CRVO. To produce arrest or regression of an advancing rubeosis without inducing significant visual loss is clearly a desirable aim.

Regression of rubeosis was reported following extensive diathermy ablation of retina anterior to the equator in 1961, and since Krill et al. demonstrated regression of iris rubeosis following panretinal photoacoagulation many studies have produced similar results. It has been suggested that rubeosis may be prevented in susceptible eyes by prophylactic photoacoagulation.

Our results of applying PRC to eyes with advancing rubeosis suggest that PRC should not be forgotten as an alternative method of selective retinal ablation when adequate photoacoagulation cannot be performed. It appears to be effective in inducing regression of the rubeotic vessels without decreasing visual acuity when the protocol described above is followed.

PRC does not feature in a major review article in 1981 on the treatment of established neovascular glaucoma. Although reported complications of PRC include traction retinal detachment, no evidence of retinal traction is present in eyes with rubeotic glaucoma we have treated so far. Cyclocryotherapy, advocated as a suitable treatment in the past, resulted in a 6% enucleation rate, with 14% of eyes becoming phthisical and 58% losing light perception in one series. Valve implants, even when preceded by photoacoagulation, fail to control intraocular pressure in many cases, often after repeated surgical procedures.

In contrast, in our series control of intraocular pressure was achieved with no additional medication in eight out of nine eyes with neovascular glaucoma. Of particular note are two eyes (eyes 3 and 7, Table

Table 3  Eyes with proliferative retinopathy

<table>
<thead>
<tr>
<th>Eye Primary disease</th>
<th>Vitreous haemorrhage</th>
<th>Acuity prior to PRC</th>
<th>Acuity at end of follow-up period</th>
<th>Regression Follow up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Diabetes Yes</td>
<td>6/36</td>
<td>6/24</td>
<td>Yes</td>
<td>48</td>
</tr>
<tr>
<td>2 Diabetes Yes</td>
<td>6/60</td>
<td>6/18</td>
<td>Yes</td>
<td>36</td>
</tr>
<tr>
<td>3 CRVO No</td>
<td>CF</td>
<td>CF</td>
<td>Yes</td>
<td>19</td>
</tr>
<tr>
<td>4 Diabetes No</td>
<td>6/9</td>
<td>6/12</td>
<td>Yes</td>
<td>8</td>
</tr>
<tr>
<td>5 Diabetes No</td>
<td>6/12</td>
<td>6/12</td>
<td>Yes</td>
<td>48</td>
</tr>
<tr>
<td>6 Diabetes Yes</td>
<td>HM</td>
<td>6/12</td>
<td>Yes</td>
<td>24</td>
</tr>
<tr>
<td>7 Diabetes Yes</td>
<td>CF</td>
<td>NPL</td>
<td>Yes</td>
<td>48</td>
</tr>
</tbody>
</table>
1), one whose acuity increased slightly from 6/24 to 6/18 and other whose acuity remained at 6/9 three years following PRC. Both had pressures over 35 mmHg before PRC, with angle neovascularisation which regressed following treatment. Intermittent peripheral anterior synechiae persisted in each eye, but intraocular pressures were maintained at 12 and 16 mmHg respectively. Treatment in five other cases preserved navigational vision, and this was particularly valuable in eye number 8, an only eye.

Although the mean follow-up of 19 months in eyes treated for rubeotic glaucoma is short in relation to the 4½-year mean follow-up of Smith, our patients appear stable at present, with light perception lost in only one eye. Neovascularisation regressed in this eye, but the drainage angle was irreversibly occluded by fibrous tissue and the glaucoma persisted.

Early treatment during the initial stages of raised intraocular pressure was emphasised when diathermy was used in retinal ablation, and we support the concept that the timing of treatment appears crucial in rubeotic glaucoma and there should be no delay if vision is to be preserved. This was well demonstrated in the first two case reports, where early treatment induced resolution of rubeotic glaucoma in eyes 6 and 7 in Table 1 and almost certainly prevented the onset of glaucoma in eye 3 in Table 2.

It has been suggested that PRC can speed the rate of clearance of vitreous haemorrhage secondary to proliferative diabetic retinopathy, and this treatment has been cited as an alternative to vitrectomy when no retinal traction exists. Our small series (Table 3) shows similar results, but the eye (eye 7 in Table 3) which progressed to rubeotic glaucoma and traction retinal detachment gives cause for concern. This eye was treated before ultrasound was available at the Oxford Eye Hospital and may have had pre-existing traction. We consider PRC should be used in the management of proliferative diabetic retinopathy with longstanding vitreous haemorrhage only when traction has been excluded by adequate retinal visualisation or ultrasound examination.

PRC is a relatively straightforward procedure to perform under local or general anaesthesia and can be quickly mastered by a surgeon with retinal experience. Regression of rubeotic vessels usually begins after a few days with complete resolution occurring after four to five weeks. Choroidal effusions are common, as is postoperative shallowing of the anterior chamber, though we have not experienced secondary angle closure to date. The intraocular pressure may also rise postoperatively, particularly in established glaucoma, and should be controlled by medical means. A transient reduction in acuity secondary to macular oedema in eyes with good vision may also occur as in case report 1, and patients should be informed that this may happen.

We believe PRC to be most effective when used in conjunction with photocoagulation at the posterior pole but have demonstrated that PRC will produce neovascular regression in certain eyes when used alone.

We recommend the use of PRC in the management of early rubeotic glaucoma, when advancing rubeosis threatens a normotensive eye, and suggest that PRC should be considered in selected cases of proliferative diabetic retinopathy where photocoagulation cannot be delivered adequately owing to media opacities.

References


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