Retinal arteriolar macroaneurysms: long term visual outcome

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Abstract

Visual outcome was analysed in 16 consecutive eyes with symptomatic retinal arteriolar macroaneurysms treated by direct laser photocoagulation and 26 consecutive symptomatic eyes followed with no treatment. No difference existed between groups in presenting visual acuity, macular involvement, presence of macular subretinal fluid, or presence or location of associated haemorrhage. The mean follow up was 41 months. In the 26 untreated eyes, visual acuity was improved by 2 or more lines in 13 (50%), was unchanged in nine (35%), and decreased in four cases (15%). In the 16 treated cases, three improved (19%), seven were unchanged (43%), and six had decreased visual acuity (38%). The average minimum angle of resolution improved 0·53 log units in untreated cases and decreased 0·14 log units in treated cases (p=0·02). Multivariable logistic regression modelling analysis revealed that laser treatment remained a significant risk factor for final visual acuity of less than 20/80 even when controlling for the effects of subretinal haemorrhage and foveal subretinal fluid (odds ratio 8·4, p=0·01). Laser photocoagulation directly to the macroaneurysm did not improve the visual outcome in this series.

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Retinal arteriolar macroaneurysms are well described.[1-17] Although macroaneurysms may involute spontaneously, there are many reports of photocoagulation of symptomatic macroaneurysms. The results of photocoagulation are variable, and it is unknown if treated patients have improved visual outcomes over patients with no treatment. We performed a retrospective analysis to compare the clinical course in our patients evaluated with symptomatic arteriolar macroaneurysms treated with laser photocoagulation versus those patients in whom treatment was deferred.

Patients and methods

All patients with documented retinal arteriolar macroaneurysms were retrieved from records of visits to the University of Iowa Department of Ophthalmology over a 16 year period from 1974 to 1990. Photographic documentation was examined independently by three different investigators and the clinical characteristics of all macroaneurysms were recorded. The location of the macroaneurysm and associated presence of subretinal fluid or haemorrhage were noted. Variables including the location of subretinal fluid (foveal or extrafoveal), location of haemorrhage (foveal or extrafoveal), as well as depth of haemorrhage (preretinal, intraretinal, or subretinal) were recorded (Fig 1). Demographic and associated systemic disease associations were retrieved from medical records, as well as presenting ocular findings and subsequent follow up examinations. Patients with a follow up of less than 6 months were excluded from analysis. Only patients with symptomatic macroaneurysms were included in both the treatment and non-treatment groups.

Criteria for treatment included decreased visual acuity secondary to either fluid or haemorrhage in the macula and the absence of overlying haemorrhage. Some vitreoretinal surgeons in our department tend to treat most symptomatic

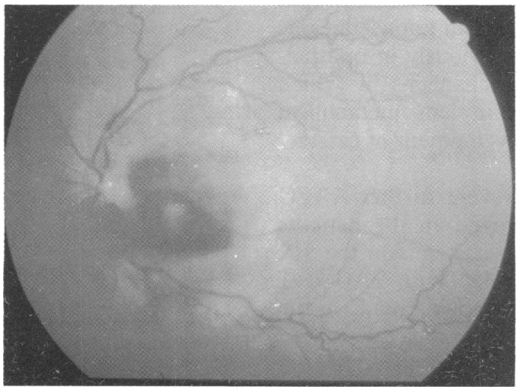

Fig 1A

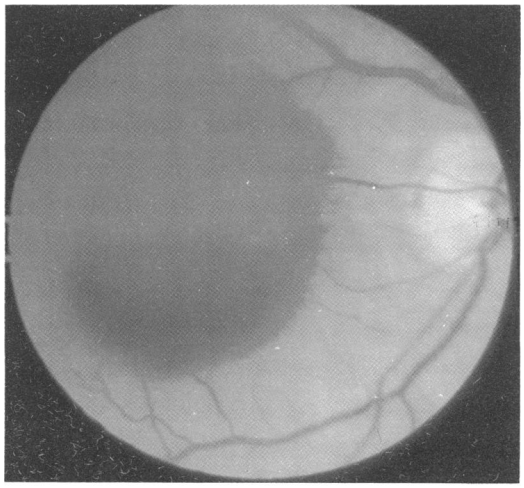

Fig 1B

Figure 1 Macular retinal arteriolar macroaneurysm in untreated case 1 demonstrates haemorrhage, subretinal fluid, and exudates (A). This patient had improved visual acuity from 20/500 to 20/100 without treatment. The macroaneurysm in untreated case 8 demonstrates preretinal, intraretinal, and subretinal haemorrhage (B). This patient improved from 20/2000 to 20/40 without treatment.

