One-year results of verteporfin therapy for subretinal neovascularization associated with type 2A parafoveal telengiectasia

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Background: To report the 12 months follow up results of verteporfin therapy for subretinal neovascularization (SRNV) associated with type 2A parafoveal telangiectasia (PFT).

Methods: A Prospective interventional case series. Patients who completed 12 months follow up following photodynamic dynamic therapy with verteporfin for subretinal neovascularistion with Type 2A PFT were studied. All patients underwent visual acuity assessment with ETDRS letter acuity chart at 4 meters, slit lamp biomicroscopy, fundus fluorescein angiography and photography. Treatment protocol of TAP study was followed. The follow up schedule was every month for 3 months and then every 3 months thereafter until 12 months. Primary outcome measure was the change in visual acuity and secondary outcome measure was the mean treatment rate. Improvement was defined as $\geq$ 10 letters gain, stabilization as $\pm$ 10 letters and deterioration as $>$ 10 letters loss.

Results: Twelve eyes of 7 patients received photodynamic therapy with verteporfin for SRNV with Type 2A PFT. Initial mean letter acuity was 25.4 and 23.4 at 12months ($p = 0.7$). At 12 months, one eye had $>$ 10 letters gain, 2 eyes had $\geq$ 10 letters loss and 9 had stabilized vision ($\pm$ 10 letters). The mean number of treatment was 2.6. Ten (83.3%) of 12 eyes had retinal pigment epithelial collateral change, observed at the end 12 months.

Conclusion: Photodynamic therapy with verteporfin is effective in stabilization of vision in SRNV associated with type 2A PFT.

Keywords: subretinal neoveascularisation, verteporfin, photodynamic therapy, parafoveal telangiectasia

Introduction

Parafoveal telangiectasia is characterized by loss of retinal transparency, small telangiectatic vessels, late fluorescein dye leakage and cystic appearance to the fovea without intraretinal leakage. Typically, loss of retinal transparency appears grayish. (Gass and Blodi 1993)

Subretinal neovascularization (SRNV) is the most important cause of severe visual loss in patients with Type 2A parafoveal telangiectasia or Idiopathic juxtafoveal telengiectasia. (Gass and Blodi 1993) This accounts for 14% of the cases. Type 2A or Group 2A have the most common form of parafoveal telangiectasia. Bilateral involvement is seen in more than 95% of patients at the time of presentation. In these patients, the telangiectatic change is often difficult to detect biomicroscopically as it is associated with minimal exudation and retinal thickening. The cause of visual loss is primarily due to progressive foveolar atrophy and SRNV in minority of patients.

Treatment of SRNV in parafoveal telangiectasia by laser photocoagulation and surgery has been generally unsuccessful, associated with poor visual outcome (Gass and Blodi 1993; Lee 1996; Berger et al 1997). The primary complication during surgical removal is the shearing of the retina due to firm vascular anastomotic connection.

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(Berger at al 1997) Hence, subretinal surgery is a relative contraindication in this subset of patients. In anecdotal series, transpupillary thermotherapy has shown encouraging results of either maintained or better vision in 88% of patients (Shukla et al 2004; Nachiappan et al 2005).

In the recent past, photodynamic therapy with verteporfin for SRNV has shown to be beneficial in regression of SRNV and improvement of visual acuity (Potter et al 2002; Hershberger et al 2003; Smithen et al 2004; Hussain et al 2005) Most of these case series had follow up of at least 7 to 9 months (Potter et al 2002; Smithen et al 2004; Hussain et al 2005) except a single case report of bilateral involvement had 21 months follow up (Hershberger et al 2003). Snyers et al (2004) also showed effective treatment with verteporfin in 3 eyes with follow up of 23, 21 and 9 months. The common feature amongst all the published reports suggests that repeated treatment is necessary to achieve closure of the subretinal new vessels.

We report 12 months follow up outcome of photodynamic therapy with verteporfin for SRNV associated with Type 2A parafoveal telangiectasia.

