Argon laser treatment of lipid keratopathy

RONALD J MARSH

From the Western Ophthalmic Hospital, London NW1 5YE, and Moorfields Eye Hospital, City Road, London EC1

SUMMARY Sixty-three cases of vascularised lipid keratopathy were treated with the argon laser to occlude feeder vessels which had been identified by fluorescein angiography. There was a reduction in extent in 62% and density in 49%. Visual acuity was improved in 48%. Six patients had keratoplasties shortly after treatment, none of which showed graft rejection. Minor complications included temporary haemorrhage into the cornea and iris atrophy. A more serious problem was severe corneal thinning after resorption of lipid. The patients had to be carefully followed up and maintained on a low dose of topical steroid.

Most lipid keratopathy is secondary to corneal inflammatory disease and is vascularised. The commonest causes are herpes simplex and herpes zoster disciform keratitis. Treatment involves firstly controlling the primary inflammatory disease and then the lipid deposits. Many attempts have been made to occlude the blood vessels supplying these deposits^{1–9} in the hope that further lipid deposition can be prevented, some resorption occur, and, in some cases, the host made safer for grafting. More recently the argon laser has been used for this purpose.^{10–12} I was pleased with our preliminary results¹³ but was struck by the extensive iris atrophy induced. The use of the Abraham contact lens has minimised this problem.¹⁴ The histopathology of treated corneas has been recorded and a mechanism of vascular closure proposed.¹³ This paper presents my results from 1975 onwards with a minimum follow-up of one year.

Material and methods

Patients with lipid keratopathy were referred for assessment and treatment from many centres, the chief of which were Moorfields and the Western Ophthalmic Hospitals. The history was recorded on a score sheet, including the suspected aetiology of the keratitis, duration, and therapy. Slit-lamp examination concentrated not only on the extent, density, and vascularity of the lipid deposit but also on the iris and lens appearance. A note was added to the score sheet on the shape and position of the deposits—whether they were central or eccentric disciform, marginal,

diffuse interstitial, or deep, and a drawing was made. A random number of patients had their fasting blood lipid profile assessed, which included serum concentrations of cholesterol, triglyceride, betalipoprotein, prebetalipoprotein, and chylomicra.

Colour photographs of the whole cornea (with a dilated pupil) were taken on a Zeiss photo slit-lamp at $\times 2$ film magnification with identical settings, lighting conditions, and film (Kodak Ektachrome 200). A careful grading was made on the density and extent of the lipid by means of a Zeiss Dokumator to project the transparency on its built-in screen over which a transparent grid was superimposed to encompass the whole cornea and divided into 100 squares. Extent was calculated from the number of grid squares involved (including those that were more than half filled) and expressed as a percentage of the whole cornea. Density was classified into four categories based on the degree of masking of underlying structures: 0=transparent, 1=slight blurring of iris crypts, 2=iris colour only appreciated, 3=pupil vaguely discerned with full illumination, and 4=total opalescence with dense creamy yellow lipid. Fluorescein angiography was carried out in all new cases with the modified Zeiss photo slit-lamp, 20% fluorescein, and video by the techniques described before.¹⁵ The 35 mm film was examined and the vascularity classified as slight (1), moderate (2), and profuse (3), while the vascular stems at the limbus were defined as single and narrow or multiple and diffuse. The video was analysed to establish the dynamic filling pattern of the vessels. These details were added to the diagram and score sheet.

Treatment was carried out with a coherent argon

Correspondence to Mr R J Marsh, FRCS, Western Ophthalmic Hospital, Marylebone Road, London NW1 5YE.

laser 900 series via the Abraham contact lens as described previously.¹⁴ In most cases it was possible to achieve initial vessels closure in one treatment session, but in cases with dense vascularisation it was best to treat three times in one day and to re-examine a few days later with a view to further lasering. Immediately after treatment prednisolone 0.3% drops were administered twice a day until the next visit. A month was usually adequate for the first follow-up visit and then three or six monthly depending on the success of vessel closure. At each follow-up examination the density, extent, and vascularity of the deposits were reassessed and colour photographs repeated, but angiography was carried out only in doubtful cases. Any remaining vessels were again treated by the laser. All relevant details were entered in the score sheet. The attempt was made to withdraw the prednisolone drops, entirely but cautiously, over one year, but they had to be used after lasering and if there was any sign of active keratitis. The intraocular pressures were regularly checked while the patients were taking steroids, and in case of raised intraocular pressure fluoromethalone drops were substituted. Where lipid deposits were very dense and central the patients received grafts as soon as vascular flow had been stopped.

