Case Series

Photodynamic Therapy for Choroidal Neovascularisation Secondary to Inflammatory Chorioretinal Disease

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Abstract

Introduction: To review the long-term outcome of photodynamic therapy (PDT) with verteporfin for inflammatory chorioretinal disease with subfoveal choroidal neovascularisation (CNV) over a 1-year period. Materials and Methods: Retrospective review of eyes with subfoveal CNV for associated choroiditis that were treated with PDT using verteporfin over a 1-year period. Main outcome measure: visual acuity. Results: Five eyes in 4 patients, with diagnoses including serpiginous choroiditis (2), ocular histoplasmosis syndrome (OHS, 1), and punctate inner choroidopathy (PIC, 2) underwent standard treatment procedure for PDT with verteporfin. Visual acuity, fluorescein angiography and treatment parameters were reviewed. Follow-up ranged from 12 months to 36 months (median, 36 months). Pre-PDT visual acuities ranged from 20/60 to 20/400 (median, 20/200). Post-PDT visual acuities ranged from 20/30 to 20/400 at 1 year (median, 20/300). Visual acuity was stabilised (within 1 line) or improved (greater than 1 line) in 3 eyes at 1 year and 4 of the 5 eyes at last follow-up. Conclusion: PDT for subfoveal CNV may stabilise, but rarely improves, visual acuity in eyes with choroidal neovascularisation secondary to inflammatory chorioretinal disease.

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Key words: Choroidal neovascularisation, Choroiditis, Photodynamic therapy, Verteporfin

Introduction

Photodynamic therapy using verteporfin (Visudyne, Novartis Ophthalmics) has been proven safe and effective for the treatment of predominantly classic, age-related macular degeneration (AMD)-related subfoveal choroidal neovascularisation (CNV), pathologic myopia-related CNV, and subgroups of AMD-related occult CNV.[1-3] Visual results following verteporfin treatment of subfoveal, non-AMD related CNV[4-14] have been variable. We report our experience utilising photodynamic therapy (PDT) for choroidal neovascularisation secondary to inflammatory chorioretinal disease.

Materials and Methods

We performed a retrospective review of all patients who underwent PDT using verteporfin for subfoveal CNV secondary to non-AMD related diseases at our institution over a year's interval. From these we extracted the patients with choroidal neovascularisation secondary to inflammatory chorioretinal disease and at least 2 years' follow-up data. Baseline examination of the patient included Snellen visual acuity, fundus biomicroscopy, fundus photography and fluorescein angiography. The greatest linear dimension of the CNV lesion was calculated based upon the lesion size measurement on the fluorescein angiogram and the image size magnification factor.

The verteporfin was administered intravenously at a dose of 6 mg per square metre of body surface area over a 10-minute time interval. Five minutes after the completion of the infusion, the patient underwent diode laser treatment to the CNV lesion using 50 J/cm^2 at an intensity of 600 mW/cm^2 for 83 seconds. A fundus contact lens was placed on the anaesthetised (topical proparacaine) cornea and utilised for the treatment. The diode laser (689 nm) treatment spot size diameter was calculated to measure 1000 microns more than the greatest linear dimension of the CNV lesion. The patients gave informed consent for PDT with verteporfin. After the PDT, the patient was instructed to

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wear sunglasses and to protect the infusion site and bare skin from direct sunlight exposure for 2 days.

Patients returned for follow-up at 3-month intervals after the first PDT. Snellen visual acuity, biomicroscopy, fundus photography and fluorescein angiography were performed at the return visits. Re-treatment was performed if the fluorescein angiogram demonstrated leakage from the CNV lesion.

Visual acuity data were recorded from the clinic record. Fluorescein angiography results were reviewed to determine lesion size and the presence or absence of leakage. Lines of visual acuity change were calculated at specific intervals post-PDT therapy. Visual acuity was considered stable if there was ≤1 line of visual acuity change. Lesion size and retreatment data were obtained from the clinic record.