Methods

Patients were recruited from the prospective patient enrollment for photodynamic therapy with verteporfin in a tertiary care hospital. The study duration was between May 2001 and July 2005. The photodynamic therapy was approved by the ethics committee of the institution in 2001. Patients were explained about the long-term unproven nature of treatment for this subset of disease and informed consent was taken accordingly.

Patients diagnosed as subretinal neovascularisation associated with type 2A parafoveal telangiectasia were included in the study. Any vascular or non-vascular causes that may adversely affect the macula were excluded from the study.

All patients underwent routine ocular examination which included ETDRS visual acuity measurement at 4 metres, Slit lamp biomicroscopy, Amsler grid and fundus examination (90/78 D and indirect ophthalmoscopy). Fundus photography and fundus fluorescein angiography (FFA) was done in all patients in each visit and pretreatment. FFA was done using a con focal scanning laser ophthalmoscope (HRA, Heidelberg Engineering Inc., Heidelberg, Germany) by trained optometrists. The follow up schedule was every month for 3 months then every three months thereafter following treatment.

Photodynamic therapy (PDT) was performed using verteporfin (Visudyne® 15 mgm, Novartis ophthalmics AG, Hettlingen, Suiza) following the protocol of TAP study (TAP Study Group 1999). A mainster focal contact lens (Ocular Instruments, USA) was used for viewing the fundus during PDT. In bilateral treatment, after completion of the first eye, the lens was shifted to the contralateral eye within 20 minutes of start of infusion as described earlier (Hussain et al 2005). The eye with more active or larger lesion was treated first than the contralateral eye (Hussain et al 2005).

Retreatment was done whenever there was evidence of leakage associated with retinal thickening. Care was taken not to misinterpret the underlying leakage pattern of the primary disease. 5400 micron was taken as the maximum permissible greatest linear dimension to be eligible for treatment.

Improvement was defined as $\geq$10 letters gain, deterioration as $>$10 letters loss and stabilization as $\pm$ 10 letters change. The primary outcome measure was the change in visual acuity at the end of 12 months and the secondary outcome measure was the mean number of treatment sessions in each eye in one year.

Statistical analysis

A Wilcoxon signed rank test was done to find out the significance of change in letter visual acuity seen till end of 12 months from the baseline.

Results

Twelve eyes of 7 patients were included in the analysis (Table 1). Five of 7 patients had bilateral involvement. The mean age was 53.6 $\pm$ 7.6 years (Range: 42 to 63 years). The male female ratio was 3:4. The initial greatest linear diameter of the SRNV ranged from 860 to 5740 (mean: 2990) microns. All the eyes had subfoveal neovascular membrane. All patients completed atleast 12 months follow up.

Letter acuity

The initial mean letter acuity was 25.4 letters with final mean letter acuity of 23.4 letters at 12 months ($p = 0.7$, standard error: 3.2), which was not statistically significant. Figure 1 shows a minimal trend of improvement in letter acuity at 3 months and then stabilization at 12 months with mean difference of 2 letters only. At 12 months, one eye gain $>$ 10 letters, 2 eyes lost $>$ 10 letters and 9 eyes (75%) had stabilized vision. 33% (4 eyes) had initial visual acuity of $\geq$ 20/40.

Snellen acuity

At 12 months, one eye (8.3%) had VA $\geq$ 20/40 and 7 eyes (58.3%) had between 20/50 and 20/80. 4 eyes remained

Table 1 Clinical characteristics of patients with subretinal neovascularization and parafoveal telengiectasis

