European Journal of Ophthalmology / Vol. 15 no. 1, 2005 / pp. 69-79

Photodynamic therapy with verteporfin of choroidal neovascularization in angioid streaks: Conventional versus early retreatment

I.D. LADAS, I. GEORGALAS, A.A. ROUVAS, S. GOTSIS, D.A. KARAGIANNIS, M. MOSCHOS

Department of Ophthalmology, Medical School of Athens University, Athens - Greece

PURPOSE. *To evaluate the effectiveness of conventional photodynamic therapy with verteporfin (PDT) in a series of patients with macular choroidal neovascularization (CNV) due to angioid streaks and to compare it to the effectiveness of early PDT retreatment.*
METHODS. *This is a retrospective study of 24 eyes (22 consecutive patients) with subfoveal or juxtafoveal CNV secondary to angioid streaks treated with PDT from September 2000 through February 2003 and that completed at least the first year of follow-up. Until August 2001, retreatments were performed according to the conventional protocol for PDT every 3 months (Group 1, consisting of 11 eyes of 9 patients). After August 2001 (13 more eyes of 13 new patients), retreatments were performed earlier (every 8 weeks) when indicated (Group 2). The follow-up time ranged from 30 to 42 months and from 12 to 30 months in Groups 1 and 2.*
RESULTS. *At the end of the follow-up, final best-corrected visual acuity decreased in 21 (87.5%), stabilized in 2 (8.3%), and improved in 1 (4.2%) of the total 24 eyes. In all, 19 of the 24 eyes (79.2%) had a final best-corrected visual acuity equal to or less than 20/400. There were not any statistically significant differences in final visual acuity between the two groups.*
CONCLUSIONS. *In this large series of patients with macular CNV secondary to angioid streaks, the functional and the anatomic results of PDT were not satisfactory, even when retreatments were performed earlier than the conventional time of 3 months. (Eur J Ophthalmol 2005; 15: 69-73)*

KEY WORDS. *Angioid streaks, Photodynamic therapy, Macular choroidal neovascularization*

Accepted: October 18, 2004

INTRODUCTION

Angioid streaks are irregular crack-like dehiscences in Bruch's membrane that invariably radiate outward from the peripapillary area in all directions. They are associated with a wide variety of systemic diseases, such as pseudoxanthoma elasticum, Ehler-Danlos syndrome, Paget's disease, and sickle-cell hemoglobinopathies.

The prognosis in patients with angioid streaks is guarded because visual impairment occurs in 70% to 86% due to the occurrence of macular choroidal neovascularization (CNV) (1-3). The natural history of such lesions is poor, with most resulting in fovea involvement and central vision loss (3, 4). Laser photocoagulation treatment of CNV may be beneficial in selected cases (5-10). However, the recurrence rate is higher than with CNV associated with other macular disor-

 1120-6721/069-05$15.00/0

ders (11, 12) and the final results reported in the literature are rather disappointing (3). Recently, limited macular translocation (13, 14) as well as photodynamic therapy with verteporfin (PDT) (15-17) were researched as alternative treatment modalities for subfoveal CNV due to angioid streaks in small series of patients with controversial results.

The purpose of this study is to evaluate the effectiveness of conventional PDT with verteporfin in a large series of patients with subfoveal or juxtafoveal CNV due to angioid streaks and to compare it to the effectiveness of early retreatment PDT (8 weeks following initial therapy) in patients who experienced disease progression.

MATERIALS AND METHODS

A retrospective analysis of 24 eyes of 22 consecutive patients with subfoveal or juxtafoveal CNV secondary to angioid streaks who were treated with PDT by the authors from September 2000 through February 2003 and completed at least the first year of follow-up was conducted. The greatest linear dimension of the entire lesion had to be 6,000 μm or less. Eyes with best-corrected visual acuity of less than 20/400 were not treated. None of the eyes had been previously treated by conventional laser photocoagulation for macular CNV.