Case Reports

Case 1. Serpiginous Choroiditis (Bilateral CNV)

A 73-year-old patient with known serpiginous choroiditis for 10 years was treated with prednisone for 6 months and extrafoveal laser for CNV in the left eye. She did well for 8 years. She then developed reactivation of her serpiginous choroiditis and was placed on immuran and prednisone. She underwent sub-Tenons steroid injections 4 times in the right eye and twice in the left eye over the next year.

She was referred to us for the evaluation of recent decreased visual acuity in both eyes while on immuran (50 mg daily). Visual acuities were 20/200 OD and 20/60 OS. The amsler grid showed areas of metamorphopsia in both eyes. Slit lamp evaluation showed early central posterior subcapsular cataracts with mild nuclear sclerosis in both eyes. The anterior chamber and posterior segments did not show any cells. Dilated fundus examination showed subfoveal greyish-white lesions with overlying subretinal fluid and dots of haemorrhage adjacent to the lesion. The posterior and midperipheral areas had several chorioretinal scars that emanated from the optic disc in a serpentine fashion. Fluorescein angiography showed subfoveal well-demarcated areas of CNV.

Bilateral PDT with verteporfin therapy was applied. The greatest linear dimensions (GLDs) were 1850 microns OD and 820 microns OS. Three months later, visual acuities were 20/400 OD and 20/100 OS. The CNV was closed OD but actively leaking OS. She underwent repeat PDT to the left eye (GLD 1100 microns). At the next follow-up, 3 months later, visual acuities were 20/400 OD and 20/60 OS. PDT was repeated OS (GLD 1000 microns). Nine months after initial treatment, visual acuities were 20/400 OD and 20/100 + 2 OS and there were bilateral active subfoveal CNVs. Bilateral PDT was performed (GLD 4400 microns OD and 1300 microns OS).

One year after initial treatment, visual acuities were 20/400 OD and 20/100 OS. Bilateral PDT was performed (GLD 2632 microns OD and 1200 microns OS). Two months after that session, visual acuities were 20/200 OD and 20/400 OS. No active CNV was seen on fluorescein angiography and cataract surgery was recommended.

Following cataract extraction and lens implantation, visual acuities were 20/200 OD and 20/100 OS. Fluorescein angiography showed closure of the CNV OD and macular oedema related to cataract surgery OS. By 1 year and 5 months after initial PDT, visual acuities were 20/300 OD and 20/100 OS. CNV leakage was noted OS and PDT was performed (GLD 1536 microns). Two months later, visual acuity dropped to 20/400 OD, with evidence of recurrent CNV OD. PDT was performed OD (GLD 2700 microns). The subfoveal CNV became inactive by the next follow-up visit. Visual acuity increased to 20/200 OD and remained 20/200 OS at 24 months and 36 months follow-up.

Case 2. Punctate Inner Choroidopathy (PIC)

A 40-year-old woman with myopia and fundus findings compatible with PIC presented with decreased vision to 20/30. A juxtafoveal CNV was diagnosed in her right eye and she underwent a 2½-month course of oral corticosteroid therapy. The CNV closed and visual acuity stabilised at 20/30. One year and 9 months later, she presented with an acute drop in visual acuity to 20/200. Evaluation disclosed the presence of a subfoveal CNV (Figs. 1a and 1b); she underwent PDT with verteporfin. Three months later, visual acuity improved to 20/40. No subretinal fluid was seen and fluorescein angiography showed closure of the CNV (Figs. 1c and 1d). At 6 months, visual acuity remained at 20/40. By 9 months, visual acuity had improved to 20/30. Visual acuity remained at 20/30 at 12, 18 and 24 months post-PDT.

