Ocular sympathetic denervation associated with ocular hypertension: a case report

D. J. BRAZIER

From the Department of Ophthalmology, St Thomas's Hospital, London SE1

SUMMARY The exact function of the sympathetic nervous system in the regulation of intraocular pressure remains unclear. Many observers have noted reduced intraocular pressure in eyes whose sympathetic supply has been interrupted. A case of ocular sympathetic denervation associated with ocular hypertension is reported. Reports on the relationship between intraocular pressure and sympathetic denervation are reviewed and their relevance to this case discussed.

Case report

A retired man aged 64 was referred to Greenwich District Hospital in November 1980 following a visit to his optician. Marked asymmetry of intraocular pressure (IOP) had been noted on noncontact tonometry (right eye 8 mmHg, left eye 22 mmHg). The patient had no visual symptoms and gave no past or family history of eye disease. He had undergone bilateral cervical sympathectomy in 1953 for Raynaud's phenomenon, which had subsequently improved. On direct questioning he admitted that the right upper lid had tended to droop since the operations and that his face did not sweat, even in warm weather.

On examination he was a fit man for his age with sympathectomy scars in both supraclavicular fossae. With a small hypermetropic correction his visual acuities were right 6/6 N5 and left 6/6 N5. There was a mild right ptosis with normal eye movements. The right pupil was smaller than the left (Fig. 1) but both reacted normally to light. Right IOP was 10 mmHg, left 28 mmHg by applanation tonometry. Both anterior chamber angles were open and showed no significant pigmentation on gonioscopy. Visual fields were normal. The optic discs were not entirely symmetrical (Fig. 2) but were thought in the absence of field loss to be consistent with a diagnosis of left ocular hypertension. He also had a clinical right Horner's Syndrome.

Three weeks later the left IOP was further elevated at 40 mmHg. Treatment of this eye was indicated and he started pilocarpine drops 4% qds and adrenaline drops 1% bd. This regimen adequately controlled the IOP. The right IOP remained normal without treatment.

In March 1982 further studies were undertaken at St Thomas's Hospital to elucidate the nature of the sympathetic denervation and possibly its relationship to the uniocular hypertension. The patient was asked...

Correspondence to Dr D. J. Brazier, Moorfields Eye Hospital, City Road, London EC1V 2PD.

Fig. 1 This photograph was taken in white light in the studio. Right ptosis and miosis are visible.
to discontinue his drops for 2 weeks and was then re-examined. With the eyes in the primary position, vertical heights of the palpebral fissures were right 8 mm and left 10 mm, while widths were equal. No enophthalmos was detected. Visual acuities remained normal. Right miosis was still clinically visible. Right IOP was 10 mmHg, left 24 mmHg. Gonioscopy and visual fields, as assessed by Friedmann Central Field Analyser and Goldmann perimetry, were unchanged. The slight asymmetry of the optic discs persisted. No facial sweating was demonstrable on either side with quinizarine dusting powder. Quinizarine is a mauve powder which becomes magenta coloured when damp. It was used by Giles and Henderson in their analysis of 216 cases of Horner's syndrome.1

Photographic studies showed bilateral pupillary dilatation lag2 and that the left pupil dilated less than the right in reduced illumination. In the absence of any iris abnormality visible on the slit-lamp the relative immobility of the left pupil was taken to be secondary to long-term pilocarpine application.

Infrared pupillometry confirmed the presence of pupillary dilatation lag (Fig. 3). Pupillometry was also performed after instillation, on different occasions, of cocaine drops 10%, hydroxyamphetamine drops 0-5%, and phenylephrine drops 2%. These examinations were performed in a standardised way separated by intervals of at least 7 days. The only treatment given at this stage was oral acetazolamide, which was stopped 3 days prior to examinations.

Pupillometry on the right revealed reduced dilatation to cocaine (1-50 mm maximum increase in pupil diameter during one hour after instillation) with exaggerated dilatation to hydroxyamphetamine (3-00 mm) and phenylephrine (4-42 mm). On the left side dilatation to cocaine was also subnormal (1-30 mm), while dilatation to hydroxyamphetamine (1-20 mm) and phenylephrine (2-56 mm) was considered to be within normal limits. When these studies were