Prior to the treatment, each patient had undergone a complete ocular examination including contact lens fundus biomicroscopy, color or red-free fundus photography, and digital fluorescein angiography (FA) using the Topcon Imagenet 2000 Digital Imaging System with TRC-50IA fundus camera (Topcon Corporation, Paramus, NJ). Fluorescein angiograms were evaluated for lesion size and leakage of the neovascular membrane. Best-corrected visual acuity was determined in all patients using standard Snellen charts.

Until August 2001, retreatments were performed according to the standard protocol followed in the Treatment of Age-Related Macular Degeneration with Photodynamic Therapy Investigation (TAP) every 12 weeks (18-21). During this time, 11 eyes of 9 consecutive patients were included in the study (Group 1). After August 2001, 13 more eyes of 13 new consecutive patients were included in the study. These eyes received early retreatments (8 weeks after the previous PDT) when indicated according to the criteria of the TAP study for conventional 3-month retreatment (Group 2).

The follow-up time ranged from 28 to 42 months (mean 34.1±4.6 months) and from 12 to 30 months (mean 20.8±5.3 months) for Groups 1 and 2, respectively. The re-examinations followed the same procedure as the first examination. Informed consent for examination and treatment was obtained from each patient after a full explanation of the procedure.

Numerical data in the text and the tables are presented as mean (±SD). Improvement or decline of visual acuity was defined as a change of at least two lines of Snellen acuity. A visual acuity of counting fingers was assigned a value of 20/1000 for statistical purposes. Fisher's exact test as well as two-tailed unpaired or paired t-test were used for the statistical analysis of the data. A p value less than 0.05 was considered statistically significant.

RESULTS

Demographics, clinical characteristics, and outcome of the eyes of Groups 1 and 2 are presented in Tables I–IV. Nine patients (11 eyes) with subfoveal (7 eyes) and juxtafoveal CNV (4 eyes) comprising Group 1 and 13 patients (13 eyes) with subfoveal (8 eyes) and juxtafoveal CNV (5 eyes) comprising Group 2 were enrolled. Evidence of predominantly classic CNV in FA was found in all 24 eyes examined.

The differences between the two groups in sex prevalence (p=0.4442), age (p=0.7598), lesion size (p=0.8708), and mean pre-treatment best-corrected visual acuity (p=0.2987) were not statistically significant. During the follow-up time, the mean number of retreatments was 8.7 (±2.5) in Group 1 and 7.9.(±2.7) in Group 2 (p=0.4647).

In Group 1, the mean final best-corrected visual acuity (0.05±0.05) was significantly lower compared to that of the baseline (0.26±0.22) (p=0.009). At the end of the follow-up time, best-corrected visual acuity decreased in 10 (90.9%) and stabilized in only 1 (9.1%) of the total 11 eyes of this group compared to the baseline. In all, 10 of the 11 eyes of Group 1 had stopped PDT during the follow-up time because they had showed conversion of the CNV into a disciform scar without leakage in FA. Nine of the 11 eyes (81.8%)

TABLE I - DEMOGRAPHICS OF PATIENTS OF GROUP 1 (conventional retreatments)

Patient no.	Age, yr	Sex	History
1	70	M	
2	45	M	PXE
Same*	46	M	PXE
3	65	F	
4	73	F	
5	50	F	
6	61	M	Paget
Same*	61	M	Paget
7	48	F	PXE
8	54	M	
9	49	M	

*The other eye of the previous patient
PXE = Pseudoxanthoma elasticum

TABLE II - DEMOGRAPHICS OF PATIENTS OF GROUP 2 (conventional retreatments)

Patient no.	Age, yr	Sex	History
1	64	M	PXE
2	46	F	
3	49	F	
4	55	M	
5	72	M	PXE
6	73	M	
7	54	F	
8	43	F	
9	60	F	SCH
10	57	M	
11	49	M	
12	50	F	
13	47	M	

PXE = Pseudoxanthoma elasticum; SCH = sickle-cell hemoglobinopathy

TABLE III - CLINICAL CHARACTERISTICS AND OUTCOME OF EYES OF GROUP 1 (conventional photodynamic therapy)