Sl no	OD/OS	Age/Sex	Initial VA	ETDRS letters	3rd mth VA	ETDRS letters	6th mth VA	ETDRS letters	12th mth VA	ETDRS letters	RPE coll.
1	OD	54/M	20/100	17	20/80	22	20/80	22	20/80	21	+
	OS		20/80	25	20/63	27	20/63	30	20/80	23	
2	OD	62/F	20/200	3	20/200	3	20/200	3	20/200	2	
	OS		20/80	23	20/100	18	20/100	18	20/100	20	+
3	OD	56/F	20/40	40	20/40	40	20/50	35	20/50	33	+
	OS		20/63	29	20/50	33	20/63	30	20/63	27	+
4	OD	51/F	20/50	35	20/50	35	20/50	35	20/32	44	+
	OS		20/200	3	20/100	18	20/160	7	20/125	13	+
5	OD	42/F	20/25	47	20/40	40	20/40	40	20/80	22	+
	OS		20/32	45	20/40	40	20/40	39	20/63	30	+
6	OS	63/M	20/125	12	20/125	16	20/125	13	20/125	13	+
7	OS	47/M	20/40	26	20/50	35	20/63	24	20/50	33	+

Abbreviations: OD, right eye; OS, left eye; M, male; F, female; mth, month; RPE coll, retinal pigment epithelial collateral damage.

same at ≥ 20/200 as the initial VA even at twelve months. Figure 2 shows that the group of eyes that had VA between 20/100 and 20/200 remained the same and 7 eyes had VA ≥ 20/80.

It can be concluded from Figures 1 and 2 that following PDT with verteporfin, there is a trend towards mild visual loss (< 5 letters) with stabilization of vision at 12 months.

Treatment sessions

The time and number of treatment sessions were shown in Figure 3. The patients received a total of 31 treatment