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macroaneurysms and some prefer observation. Clinical judgment at the time of presentation and preference of the surgeon determined which patients meeting these criteria underwent laser photocoagulation. Laser treatment in all cases was directed to the macroaneurysm to achieve a light to medium burn. In some cases, the surrounding retina was treated along with macroaneurysm. The argon laser was used in eight eyes and the dye yellow laser in eight eyes.

The demographic and presenting ophthalmic findings in patients treated with laser photocoagulation were compared with the untreated group. Age, sex, presenting visual acuity expressed as logarithm minimum angle of resolution (logMAR), known present or prior hypertension, location of aneurysm (macular or extramacular), presence of associated macular oedema, and presence and location of any associated haemorrhage (preretinal, intraretinal, or subretinal) were analysed independently between treatment and control groups. Follow up visual acuity (logMAR) and delta logMAR (from presentation to last follow up) were compared in treatment and non-treatment groups.

DATA ANALYSIS

Statistical analysis was performed with the computerised program SYSTAT. Significance was tested with the χ^2 or Student's t test where appropriate. Two tailed analyses were performed on all parameters except vision. All visual acuity data were converted to logMAR scores[18] before a one tailed Student's t test was performed. Multiple logistic regression analysis modelling strategies were employed utilising the computer program MULTLR.[19] Univariable analysis was performed to identify variables with statistical significance at the $p<0{\cdot}25$ level associated with an outcome of final visual acuity 20/80 or worse. These factors were utilised in a modelling technique to identify factors associated with an increased likelihood of having a visual acuity worse than 20/80 at the end of follow up.

Results

Sixteen consecutive eyes undergoing laser photocoagulation and 26 untreated eyes met the study criteria. Average follow up was 43 months (median 35 months) in the treated group and 40 months (median 34 months) in the untreated group. The average age was 74 years old in the treated group and 70 years old in the untreated group. The duration of symptoms before presentation was 64 days (median 30 days) in the treated group and 44 days (median 14 days) in the untreated group. Twelve of 16 treated cases had a documented history of hypertension compared with 17 to 26 controls. Average presenting visual acuity was 1·05 logMAR (Snellen equivalent 20/224) in treated eyes and 1·08 logMAR (Snellen equivalent 20/225) in untreated eyes. Fourteen of 16 treated eyes and 21 of the 26 untreated eyes had macroaneurysms located in the macula between the temporal arcades.

No significant difference was found at presentation between those cases treated with laser photocoagulation and those followed conservatively when the following variables were considered by univariate analysis: presenting visual acuity ($p=0{\cdot}89$), age ($p=0{\cdot}95$), presence of hypertension ($p=0{\cdot}52$), presence of macular involvement ($p=0{\cdot}57$), presence of macular oedema ($p=0{\cdot}27$), or presence and locations of haemorrhages ($p=0{\cdot}60$–$0{\cdot}79$). Although the average duration of symptoms in the treated group was longer than in the untreated group, longer duration of symptoms (greater than 1 month) was not statistically associated with worse visual acuity ($p=0{\cdot}35$).