Case 3. Ocular Histoplasmosis Syndrome (OHS)

A 78-year-old man with OHS diagnosed at 18 years of age had previously undergone bilateral thermal laser treatment for CNV (10 years ago, OD, and 5 years ago, OS). He presented complaining of blurred central vision, metamorphopsia and an enlarging scotoma in the right eye. Visual acuities were 20/400 in the right eye and 20/25 in the left eye. Dilated examination revealed a subfoveal greyish-green membrane with overlying neurosensory detachment adjacent to the old temporal laser scar. In contrast, the left macular region showed a flat laser scar inferior to the fovea without any subretinal fluid, haemorrhage or hard exudates. The periphery of both eyes showed numerous punched out lesions consistent with histoplasmosis.

A fluorescein angiogram showed a classic subfoveal CNV lesion (GLD 1600 microns) adjacent to the old laser scar OD. PDT was performed. One month later, visual

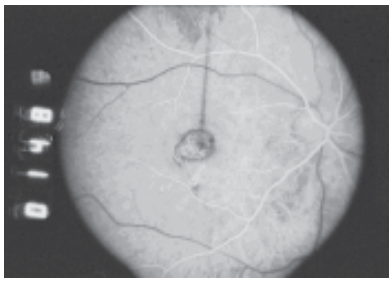

Fig. 1a. Early frame fluorescein angiogram shows a subfoveal CNV lesion in a patient with PIC. Visual acuity was 20/300.

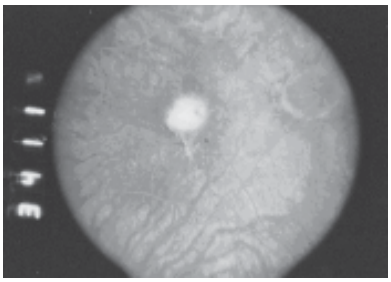

Fig. 1b. Late frame fluorescein angiogram shows leakage from the CNV lesion.

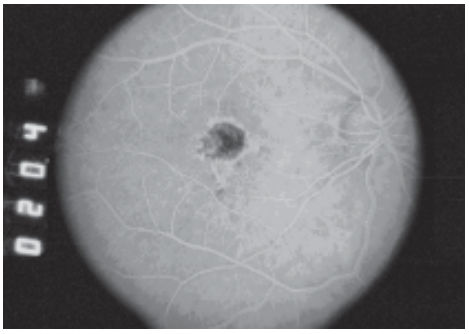

Fig. 1c. 3 months after PDT, visual acuity was improved to 20/40 and the lesion was now flat. Late frame fluorescein angiogram shows no leakage.

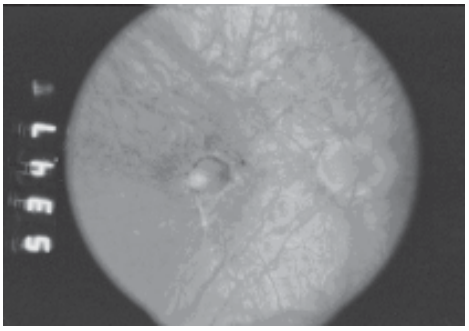

Fig. 1d. Late frame fluorescein angiogram shows staining but no subfoveal leakage.

acuity had improved to 20/200. By 3 months post-treatment, visual acuity had decreased to 20/400 and fluorescein angiography confirmed the presence of subfoveal CNV leakage. PDT was repeated (GLD 2500 microns). Six months after initial treatment, visual acuity had improved to 20/100 in the right eye. However, 7 months after initial treatment, visual acuity decreased to 20/400, CNV leakage was present on fluorescein angiography and PDT was performed. Three months later, visual acuity improved to 20/100. Visual acuity dropped 2 months later to 20/400 because of recurrent CNV and PDT was repeated (GLD 3200 microns). The patient was lost to follow-up for 6 months. When he returned, his visual acuity was 20/400 and macular atrophy was visible. He has remained 20/400 at 24 and 36 months after his initial PDT.

Case 4.