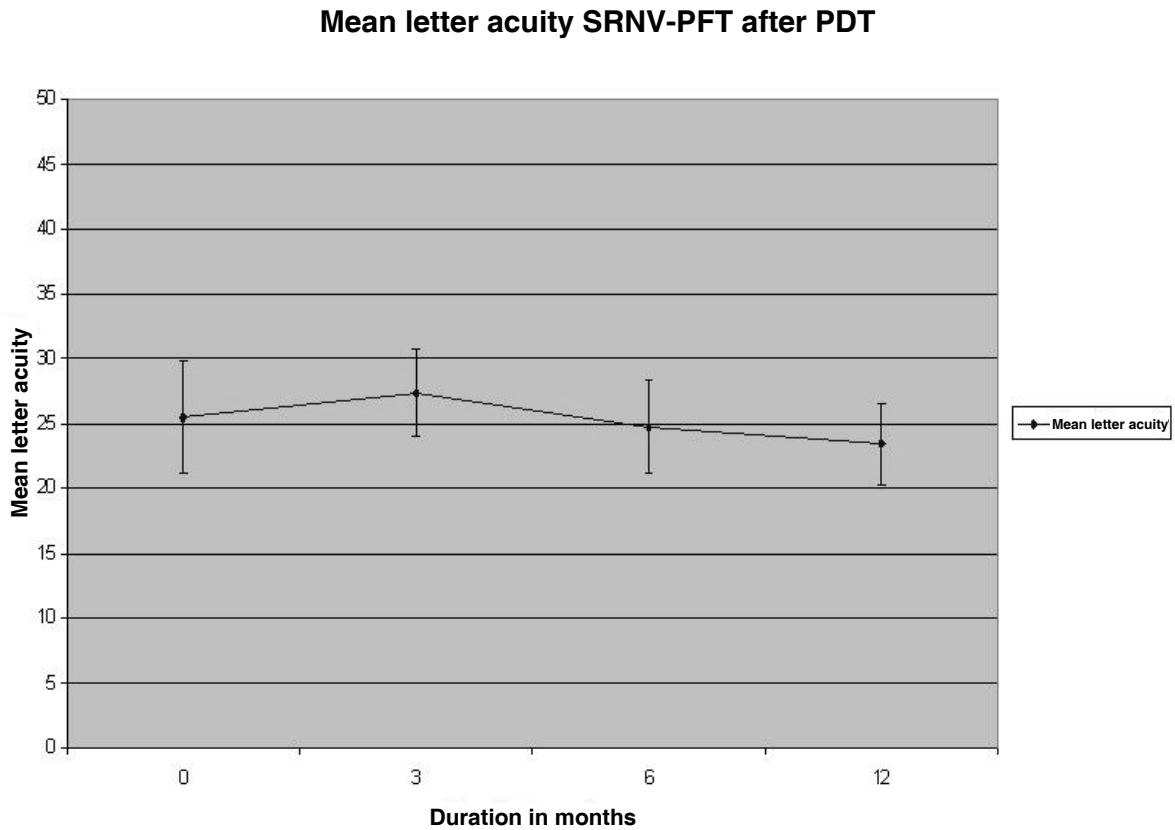

Figure 1 Graph showing change in mean letter acuity in 12 months period. The change in letter was not statistically significant (p = 0.7).

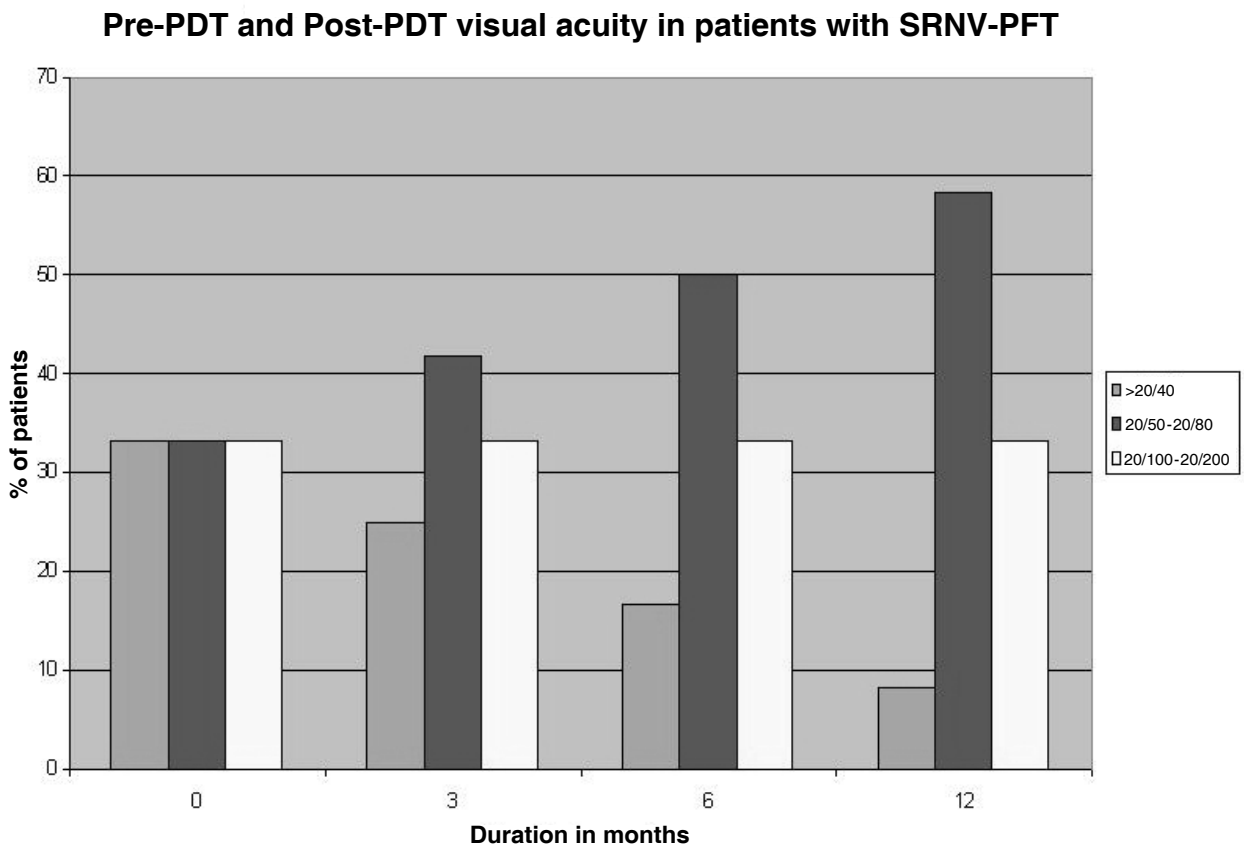

Figure 2 Bar diagram showing Pre- and post-PDT snellens visual acuity in 12 months. 66.6% of eyes had VA ≥ 20/80 at baseline and 12 months.

sessions with a mean of 2.6 for each eye. 28 of 31 treatment sessions (93.5%) were done within 6 months suggesting repeated and shorter interval of treatment is necessary.