Eye no.	Lesion size, µm	Lesion location	PDT no.	Follow-up, mo	Initial BCVA	Final BCVA	Anatomic outcome	FA outcome
1	3100	Subfoveal	10	42	20/200	Counting fingers	Larger, scar	No leakage
2	2700	Subfoveal	9	41	20/400	Counting fingers	Larger, scar	No leakage
3*	2400	Juxtafoveal	11	30	20/50	20/200	Larger, scar	No leakage
4	4000	Subfoveal	11	39	20/100	20/800	Stable, scar	No leakage
5	1100	Subfoveal	8	34	20/200	Counting fingers	Larger, scar	No leakage
6	800	Juxtafoveal	7	33	20/40	20/400	Larger, scar	No leakage
7	6000	Subfoveal	6	32	20/200	20/800	Stable, scar	No leakage
8*	700	Juxtafoveal	7	28	20/25	Counting fingers	Larger, scar	No leakage
9	2900	Juxtafoveal	12	34	20/80	20/100	Stable	No leakage
10	5200	Subfoveal	4	32	20/100	Counting fingers	Stable, scar	No leakage
11	3300	Subfoveal	11	30	20/80	20/400	Larger	Leakage

*The other eye of the previous patient.
PDT = Photodynamic therapy; BCVA = Best-corrected visual acuity; FA = Fluorescein angiography

TABLE IV - CLINICAL CHARACTERISTICS AND OUTCOME OF EYES OF GROUP 2 (early retreatments)

Eye no.	Lesion size, µm	Lesion location	PDT no.	Follow-up, mo	Initial BCVA	Final BCVA	Anatomic outcome	FA outcome
1	1100	Subfoveal	12	30	20/20	20/800	Larger, scar	No leakage
2	3400	Subfoveal	10	27	20/100	Counting fingers	Larger, scar	No leakage
3	4600	Subfoveal	9	21	20/200	Counting fingers	Stable,scar	No leakage
4	2100	Juxtafoveal	9	25	20/25	Counting fingers	Larger, scar	No leakage
5	700	Juxtafoveal	10	25	20/80	Counting fingers	Larger, scar	No leakage
6	4200	Subfoveal	11	23	20/100	20/400	Larger, scar	No leakage
7	900	Juxtafoveal	8	21	20/40	20/400	Larger, scar	No leakage
8	2400	Subfoveal	9	20	20/100	20/50	Smaller	Leakage
9	5800	Subfoveal	6	19	20/100	Counting fingers	Larger, scar	No leakage
10	3200	Subfoveal	7	18	20/200	20/200	Stable	No leakage
11	3400	Subfoveal	4	15	20/80	20/200	Larger	Leakage
12	2700	Juxtafoveal	4	14	20/50	Counting fingers	Larger, scar	No leakage
13	5000	Juxtafoveal	4	12	20/25	20/200	Larger	Leakage

PDT = Photodynamic therapy; BCVA = Best-corrected visual acuity; FA = Fluorescein angiography

of Group 1 were found to have a final best-corrected visual acuity equal to or less than 20/400. Enlargement of the CNV was documented in 7 eyes of Group 1 (63.6%) at the final follow-up.

The results were similar in Group 2. The mean final best-corrected visual acuity did not differ significantly between the two groups (p=0.5228). In Group 2, the mean final best-corrected visual acuity (0.07±0.1) was significantly lower compared to that of the baseline (0.38±0.3) (p=0.0056). At the end of the follow-up time, the best-corrected visual acuity decreased in 11 (84.6%), stabilized in 1 (7.7%), and improved in 1 (7.7%) of the total 13 eyes of this group compared to the baseline. In all, only 3 of the 13 eyes of Group 2 (among them the one with better visual acuity) continued PDT because of the presence of leakage at the end of the follow-up time. Nine of the 13 eyes (69.2%) of Group 2 were found to have a final best-corrected visual acuity equal to or less than 20/400. Enlargement of the CNV was documented in 9 eyes of Group 2 (69.2%) at the final follow-up.