A 30-year-old woman with a known history of PIC, who had undergone thermal laser treatment for an extrafoveal CNV lesion in the right eye, presented complaining of an acute drop in vision. Visual acuity was 20/400 and a fluorescein angiogram showed a subfoveal classic CNV lesion. PDT with verteporfin using a GLD of 1800 microns was performed. Three months later, visual acuity remained 20/400 and subretinal fluid was present. PDT was repeated (GLD 2700 microns). The patient was lost to follow-up until 10 months after her initial PDT. She returned with 20/400 visual acuity and a fluorescein angiogram confirmed the presence of CNV. She was recommended additional PDT treatment. The patient believed her visual acuity was stable at 1 year (after the initial PDT) and deferred further treatment.

Results

Four patients (5 eyes), ranging in age from 30 to 78 years, presented with subfoveal CNV due to serpiginous choroiditis (2), ocular histoplasmosis (1 eye) and punctate inner choroidopathy (2). There were 3 females and 1 male. All 5 eyes of 4 patients underwent PDT with verteporfin using standard treatment parameters as described above. One patient with serpiginous choroiditis presented with bilateral active subfoveal CNV and underwent bilateral sequential PDT at the same sitting. The other 3 patients had unilateral active CNV and underwent unilateral PDT. All of the patients were offered alternative treatments (such as submacular surgery, translocation, steroid injection) and chose PDT. The CNV was predominantly classic in composition in all patients.

Pre-PDT visual acuities ranged from 20/60 to 20/400 (median, 20/200). Post-PDT visual acuities ranged from 20/30 to 20/400. Follow-up ranged from 12 to 48 months (median, 36 months). Follow-up visits occurred at approximately 12-week intervals. At the follow-up visits, patients were retreated if the fluorescein angiogram showed

Table 1. Visual Acuity Results after PDT with Verteporfin for Choroiditis-related CNV

	N (eyes)	Stable*	Decreased	Increased
10-12 weeks	5	2	2	1
6 months	4	1	1	2
9 months	4	0	2	2
12 months	5	2	2	1
2 years	4	2	1	1
3 years	4	2	1	1

CNV: choroidal neovascularisation; PDT: photodynamic therapy
* within 1 line of baseline visual acuity

Table 2. Visual Acuity Results after PDT with Verteporfin for Choroiditis-related CNV

	N (eyes)	Stable*	Decreased	Increased
10-12 weeks	5	3	1	1
6 months	4	1	1	2
9 months	4	2	1	1
12 months	5	3	1	1
2 years	4	2	1	1
3 years	4	2	1	1

CNV: choroidal neovascularisation; PDT: photodynamic therapy
* within 2 lines of baseline visual acuity

evidence of leakage and if no subfoveal fibrotic scar was noted.

Tables 1 and 2 show the visual acuity results for specific time intervals post-PDT. Visual acuity was stable or improved (2 or more lines) in 3 of 5 eyes (60%) at 3 and 12 months and in 3 of 4 eyes at 2 and 3 years. Visual acuity was increased 2 or more lines in 1 of 5 eyes (20%) at 3 and 12 months. Visual acuity was decreased 2 or more lines in 2 of 5 eyes (40%) at 3 and 12 months.

Eyes with serpiginous choroiditis had the worst outcomes at year 4, with both eyes losing 2 or more lines of visual acuity from baseline. Cataract surgery after 1 year led to stabilisation in 1 eye; the other eye still lost more than 2 lines of visual acuity.

Retreatment was performed in 3 of the 5 (60%) eyes within 3 months of the initial treatment, 2 (40%) eyes at 6 months, 3 (60%) eyes at 9 months, 2 (40%) eyes at 12 months and 2 (40%) eyes in the second year. The mean number of treatments ranged from 1 (PIC) to 4 treatments [serpiginous (1) and OHS (1)] in the first year.

By the last follow-up visit, the subfoveal CNV was closed in 3 of 5 eyes and active in 2 (serpiginous, PIC) of the 6 eyes. There was advanced subfoveal retinal pigment epithelial atrophy in 1 eye each with serpiginous choroiditis and OHS.