Results

Sixty-three patients were reviewed with a minimum follow-up of 12 months. The sex distribution was equal and the average age was 52. Table 1 depicts the morphology and aetiology of the cases. Two of these cases were old corneal grafts with marginal lipid deposits at the graft-host junction and the bacterial infection was related to contact lens wear.

Thirty-nine cases (62%) showed a reduction in the

extent of the lipid, 13 (21%), no change and 11 (17%) an increase. If the patients were divided into two groups, one with lipid involving less than 20% of the cornea and the other with more than 20%, there was a highly significant improvement after treatment (Table 2). The density of deposits was reduced in 31 (49%), the same in 26 (41%), and worse in six (10%). Dividing the patients into two groups again, one with density of lipid of 3 units or more and the other 2 units or less, showed a significant reduction in density after treatment, particularly in the second group (Table 3). There was improvement in both extent and density in 23 cases (36%) (Figs. 1, 2, 3). Snellen visual acuity was improved in 30 cases (48%), unchanged in 19 (30%), and worse in 14 (22%). However if the patients were divided into two groups, one with vision of 6/18 or worse and the other with 6/12 or better, there was a small but non-significant improvement in both groups (Table 4). Combined improvement in all three aspects occurred in 14 cases (22%) apart from those cases that were grafted (Fig. 4). We compared the number of burns per degree of vascularity and per mm² of corneal opacity, but there were no enough cases in the former measurement to give a significant result, and the latter was equivocal (Table 5).

Six grafts were carried out after treatment by laser, four of which were elective and two carried out urgently because of descemetocoele formation. Two of these six required regrafting, one because of poor

Table 1 Aetiology and morphology of lipid keratopathy

Aetiology	Central disciform	Eccentric disciform	Marginal	Diffuse interstitial	Diffuse deep
Herpes simplex	13	14	3	5	0
Herpes zoster	5	14	2	0	0
Acne rosacea	0	0	1	0	0
Bacterial	0	1	0	0	0
Unknown	0	2	1	0	2

Table 2 Effect of laser on the extent of opacity (expressed as a percentage of the corneal surface)

	More than 20%	Less than 20%
Before treatment	36 (57%)	27 (43%)
After treatment	18 (29%)	45 (71%)

$\chi^2=9.36$. $p<0.01$, highly significant.

Table 3 Effect of treatment on the density of opacities

	3 Units or more	2 Units or below
Before treatment	35 (56%)	28 (44%)
After treatment	22 (35%)	41 (65%)

$\chi^2=4.61$. $p<0.05$, significant.

Table 4 Effect of laser treatment on visual acuity

	6/18 or worse	6/12 or better
Before treatment	42 (66%)	21 (34%)
After treatment	34 (54%)	29 (46%)

$\chi^2=1.66$. p Non-significant.

Table 5 Effect of intensity of treatment

Number of burns per mm ² of opaque cornea	Better	Worse
Below 75/mm ²	47 (75%)	16 (25%)
Above 75/mm ²	37 (58%)	26 (42%)

$\chi^2=1.56$. p about 0.1. If 1 in 10 is the criterion of significance, this is significant.

Fig. 1A *Herpes simplex disciform scarring.*

Fig. 1B *Same case two years after treatment.*

donor endothelium and the other because of recurrence of herpes simplex keratitis spreading into the donor cornea. All were clear after a minimum follow-up of 36 months.

The most spectacular result was in a woman with an old herpes simplex diffuse interstitial keratitis, vision of hand movements, lipid density three, extending over the entire cornea, vascularity four with multiple stems. She received 13 000 burns in 18 treatment sessions over five years. Now eight years later her visual acuity is 6/36, lipid density is 1, extent 0.3, and the great majority of the vessels have been closed (Fig. 3). It is interesting that despite extensive iris atrophy there is no sign of lens opacities or retinal damage.