### Table 1 Intraocular pressures and treatment

<table>
<thead>
<tr>
<th>Date</th>
<th>Intraocular pressure mmHg</th>
<th>Treatment (left eye only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td>Left</td>
<td></td>
</tr>
<tr>
<td>2 June 1980</td>
<td>8</td>
<td>Nil</td>
</tr>
<tr>
<td>11 Nov 1980</td>
<td>10</td>
<td>Nil</td>
</tr>
<tr>
<td>3 Dec 1980</td>
<td>10</td>
<td>Nil</td>
</tr>
<tr>
<td>17 Dec 1980</td>
<td>8</td>
<td>Gutt. pilocarpin. 4% qds and Gutt. adrenalin. 1% bd</td>
</tr>
<tr>
<td>9 Jan 1981</td>
<td>10</td>
<td>Gutt. pilocarpin. 4% qds and Gutt. adrenalin. 1% bd</td>
</tr>
<tr>
<td>1 May 1981</td>
<td>8</td>
<td>Gutt. pilocarpin. 4% qds and Gutt. adrenalin. 1% bd</td>
</tr>
<tr>
<td>13 Nov 1981</td>
<td>9</td>
<td>Gutt. pilocarpin. 4% qds and Gutt. adrenalin. 1% bd</td>
</tr>
<tr>
<td>6 Apr 1982</td>
<td>10</td>
<td>Nil</td>
</tr>
<tr>
<td>20 Apr 1982</td>
<td>10</td>
<td>Nil</td>
</tr>
<tr>
<td>18 May 1982</td>
<td>7</td>
<td>Gutt. timolol. 0-5% bd</td>
</tr>
</tbody>
</table>
These results whether the reduced facility. Alteration and facility. Further of the venous pressure appearance formation aqueous nerves short-term resulted to tomy was was excision lasting detail.

**Discussion**

**OCULAR SYMPATHETIC DENERVATION AND INTRAOCULAR PRESSURE**

The relationship between these two has been studied both in animal experiments and by clinical observation in humans who have suffered ocular sympathetic denervation.

Experimental studies, mainly in rabbits and cats, have been based on interruption of the cervical sympathetic pathway proximal to the superior cervical ganglion (preganglionic sympathectomy) or distal to it (postganglionic sympathectomy). The latter lesion is also produced by destruction or excision of the superior cervical ganglion.

In 1948 Jaffe reported that section of the cervical sympathetic nerves in cats produced a reduction of IOP lasting 2 days. Over several weeks he noted that postganglionic sympathectomy caused persistent depression of IOP, while preganglionic sympathectomy resulted in normal or elevated IOP. The short-term reduction of IOP following sympathectomy was subsequently confirmed and studied in detail by many observers; long-term effects of sympathectomy appear to have been variable or absent. Linner and Prijot, working with rabbits, concluded that the reduced IOP during the day after extirpation of the superior cervical ganglion was due to reduced aqueous formation while outflow facility and episcleral venous pressure remained constant. These findings were confirmed by Lieb et al.

Langham and Taylor, although unable to obtain consistent results working with cats, also reported transient reduction of IOP in rabbits following ganglionectomy. Further studies demonstrated that the reduced pressure was due to increased outflow facility while aqueous production remained constant. These results were similar to those of Sears and Bárány and Tomar and Agarwal. It is still not clear whether the reduced IOP in these animals is mediated through alteration of aqueous production or outflow facility. Potter observed there is marked species variation in the anatomy of the outflow tract including innervation and adrenoreceptor populations. It seems prudent, therefore, to avoid drawing firm conclusions about control of IOP in man from animal experiments.

Clinical studies are mostly linked to the description by the Swiss ophthalmologist Horner of the collection of physical signs which became known as Horner’s syndrome. He described a patient with ptosis, miosis, facial anhidrosis associated with flushing and temperature changes, reduced ipsilateral IOP (measured by tonometry), and enophthalmos. It is now accepted that the enophthalmos is only apparent.

Thompson suggested that reduced IOP is a transient sign of Horner’s syndrome which cannot be relied upon in making a diagnosis. There are, however, reports of sustained reduction of IOP following interruption of the cervical sympathetic system. Cobb and Scarlett reported reduction of IOP in the ipsilateral eye in 7 cases of Horner’s syndrome while pressures were equal in an eighth case. Davson and Matchett alluded to clinical studies in man suggesting chronically lowered IOP following stellactomy. Swegmark studied aqueous dynamics in a patient with unilateral postganglionic Horner’s syndrome. He showed that reduced IOP in the ipsilateral eye was due to reduced aqueous production. By treatment with guanethidine drops (blocking release of noradrenaline at postganglionic nerve endings) he produced a comparable reduction of aqueous production in the normal eye. He concluded that sympathetic denervation reduced aqueous production and thus IOP. Similar findings were subsequently reported by Langham and Weinstein and Bron. Wentworth and Brubaker found a statistically significant reduction of IOP in 21 cases of Horner’s syndrome. Alteration of aqueous production in this series was not consistent.