In the 26 untreated eyes, visual acuity was improved by 2 or more lines in 13 (50%), was

Table 1 Non-treated series

Case	Symptom duration (days)	Follow up (months)	Foveal involvement			Snellen VA (20/×)		Comments
			SRF	Hard ex	Haem	Presenting	Follow up	
1	14	50	+	+	+	500	100	
2	1	135	+	+	+	500	25	
3	30	127	−	−	−	40	80	Cataract decreased vision
4	210	28	+	+	+	200	70	
5	4	17	+	+	−	15	20	
6	10	6	+	+	+	50	50	
7	7	9	−	−	+	4000	40	
8	1	17	+	−	+	2000	40	
9	6	55	−	−	−	50	15	
10	21	68	+	+	+	500	1000	Scarring after subretinal haemorrhage
11	5	44	+	+	+	25	100	
12	30	33	+	+	+	20	30	
13	14	11	+	−	+	1400	40	
14	210	34	+	+	+	8000	200	
15	240	34	−	−	−	20	20	Symptomatic extrafoveal haemorrhagic PED
16	7	6	+	−	+	2000	500	Scarring after subretinal haemorrhage
17	60	87	+	+	+	200	200	
18	60	62	+	+	−	500	2000	Persistent hard exudates, fluid
19	60	7	−	+	−	70	30	
20	14	13	+	+	+	30	30	
21	11	37	+	+	+	8000	40	
22	30	9	−	−	−	200	30	
23	60	8	+	+	+	2000	3000	Scarring after subretinal haemorrhage
24	5	35	+	+	−	25	25	
25	17	38	+	+	+	4000	30	
26	4	58	+	+	−	20	20	
Mean	44 days	40 months						
Median	14 days	34 months						

Duration of symptoms (days), follow up duration (months), and visual acuity expressed as Snellen fraction (20/×).
SRF=subretinal fluid involving fovea; Hard ex=hard exudates; Haem=haemorrhage involving the fovea; PED=pigment epithelial detachment.

Table 2 Treatment series

Case	Symptom duration (days)	Follow up (months)	Foveal involvement			Snellen VA (20/×)		Laser	Comments
			SRF	Hard ex	Haem	Presenting	Follow up		
1	30	44	+	+	+	500	8000	argon	Scarring after subretinal fluid
2	270	44	+	−	+	2000	8000	dye-yel	Laser scar extended to fovea and foveal capillary loss
3	56	45	+	+	+	20	100	argon	Scarring after subretinal fluid
4	14	190	−	+	−	20	40	argon	
5	28	8	+	+	−	200	80	dye-yel	
6	7	8	+	+	+	2000	8000	dye-yel	Scarring after subretinal fluid and foveal capillary loss
7	180	61	+	+	−	200	100	argon	
8	90	78	+	+	+	100	500	argon	Persistent hard exudates, fluid
9	20	24	+	−	+	400	200	dye-yel	
10	5	14	+	+	−	200	200	dye-yel	Scarring after subretinal fluid
11	30	9	−	−	+	200	100	dye-yel	
12	14	9	+	+	+	70	70	argon	
13	64	60	+	+	+	2000	2000	argon	Scar after subretinal haemorrhage
14	2	22	+	+	+	4000	100	dye-yel	
15	30	41	−	+	−	60	1000	dye-yel	Persistent hard exudates, fluid
16	180	29	+	+	+	70	50	argon	
Mean	64 days	43 months							
Median	30 days	35 months							

Duration of symptoms (days), follow up duration (months), and visual acuity expressed as Snellen fraction (20/×).
SRF=subretinal fluid involving fovea; Hard ex=hard exudates; Haem=haemorrhage involving the fovea; dye-yel=dye yellow laser; argon=argon laser.

unchanged in nine (35%), and decreased in four cases (15%) (Table 1). Of the 16 treated eyes, three improved (19%), seven were unchanged (43%), and six had decreased visual acuity (38%) (Table 2). Comparing groups in this fashion suggests a trend that untreated patients do better over follow up although statistical significance is not demonstrated with our sample size ($\chi^2=0{\cdot}091$). The change in visual acuity from presentation to follow up was also compared. Untreated cases showed −0·53 log units change (improvement from 20/220 to 20/70) and treated cases changed +0·14 log units (decrease from 20/220 to 20/300). This difference is significant (p=0·02 level).