It was possible to close all the blood vessels at the end of a treatment session. However, in cases of very vascular keratopathy there was a tendency for some vascular channels to reopen soon afterwards, but eventually, after repeated treatment, all but some very small vessels with very slow flow were successfully closed.

The commonest immediate complication is

haemorrhage around the treated vessels, which rarely spreads widely between corneal lamellae. However, this is a temporary phenomenon and, though a little disturbing to the patient, always resorbs. Less commonly there is temporary peaking of the pupil in the sector underlying that treated with the laser. Patients who had multiple laser treatments all developed some degree of iris atrophy underlying the treatment zone. There was occasional reactivation of keratitis, but all except one responded well to increasing topical steroids (with antiviral cover when appropriate). The exception was a patient who did not take his drops and failed to attend follow-up for over a month, in whom a marked stromal swelling with cellular infiltration and increase in opacity resulted. Two cases of dense disciform lipid deposits developed rapid central stromal thinning within one month of treatment, culminating in the development of descemetocoeles at four and six months respectively. Both received grafts shortly afterwards and have remained clear over a follow-up period exceeding two years. All cases of disciform keratopathy that responded successfully to treatment showed some

Fig. 2A *Old bacterial keratitis with eccentric disciform scar.*

Fig. 2B *Same case three years after treatment.*

Fig. 3A Old diffuse scarring from herpes simplex.

Fig. 3B Same case four years later after 13 000 burns.

degree of stromal thinning. Two patients developed open-angle glaucoma and appreciable field loss due to a combination of chronic keratouveitis and topical steroids. I am not aware of any lens or retinal damage as a result of the therapy.

Fourteen randomly selected patients had their fasting blood lipid profile assayed. Nine of these were normal, four had hyperlipoproteinaemia (two Fredrickson's type 2A and 2 Fredrickson's type 2B).

Discussion

The results of argon laser treatment of lipid keratopathy are encouraging, but clearing of the lipid is slow and may take several years to be apparent. Even though Snellen tested visual acuity improved in only 30 cases, many other patients noted an improvement in photophobia and quality of sight. It is important to stress that the usual natural history of a vascularised lipid keratopathy is to advance with deterioration of

vision, so that arresting the condition is a significant achievement. The results of grafting treated cases were excellent, and a number of other successful cases were not included in this series because of inadequate personal follow-up. It seemed best to arrange for laser treatment three days prior to grafting under topical steroid cover, which rendered the cornea avascular at surgery and precluded descemetocoele formation.

Patients on the whole tolerated the treatment very well. The Abraham lens not only made the application of the burns more accurate but also kept the eye steady. The main complaint from patients was that the laser beam dazzled their other eye (it was worth covering it with the operator's hand during firing). It should be admitted that prolonged treatment sessions were also uncomfortable for the surgeon and that on the rare occasions when fluorescein angiography had been carried out just previously the dazzle was even more bothersome. The importance of using the postoperative drops was stressed to the patients, and regular applanation was important.

The video corneal angiograms proved very useful for identifying feeder vessels and flow. They also clearly showed that many of the eccentric disciform keratopathies and all the marginal and half of the idiopathic deep keratopathies had marked ischaemic changes in neighbouring episclera. The first two types were usually caused by herpes zoster and probably at the time of the preceding acute keratitis had an ischaemic episcleritis.

The mechanism of lipid clearance is uncertain but is probably due to ingestion by macrophages wandering between corneal lamellae which then migrate to the limbus, whence they gain access to lymph and blood vessels. Successful closure of vessels will obviously prevent further deposition of lipid. Another factor is the obvious disruption in the corneal tissues caused by the laser burns, which may facilitate diffusion of lipid away from the kerato-

Fig. 4 The effect of laser treatment on visual acuity (expressed as those cases better than 6/18), lipid density (those cases less than 3), and extent (those cases less than 20% of the cornea).

pathy. As expected, fibrous scarring of the corneal stroma did not clear. Thinning occurred as the lipid 'leached out', implying that the lipid deposits had artificially contributed to corneal thickness and in fact revealed how much corneal stroma had been destroyed by the pre-existing keratitis.