Discussion

In this non-randomised, small, retrospective case series of inflammatory chorioretinal disease with subfoveal CNV, the standard regimen of PDT using verteporfin resulted in stabilised (within 1 line) or improved visual acuity in 60% of patients at 1 year. At 6 months, 3 eyes had improved by 2 or more lines and it is unlikely that laser photocoagulation could have resulted in similar results. In fact, thermal laser photocoagulation for these eyes with subfoveal CNV would have resulted in significant visual acuity loss. However, at 1 year, the advantage in 2 of these eyes was lost. Alternative treatments for this group of eyes include submacular surgery, translocation surgery, steroid injection and transpupillary thermotherapy. The published results for submacular surgery include only 1 patient each with PIC[15]and serpiginous choroiditis[16] in a series of submacular surgery. There is limited information regarding macular translocation for OHS.[17] Only OHS consistently shows benefit from submacular surgery[15,16] as compared to the natural history for subfoveal OHS.[18,19] PDT with verteporfin appears to be a reasonable, less invasive, initial treatment option that may stabilise or improve visual acuity for eyes with non-AMD subfoveal CNV. Sickenberg et al[4] first reported a favourable outcome [mean increase was 2.6 (+/- 3.0) lines of visual acuity] of photodynamic therapy using verteporfin drug in 13 patients with diagnoses other than AMD [myopia (10), angioid streaks (1), OHS (1) and idiopathic CNV (1)]. Since then, there have been published reports of the use of verteporfin PDT for treatment of eyes with subfoveal CNV secondary to histoplasmosis,[5] multifocal choroiditis,[6] juxtafoveal telangiectasia,[7] IPCV,[8] idiopathic[9,10] angioid streaks,[11,12] rubella[13] and Sorsby's macular dystrophy[14] CNV. Treatments have resulted in stable or improved visual acuities without complications for most of the diagnoses.

Saperstein et al[5] reported the results of a prospective, open label, 3-centre case series of OHS eyes treated with verteporfin for ocular histoplasmosis. Initial visual acuity Snellen equivalents ranged from 20/40 to 20/200. Median visual acuity improved by 7 or more letters from baseline Early Treatment of Diabetic Retinopathy Study (ETDRS) visual acuity at 1 year in 56% of patients. Overall, 84% were stable or improved at 1 year following treatment. Our patient had worse initial visual acuity than those included in the study.

Most recently, Rogers et al[10] have reported a beneficial effect for the use of PDT with verteporfin for eyes with idiopathic (10), PIC (5) and multifocal choroiditis (3), multifocal choroiditis (MFC) or PIC (1). In our series, the PIC eyes did have a good initial response to PDT. One eye with PIC was lost to follow-up for a few months and then refused more PDT; that patient may have had a better final

visual acuity outcome if additional treatment had been performed.

In our series, we noted that overall visual acuity was within 1 line of initial visual acuity or improved in 60% of eyes at 1 year after treatment. Using the chi-square test for binomial proportions given an expected proportion improving 3 or more lines of visual acuity of 8% (high estimate), the results seen in this series appear significant. As has been shown in other studies, we found that the mean number of treatments decreased over time.[1-3,5]

Although there appears to be an initial response in serpiginous eyes, the ultimate result is limited compared to PIC and OHS. Even though both eyes with serpiginous choroiditis showed an eventual response to PDT (with closure of the CNV), 1 serpiginous eye developed significant subfoveal atrophy and decreased vision on follow-up. However, since the natural history of subfoveal CNV due to serpiginous choroiditis and PIC is poor, it is reasonable to try PDT. At least transient visual acuity improvement can be offered to the patient.

Due to the limited number of patients with subfoveal CNV secondary to serpiginous choroiditis and PIC, it is unlikely that a significant number of patients would ever be recruited for a randomised clinical trial. Based on these limited data, it appears that PDT may be a useful initial option for stabilisation of visual acuity in eyes with chorioretinal disease and CNV. Patients should be informed that visual acuity improvement as a final outcome is not likely.

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