A multiple logistic regression modelling technique was employed to determine which factors implicate a greater risk of having a visual outcome worse than 20/80. Univariable analysis showed that the following factors had a p value less than 0·25 associated with a final visual acuity of 20/80 or worse: macular location of the macroaneurysm within the temporal arcades (p=0·12), presence of subretinal haemorrhage (p=0·21), presence of subretinal fluid (p=0·11), presence of subretinal blood involving the fovea (p=0·03), and treatment by laser photocoagulation (p=0·01). Multivariable logistic regression modelling was used to determine which of these factors (when controlled for each other) implicate a worse visual acuity. The three most important factors were: presence of subretinal haemorrhage (odds ratio 2·36, p=0·33), presence of subretinal fluid involving the fovea (odds ratio 4·3, p=0·09), and treatment by laser photocoagulation (odds ratio 8·4, p=0·01) (Fig 2). In other words, when final visual acuity was analysed (controlling statistically for subretinal haemorrhage and foveal subretinal fluid), treated cases had an eightfold greater likelihood over non-treated cases to have a follow up visual acuity of 20/80 or worse.

All patients in the treated group had laser photocoagulation directly to the macroaneurysm with either argon laser or dye yellow laser photocoagulation. Twelve of 16 eyes required only one treatment session whereas four had multiple treatment sessions for persistent macular oedema. Eight cases were treated by argon green laser and eight by dye yellow laser. Four of the eight cases treated with dye yellow laser had improved visual acuity over follow up compared with two cases treated by argon green laser. Complications included documented arteriolar occlusion in four cases (two by dye yellow treatment and two by argon green laser treatment).

Follow up clinical photographs and angiograms were examined in an attempt to determine the aetiology of poor visual outcomes in treated and untreated patients. Severe foveal capillary dropout was seen in two treated patients (Table 2, cases 2 and 6) and in one of these patients, subretinal scar from laser treatment extended into the fovea (Table 2, case 2). Two patients had heavy exudates in the fovea that did not resolve following treatment (Table 2, cases 8 and 15) and an additional four treated patients had subretinal fibrosis following resorption of subretinal fluid (Table 2, cases 1, 3, 6, and 10) and subsequent

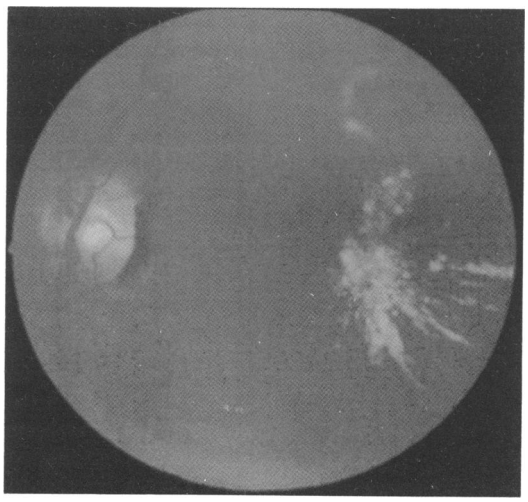

Figure 2 Subretinal fluid with exudates involving the fovea is an important risk factor for worse visual acuity. Treated case 8 demonstrates marked lipid exudation involving the fovea on presentation. Visual acuity declined from 20/100 to 20/500 with persistent hard exudates despite argon laser treatment.