Prevention of the lipid keratopathy is an important element in any discussion on treatment. Probably all patients should have their fasting blood lipid profile assessed and any lipid abnormality appropriately corrected. (Although no data are available on the effect of hyperlipidaemia on the development of secondary lipid keratopathy in humans, there is in rabbits.¹⁶) More importantly, a vascularising active keratitis, particularly due to herpes zoster, should be adequately treated with topical steroid to prevent excessive scarring.¹⁷⁻¹⁹

I thank my colleagues for referring their patients, Professor R F Fisher of the Western Ophthalmic Hospital for his statistical advice, Miss S Ford for her invaluable help with the photography, and Coherent Lasers for helping finance the colour photographs.

References

- 1 Ey RC, Hughes WF, Bloome TA, Tallman CB. Prevention of corneal vascularisation. *Am J Ophthalmol* 1968; **66**: 1118-31.
- 2 Lederman M. Radiotherapy of diseases of the cornea. *J Fac Radiol* 1952; **4**: 97-114.
- 3 Michaelson IC, Schreiber H. Influence of low-voltage x radiation on regression of established corneal vessels. *Arch Ophthalmol* 1955; **56**: 48-51.
- 4 Mandras G. Beta-therapy in ophthalmology. *Arch Ophthalmol (Paris)* 1956; **16**: 811-6.
- 5 Fraser H, Naunton WJ. Treatment on non-malignant corneal conditions with radioactive isotopes: a five year survey. *Br J Ophthalmol* 1961; **45**: 358-64.
- 6 Ainslie D, Snelling MD, Ellis RE. Treatment of corneal vascularisation by Sr-90 beta plaque. *Clin Radiol* 1962; **13**: 29.
- 7 Langham ME. The inhibition of corneal vascularisation by triethylene thiophosphoramide (part 2). *Am J Ophthalmol* 1960; **49**: 1111-25.
- 8 Laverne G, Colmont IA. Comparative study of the action of thiotepa triamcinolone on corneal vascularisation in rabbits. *Br J Ophthalmol* 1964; **48**: 416.
- 9 Mayer W. Cryotherapy in corneal vascularisation. *Arch Ophthalmol* 1967; **77**: 637-41.
- 10 Cherry PMH, Faulkner JD, Shaver RP, Wise JB, Witter SL. Argon laser treatment of corneal vascularisation. *Ann Ophthalmol* 1973; **5**: 911-20.
- 11 Read JW, Fromer C, Klintworth GK. Induced corneal vascularisation remission with argon laser therapy. *Arch Ophthalmol* 1975; **93**: 1017-9.
- 12 Cherry PMH, Garner A. Corneal vascularisation treated with argon laser. *Br J Ophthalmol* 1979; **63**: 464-72.
- 13 Marsh RJ, Marshall J. Treatment of lipid keratopathy with the argon laser. *Br J Ophthalmol* 1982; **66**: 127-35.
- 14 Marsh RJ. Lasering of lipid keratopathy. *Trans Ophthalmol Soc UK* 1982; **102**: 154-7.
- 15 Marsh RJ, Ford SM. Cine photography and video recording of anterior segment fluorescein angiography. *Br J Ophthalmol* 1978; **62**: 657-9.
- 16 Mendelsohn AD, Lee Stock E, Lo GG, Schneck GL. Laser photocoagulation of feeder vessels in lipid keratopathy. *Ophthalmic Surg* 1986; **17**: 502-7.
- 17 Langham ME. The action of cortisone on the swelling and vascularisation of the cornea. *Trans Ophthalmol Soc UK* 1953; **72**: 253-60.
- 18 Duke-Elder S, Ashton N. Action of cortisone on tissue reactions of inflammation and repair with special reference to the eye. *Br J Ophthalmol* 1951; **35**: 695-707.
- 19 Cook C, MacDonald RK. Effect of cortisone on the permeability of the blood aqueous barrier to fluorescein. *Br J Ophthalmol* 1951; **35**: 730-40.

Accepted for publication 16 September 1987.