The concept of reducing IOP by alteration of the sympathetic nerve supply to the eye has formed the basis of both investigation and treatment of glaucoma. Miller studied the effect of stellate ganglion block with procaine on IOP. In patients with chronic simple glaucoma he reported an immediate rise in IOP followed by a fall to the original pressure or below during an hour. This change was thought to be due to dilatation of intraocular capillaries. The treatment of chronic simple glaucoma by excision of the superior cervical ganglion was reported by Abadie and Jonnesco. It appears that the resulting improvement in IOP was not sustained, and the procedure was eventually abandoned. Many drugs now in use for treating glaucoma act on ocular sympathetic mechanisms. They include adrenaline (mainly α-adrenergic receptor agonist), timolol (β-
adrenergic receptor blocker), and guanethidine. Their exact modes of action remain to a large extent obscure.

The author has not located any reports of ocular hypertension or glaucoma developing with pre-existing ocular sympathetic denervation.

**Present Case**

The reported patient has a right preganglionic Horner's syndrome. This is suggested by ptosis and miosis, pupillary dilatation lag, pharmacological studies, and the absence of facial sweating. On the left side the situation is less clear. The relative immobility of the pupil makes interpretation of the pupillometric studies more difficult. However, preganglionic sympathetic denervation is strongly suggested by pupillary dilatation lag, reduced dilatation to cocaine 10%, and absent facial sweating. The ptosis and miosis appear to have been relatively less obvious on this side, and it is therefore difficult to describe this clinical picture as Horner's syndrome.

He undoubtedly has left ocular hypertension on the basis of persistently elevated IOP in the presence of visual fields and optic discs which are within normal limits. The average left IOP untreated was 29.2 mmHg; this was reduced by treatment to an average 16.0 mmHg. The association of ocular sympathetic denervation and ocular hypertension appears most uncommon.

The average IOP in the right eye was 9.0 mmHg. Duke-Elder states that only 2% of the normal population have pressures under 10 mmHg. This eye has therefore maintained a pressure very much at the lower end of the normal range.

Outflow facilities were the same at 0.13 μl mmHg⁻¹ min⁻¹ left eye and average 0.13 μl mmHg⁻¹ min⁻¹ right eye. These values also fall at the lower end of what may be considered to be the normal range (0.12–0.57 μl mmHg⁻¹ min⁻¹). With similar outflow facilities the most likely cause for asymmetry of IOP is a difference in rates of aqueous production. While it is possible that the sympathetic denervation and ocular hypertension are entirely independent, it seems reasonable to suggest that the relatively low IOP in the right eye may be due to some protective effect of the Horner's syndrome on that side. If so, it has probably been mediated by alteration of aqueous production. This would be entirely consistent with the quoted reports of reduced aqueous production in Horner's syndrome.

There does not appear to be similar evidence that the IOP rises as a result of ocular sympathetic denervation in humans. It would certainly be surprising that this patient had maintained normal optic discs and visual fields if his ocular hypertension dated from cervical sympathectomy in 1953. It is much more likely that the IOP has increased in recent years in the presence of pre-existing sympathetic denervation.

The different behaviour of the 2 eyes might be explained by the completeness of sympathetic denervation that they have respectively suffered. On the right side the clinical and pharmacological evidence suggests a typical Horner's syndrome. On the left side 2 of the main features of Horner's syndrome, ptosis and miosis, were minimal or absent. Romano et al. have drawn attention to variation in ocular signs after upper dorsal sympathectomy, which is explained by variation either in nerve fibre pathways or by the degree of sympathetic injury inflicted at surgery. It is possible that the reported patient has suffered a more complete sympathectomy on the right side. This asymmetry may have contributed to the maintenance of low normal IOP in the right eye while ocular hypertension has developed in the left eye.

I thank Mr J. Shilling for permitting me to report this patient under his care and Professor S. E. Smith, Department of Pharmacology, St Thomas's Hospital, for performing the pupillometry and advising me on interpretation of the results.

**References**

Ocular sympathetic denervation associated with ocular hypertension: a case report