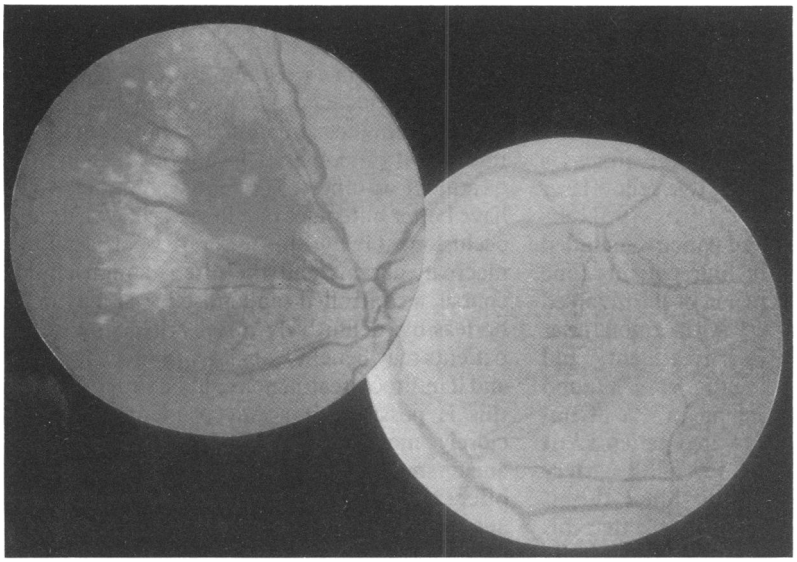

Fig 3A

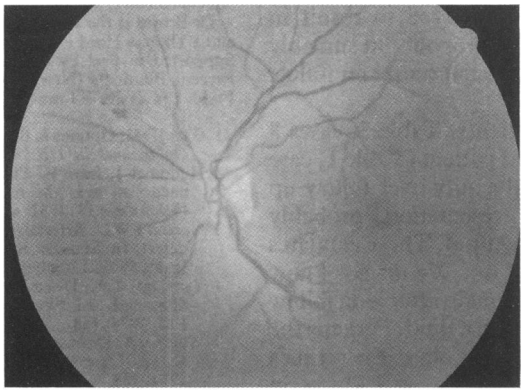

Fig 3B

Figure 3 Treatment case 10 demonstrates superior nasal macroaneurysm with subretinal fluid extending into the fovea (A). Following laser treatment, visual acuity remained 20/200 secondary to subretinal scarring following resolution of subretinal fluid (B).

worse visual acuity (Fig 3). Three untreated patients had scars following subretinal haemorrhage (Table 1, cases 10, 16, and 23) and one of these also had coexistent foveal capillary dropout (Table 1, case 10). One untreated patient had persistent hard exudates involving the fovea (Table 1, case 18).

Discussion

In 1972, Gass described a patient with an arteriolar macroaneurysm treated by argon laser photocoagulation with eventual disappearance of the macroaneurysm and improvement in visual acuity.[1] Additional early case reports[2-5 9] documented improved visual acuity in five of six treated patients. Subsequent treatment series also suggested that laser photocoagulation might be beneficial, but included patients who either did not benefit from treatment or actually suffered decreased visual acuity possibly from the treatment itself.[8 10-12 14 16] The average presenting logMAR of these combined published symptomatic macroaneurysms (those with 6 months' follow up and documented visual acuity) treated by laser photocoagulation (44 patients) was 0·98 log units and the average follow up logMAR was 0·58 log units. This literature review series shows that treated patients, on average, improve from approximately 20/190 to 20/80.

The average presenting visual acuity of the combined published non-treated cases of arteriolar macroaneurysms affecting the macula (72 patients)[6-11] was 1·06 log units logMAR (including only patients with 6 months' follow up and documented visual acuity). Average visual acuity at follow up examination in this combined series was 0·58 log units logMAR. This literature series of untreated patients equates to an average improvement in visual acuity from 20/230 to 20/80, very similar to the results of the published treatment series summarised above.

The current series shows that patients with treatment directly to the macroaneurysm experienced an average decrease in visual acuity. As in all non-randomised studies, it is possible that patient selection for laser favoured those with more severe disease. However, presenting visual acuity was virtually identical in each group. Other presenting factors such as location of the macroaneurysm within the temporal arcade, presence of preretinal or subretinal haemorrhage, and presence of subretinal fluid involving the fovea were not statistically different between our groups. Laser photocoagulation remained a significant risk factor for visual loss even when the effects of subretinal haemorrhage and foveal subretinal fluid were controlled by multiple logistic regression analysis.

As patients in our series improved, they were generally referred back to their primary ophthalmologist. Hence the follow up time in improved cases (mean=31 months) is not as long as the follow up in cases with decreased vision (mean=66 months). It is possible that the improvements in visual acuity may be transient and this might be a bias influencing the results. However as the average follow up in the patients who improved was 31 months and vision was usually stable after the first year, we doubt whether significant deterioration occurred after this interval.