Retinal pigment epithelial collateral damage from the baseline characteristics was seen in 10 eyes (83.3%) till the end of 12 months. The change has been seen around the SRNV and within the area of the spot size. No adverse ocular or systemic ocular events were observed during the follow up period.

Discussion

Subretinal neovascularisation may occur in advanced stages of primarily bilateral parafoveal telangiectasia (Stage 5, Type 2A) (Gass and Blodi 1993; Lee 1996). Management options in this subset of eyes are limited and studies have already shown the adverse outcome and limitations of medical and surgical treatment (Berger et al 1997; TAP Study Group 1999; Potter et al 2002; Hershberger et al 2003; Shukla et al 2004; Smithen et al 2004; Snyers et al 2004; Hussain et al 2005; Nachiappan et al 2005). The difficulty lies in the inability to achieve easy closure of the neovascular membrane. This is due to different internal milieu and origin of subretinal neovascular membrane (Gass 2003; Hussain et al 2005) than seen in neovascular membrane secondary to age related macular degeneration or myopia or etc.

Present study has shown that photodynamic therapy with verteporfin is effective in maintaining vision atleast till 12 months of follow up. This result also suggest that PDT can prevent moderate to severe visual loss and better the initial VA, better is the outcome in maintaining vision. Syners et al (2004) have also reported similar results in maintenance of vision in 4 eyes (4 patients). Except in one eye where vision deteriorated to 20/200. The average follow up in these 4 patients were 16.7 months.

The reason for apparent non-improvement of vision in the study was possibly due to associated retinal pigment epithelial (RPE) collateral damage seen (83.3%) around the lesion following PDT. This finding was also shown in the earlier reports. (Potter et al 2002; Hussain et al 2005; Shanmugam 2005) It is possible that the microvascular abnormality of telangiectasia vessels besides the SRNV may leak verteporfin