Among the total 24 eyes that were treated with PDT because of macular CNV due to angioid streaks, the mean final best-corrected visual acuity (0.06±0.08) was extremely significantly lower compared to that of the baseline (0.33±0.27) (p = 0.0001). The final best corrected visual acuity decreased in 21 (87.5%), stabilized in 2 (8.3%) and improved in only one (4.2%) of the total 24 eyes. In all, 19 of the 24 eyes (79.2%) had a final best corrected visual acuity of equal or less than 20/400 and 16 (66.7%) presented an enlargement of the CNV in FA at the end of the follow-up time.

Among the 15 eyes with subfoveal CNV the mean final best-corrected visual acuity (0.06±0.1) was significantly lower compared to that of baseline (0.22±0.23) (p=0.0295). The results were similar or worse in the nine eyes with juxtafoveal CNV. Among these latter eyes the final best-corrected visual acuity (0.06±0.06) was significantly lower compared to that of baseline (0.52±0.23) (p = 0.0006). PDT-related ocular complications were not reported in any of the study patients.

DISCUSSION

The most serious complication of angioid streaks is the development of CNV, which if left untreated leads to irreversible loss of central vision (3, 4).

Laser photocoagulation is of limited value in patients with CNV due to angioid streaks (5-10) as the recurrence rate is high (11, 12) and the final results rather disappointing (3). Recently, limited macular translocation was used as a new surgical approach to the management of a few eyes with subfoveal CNV secondary to angioid streaks with encouraging preliminary results (13, 14).

PDT was also researched as an alternative treatment for subfoveal CNV due to angioid streaks with controversial results. In 2000, Sickenberg et al (15) reported that PDT achieved a short-term (12-week) cessation of FA leakage from CNV secondary to angioid streaks in only one eye. Two years later, Karacorlu et al (16) concluded that "PDT generally achieved short-term cessation of/or decrease in FA leakage from subfoveal CNV without loss of vision" in a small series of patients with angioid streaks (8 eyes of 8 patients). However, 1 year later, Shaikh et al (17), studying 11 eyes of 9 patients, concluded that "PDT for CNV associated with angioid streaks does not appear to significantly alter the course of this disease with most eyes undergoing enlargement and disciform transformation of the neovascular process."

Our results in a larger series of patients (24 eyes of 22 patients) with a long follow-up confirm the disappointing functional and anatomic results of Shaikh et al (17). The greatest number of our patients showed progression of CNV to disciform scar (75%) and a best-corrected visual acuity of less than 20/400 (79.2%).

Further, we examined the effectiveness of aggressive PDT management of eyes with macular CNV secondary to angioid streaks performing early retreatments every 8 weeks when indicated. The results of PDT in this group of patients were similarly not encouraging as they did not differ significantly from the results in the group of patients with conventional PDT.

Only one of our study eyes presented a functional and anatomic improvement after 20 months of follow-up and 9 PDTs (Case 8 of Tab. IV). However, even for this eye the results cannot be considered final, since during the last follow-up examination leakage from the macular CNV persisted on FA and retreatment with PDT was administered.

In conclusion, PDT is not an effective treatment for macular CNV associated with angioid streaks even when retreatments are performed earlier than the conventional time of 3 months. Most likely, the combi-

nation of PDT with other macular CNV treatment modalities, such as intravitreal triamcinolone acetonide, anecortave acetate, or antivascular endothelial growth factor, or a surgical approach such as limited macular translocation will prove more effective in the management of this disease with guarded prognosis in the future.