All patients in our series received direct photocoagulation to the macroaneurysm, with or without treatment to the surrounding retina. Direct treatment was used by Lewis *et al*,[8] Abdel-Khalek and Richardson,[11] and others with no reports of haemorrhage or rupture of the macroaneurysm. Some authors argue that indirect treatment to the surrounding retina is equally effective in obliterating the lesion.[15] Theoretically, indirect treatment of the aneurysm avoids the risk of rupture and haemorrhage and may decrease the incidence of arteriolar occlusion. Palestine *et al* recommended photocoagulation to the small, incompetent vessels surrounding the aneurysm (which contribute to the retinal swelling) and also to the trunk and distal tributaries of the retinal arteriole in an effort to decrease the blood flow and intraluminal pressure in the macroaneurysm to promote healing.[10] Joondeph *et al* recommended a treatment technique consisting of long duration, relative low power burns directly on the surface of the macroaneurysm intentionally avoiding the feeding and draining arterioles.[16] These techniques may lower the incidence of arteriolar occlusion but cases of arteriolar occlusion with this technique have been reported.[17]

Recent treatment series have advocated dye yellow laser to treat arteriolar macroaneurysms.[14 16] Yellow dye laser has theoretical

advantages in the occlusion of macroaneurysms because the yellow wavelength (577 nm) is highly absorbed by haemoglobin and oxyhaemoglobin. The small numbers of patients treated by each type of laser in this study (eight each) actually preclude judgment on which type of treatment is better but no definitive benefit of dye yellow laser was demonstrated.

Complications in our treated patients included occlusion of the arteriole in four patients (one previously reported[13]). Occlusion of the involved arteriole has been reported with argon laser treatment,[8 12 17] dye yellow laser treatment,[13] and in untreated patients.[6 17] Panton *et al*, found spontaneous arteriolar occlusion in 8% of untreated patients and 16% of treated patients.[17] It is difficult to assess the patency of the artery without follow up angiography. Since this is frequently not performed, it is possible that this complication is more common than is clinically appreciated. In at least two of our treated patients (Table 2, cases 2 and 6), arteriolar occlusion by laser close to the fovea appeared to result in increased foveal capillary dropout presumably accounting for decreased visual acuity on follow up.

Two of our treated patients (Table 2, cases 8 and 15) and one untreated patient (Table 1, case 18) with decreased visual acuity over follow up had lipid exudates on presentation, probably indicative of long standing fluid. These exudates remained through follow up. We do not know why hard exudates often remain after long follow up and resolution of subretinal fluid. Perhaps the advanced age of these patients alters the retina's ability to clear lipid exudates as quickly as in younger patients with hard exudates typically from diabetic retinopathy. Alternatively, permanent capillary damage may exist with continued slow leakage of fluid insufficient to cause subretinal fluid but enough to cause persistent hard exudates. Several other treated patients had decreased visual acuity secondary to subretinal fibrosis and scarring after resolution of subretinal fluid. These patients seem to have more fibrosis following subretinal fluid resorption compared with disorders such as central serous retinopathy. This may be related to an increased disruption of the blood-retinal barrier in leaking macroaneurysms with a resultant increase in macromolecule concentration in the exudation. These patients are also much older and many have coexistent hypertension, atherosclerosis, and retinal pigment epithelial changes associated with aging which may adversely influence the prognosis. Laser photocoagulation applied to arteries proximal to the fovea may compromise blood supply and add further insult to the foveal area.

Direct laser photocoagulation to macroaneurysms did not improve the visual outcome in our series of patients. Likewise, cumulative examination of published cases demonstrates that the majority of untreated cases have improved visual acuity of two or more lines and that laser photocoagulation does not seem to alter this visual outcome. It is unknown if indirect treatment or other treatment techniques would have better outcomes or a lower risk of arteriolar occlusion. Owing to the rarity of arteriolar macroaneurysms and the often benign clinical course, a controlled randomised trial may never be feasible definitively to set criteria for which patients may benefit from laser photocoagulation and if indirect treatment might be superior. Until this is possible, it seems prudent to observe closely most patients with arteriolar macroaneurysms without treatment. If treatment is offered, direct photocoagulation to the macroaneurysms cannot be recommended.

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