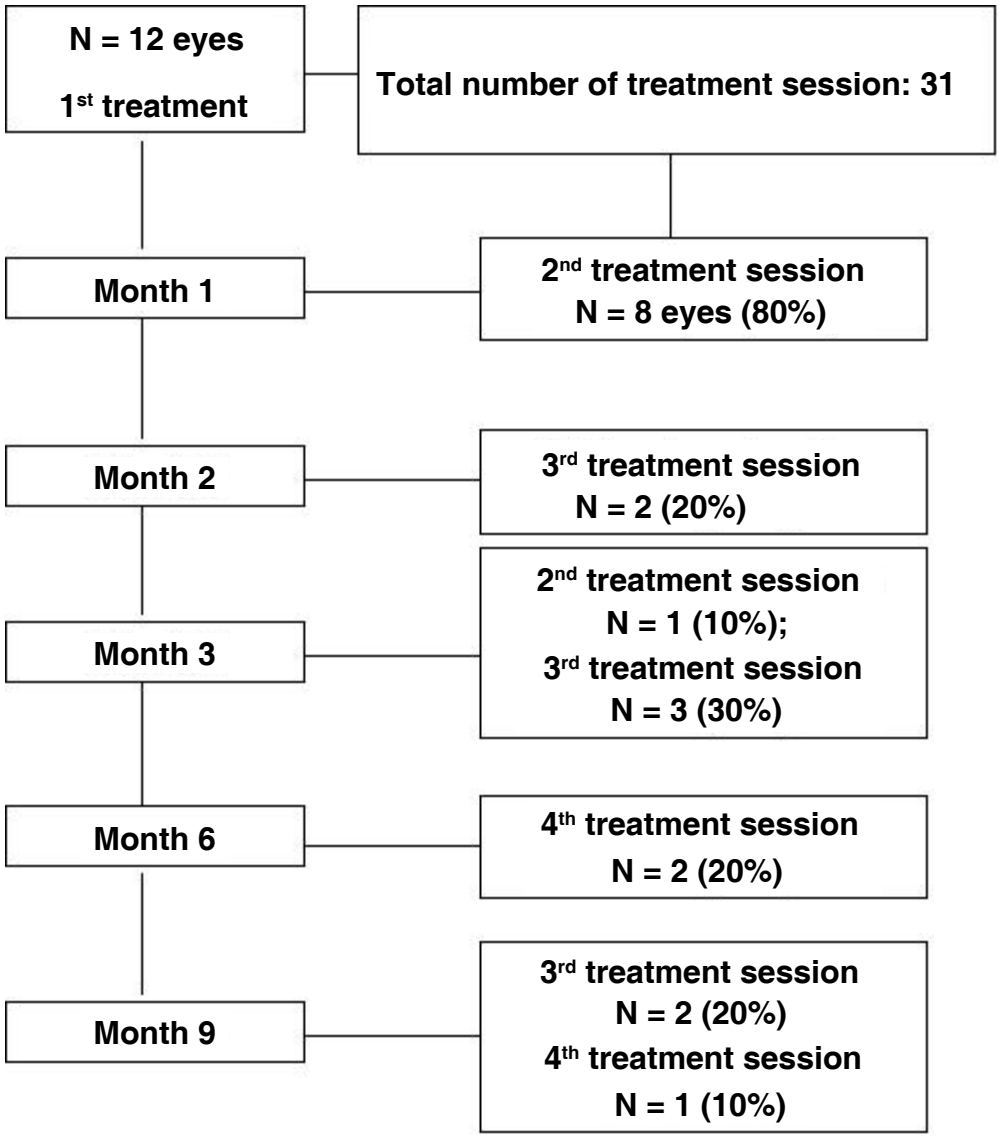

Figure 3 Flow chart showing the time of treatment sessions in 12 months. 93.5% of the treatments were done within 6 months.

and theoretically may cause collateral change at the level of RPE. (Hussain et al 2005) This is a specific possibility due to leakage of verteporfin and frequent repeated treatment in these subsets of eyes.

The mean number of treatment was 2.6 in the present study, which is more than that treated for choroidal neovascularization secondary to age related macular degeneration (mean: 2.1 at the end of 12 months) (Hussain et al 2006) in the eyes of similar ethnic origin. It has also been seen that 93.5% of the eyes required treatment session within 6 months. Most of the small series of patients and case report with less than one year follow up published so far suggest number of treatment sessions ranging from 2 to 4 (mean 2.2) (Potter et al 2002; Hershberger et al 2003; Smithen et al 2004; Snyers et al 2004; Hussain et al 2005) which is also seen in the present series of patients. The highlight of PDT in PFT with SRNV can be stated that frequent repeated treatment is necessary to achieve successful closure. This may be attributed to the high flow microvascular connections to the subretinal lesions (Hussain et al 2005).

It has recently been shown that transpupillary thermotherapy (TTT) is effective in closure of SRNV associated with parafoveal telengiectasis. (Shukla et al 2004; Nachiappan et al 2005; Shanmugam 2005) The two anecdotal series also shows that visual acuity can be maintained following TTT. However, RPE collateral damage has not been reported. The long-term thermal effect of TTT cannot be ruled out on an already compromised RPE associated with PFT.

Hence, photodynamic therapy with verteporfin is effective in successful closure of SRNV and stabilization of vision atleast at the end of 12 months. The limitations of the study are small sample size and long-term outcome or recurrence is not known. We feel the sample size of (12 eyes) appears adequate to see the effect at 12 months, as this entity with SRNV is also a rare clinical finding. We do agree that a long-term follow up study is also necessary.

Note

Financial interest: None.

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