Reprint requests to:
Ioannis D. Ladas, MD
8 Meg. Alexandrou Str.
GR-152 36 P. Penteli
Athens, Greece
ladas@ath.forthnet.gr

REFERENCES

1. Connor PH, Juergens JL, Perry HO, et al. Pseudoxanthoma elasticum and angioid streaks: a review of 106 cases. Am J Med 1961; 30: 537-43.
2. Shields JA, Federman JL, Tomer TL, et al. Angioid streaks. I. Ophthalmoscopic variations and diagnostic problems. Br J Ophthalmol 1975; 59: 257-66.
3. Clarkson JG, Altman RD. Angioid streaks. Surv Ophthalmol 1982; 116: 414-23.
4. Piro PA, Scheraga D, Fine L. Angioid streaks: natural history and visual prognosis. In: Fine SL, Owens SL, eds. Management of retinal vascular and macular disorders. Baltimore: Williams & Wilkins, 1983; 136-290.
5. Meislik J, Neldner K, Reeve EB, et al. Laser treatment in maculopathy of pseudoxanthoma elasticum. Can J Ophthalmol 1978; 13: 210-2.
6. Kayazawa F. A successful argon laser treatment in macular complications of angioid streaks. Ann Ophthalmol 1981; 13: 581-4.
7. Lim JI, Bressler NM, Marsh MJ, et al. Laser treatment of choroidal neovascularization in patients with angioid streaks. Am J Ophthalmol 1982; 26: 235-46.
8. Brancato R, Menchini U, Pece A, et al. Laser treatment of macular subretinal neovascularizations in angioid streaks. Ophthalmologica 1987; 195: 84-7.
9. Van Eijk AW, Oosterhuis JA. Kryptonlaserbehandlung von gefabneubildungen bei angioiden streifen. Klin Monatsbl Augenheilkd 1987; 191: 443-8.
10. Geliksen O, Hendrikse F, Deutman AF. A long-term follow-up study of laser coagulation of neovascular membranes in angioid streaks. Am J Ophthalmol 1988; 105: 299-303.
11. Deutman AF, Kovacs B. Argon laser treatment in complications of angioid streaks. Am J Ophthalmol 1979; 88: 12-7.
12. Singerman LJ, Hatem GF. Laser treatment of choroidal neovascular membranes in angioid streaks. Retina 1981; 1: 75-85.
13. Fujii GY, Humayun MS, Pieramici DJ, et al. Initial experience of inferior limited macular translocation for subfoveal choroidal neovascularization resulting from causes other than age-related macular degeneration. Am J Ophthalmol 2001; 131: 90-100.
14. Roth DB, Estafanous M, Lewis H. Macular translocation for subfoveal choroidal neovascularization in angioid streaks. Am J Ophthalmol 2001; 131: 390-2.
15. Sickenberg M, Schmidt-Erfurth U, Miller JW, et al. A preliminary study of photodynamic therapy using verteporfin for choroidal neovascularization in pathologic myopia, ocular histoplasmosis syndrome, angioid streaks, and idiopathic causes. Arch Ophthalmol 2000; 117: 327-36.
16. Karacorlu M, Karacorlu S, Ozdemir H, et al. Photodynamic therapy with verteporfin for choroidal neovascularization in patients with angioid streaks. Am J Ophthalmol 2002; 134: 360-6.
17. Shaikh S, Ruby AJ, Williams GA. Photodynamic therapy using verteporfin for choroidal neovascularization in angioid streaks. Arch Ophthalmol 2003; 135: 1-6.
18. Miller JW, Scmidt-Erfurth U, Sickenberg M, et al. Photodynamic therapy with verteporfin for choroidal neovascularization caused by age-related macular degeneration: results of a single treatment in a phase 1 and 2 study. Arch Ophthalmol 1999; 117: 1161-73.
19. Scmidt-Erfurth U, Miller JW, Sickenberg M, et al. Photodynamic therapy with verteporfin for choroidal neovascularization caused by age-related macular degeneration: results of retreatments in a phase 1 and 2 study. Arch Ophthalmol 1999; 117: 1177-87.
20. TAP Study Group. Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: one-year results of randomized clinical trials–TAP Report 1. Arch Ophthalmol 1999; 117: 1329-45.
21. TAP Study Group. Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: two-year results of randomized clinical trials–TAP Report 2. Arch Ophthalmol 2001; 119: 198-207.