·Clinical Research·

Comparison of outcomes between overlapping-spot and single-spot photodynamic therapy for circumscribed choroidal hemangioma

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Abstract

• AIM: To compare the efficacy and safety of photodynamic therapy (PDT) with overlapping multiple spots and single spot for treating circumscribed choroidal hemangioma.

• METHODS: Twenty-two patients (22 eyes) with symptomatic circumscribed choroidal hemangioma received PDT treatment. Fourteen patients received overlapping spots (two to three spots) PDT, whereas eight patients received single-spot PDT. Laser was used at 50J/cm² for 83s in the overlapping-spot group and 50J/cm² for 166s in the single-spot group. Clinical examination, funduscopy, fluorescein angiography, and ultrasonography were performed at baseline and after treatment.

• RESULTS: The mean follow-up time was 28.5±8.0 months in the overlapping-spot group and 27.0±5.0 months in the single-spot group. Nine patients (64.2%) had their vision improved over two lines on the Snellen chart, and five patients showed stable visual acuity in the overlapping-spot group. The mean thickness of tumor decreased from 2.7±0.8mm to 1.2±0.9mm, and the mean greatest tumor linear dimension decreased from 7.4±1.5mm to 4.5±3.5mm after treatment. In the single-spot group, two patients (25%) had their vision improved over two lines on the Snellen chart, and six patients had unchanged stable vision. The mean tumor thickness in this group decreased from 2.5±0.7mm to 1.4±1.0mm, and the mean greatest tumor linear dimension decreased from 7.2±1.3mm to 4.7±3.6mm. No significant differences in visual improvement and tumor regression were found between the two groups.

• CONCLUSION: Overlapping-spot PDT under appropriate treatment parameters and strategies is as effective and safe as single-spot PDT for treating symptomatic circumscribed choroidal hemangioma. Improved or stabilized visual acuity was achieved as a result of tumor regression.

• **KEYWORDS:** photodynamic therapy; circumscribed choroidal hemangioma; spot pattern

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INTRODUCTION

Circumscribed choroidal hemangioma is a benign choroidal vascular tumor caused by congenital vascular malformation. This choroidal hemangioma induces vision loss when it is located in the macula or it leaks fluid, which causes retinal detachment or cystic changes in the retina[1-4]. A number of technical approaches are available for the treatment of choroidal hemangioma, including laser photocoagulation, transpupillary thermotherapy, ruthenium plaque therapy, external beam irradiation, and proton-beam irradiation [5-9]. Although these approaches are effective for extramacular lesions, their use in the treatment of macular lesions is problematic because irreversible foveal damage often occurs after treatment[9].

Recently, several studies have reported that photodynamic therapy (PDT) is effective and safe for circumscribed choroidal hemangioma[10-15]. Isolated single or multiple spots, as well as multiple partially overlapping-spot pattern, have been used in these studies. Overlapping-spot pattern is usually avoided because it is believed to induce choroidal atrophy caused by the intensive treatment of the overlapping spots [16-18]. However, no study has compared the outcomes between these two spot patterns. Thus, we compared the visual and anatomic outcomes of overlapping-spot PDT and single-spot PDT to evaluate their efficacy and safety for the treatment of symptomatic circumscribed choroidal hemangioma.

SUBJECTS AND METHEODS

Subjects The data used for this retrospective study were from a series of patients who underwent PDT for

circumscribed macular or peripapillary choroidal hemangioma at the Eye Center, the Second Affiliated Hospital of Zhejiang University School of Medicine. A total of 22 patients (22 eyes) diagnosed with macular or circumscribed choroidal hemangioma between September 2006 and September 2010 were included. Diagnosis of circumscribed choroidal hemangioma was conducted through clinical examination, fluorescein angiography, and B-scan ultrasonography. Fourteen patients received overlapping-spot PDT with two to three partially overlapping spots between September 2006 and August 2008. Eight patients received single-spot PDT between September 2008 and September 2010. None of the patients in the study received prior treatment for choroidal hemangioma. Informed consent was obtained from all of the patients in accordance with the Zhejiang Institutional Review Board approval.

Photodynamic Therapy Parameters and Strategies PDT was performed using a laser (Activis, Quantel Medical, Clermont-Ferrand, France), which emits light at 689nm, for photosensitization. Verteporfin (Visudyne, Novartis Ophthalmics AG, Basel, Switzerland) was administered at 6mg/m^2 body surface area. Verteporfin infusion was performed over a 10min period under the control of an injection pump (Syringe Pump SP6000, Arcomed AG, Regensdorf, Switzerland) at 3mL/min. Light exposure was commenced 15min after the start of intravenous infusion, according to the standard PDT protocols.

In the overlapping-spot group, two or three partially overlapped spots (, , and) were applied according to the size and shape of the choroidal hemangioma as indicated on fluorescein angiography; the diameter of the treatment spot was 3.0mm to 5.0mm. The overlapping spots were treated under 50J/cm^2 laser and 83s exposure time at the most prominent part of the tumor. By contrast, 50J/cm^2 laser for 166s was used for the single-spot group.

Evaluation and Follow-ups Assessment of the patients included visual acuity test, dilated stereoscopic evaluation of the fundus with a 120-diopter lens, color photography with a 45-degree field, fluorescein angiography, and B-scan ultrasonography. The occurrence of ocular or systemic adverse reaction during or after the treatment was also observed to evaluate the safety of the treatment. All patients were examined at baseline and then at one and three months post treatment, with subsequent follow-ups every three to six months.

Statistical Analysis Statistical analysis was performed using SPSS software for Windows, Version 16.0 (SPSS Inc., Chicago, Illinois, USA). Changes in the best corrected visual acuity (BCVA) and thickness as well as the greatest linear dimension of choroidal hemangioma were analyzed and compared using Fisher's exact probabilities in a 2×2 table. P<0.05 was considered statistically significant.

Table 1 Patients' characteristics

Characteristic	Overlapping-spot PDT	Non-overlapping-spot PDT
Patients (*n*)	14	8
Eyes (*n*)	14	8
Sex (M/F)	9/5	6/2
Mean age (*a*)	38±5.0	40±6.2
Mean follow-up time (months)	28.5±8.0	27.0±5.0

RESULTS

Twenty-two patients (15 males and 7 females) aged 33 years to 52 years were included in this study. Presenting symptoms included blurred vision and metamorphopsia for 3 to 24 months prior to the clinic visit. The mean follow-up time was 28.5±8.0 months (15 months to 38 months) in the overlapping-spot group and 27.0±5.0 months (17 months to 34 months) in the single-spot group. The demographics of the patients/eyes in the study are reported in Table 1.

Visual Outcomes The mean decimal BCVA of the overlapping-spot group was 0.08±1.00 (CF-0.4) at pre-treatment, which increased to 0.33±0.38 (CF-1.0) at the end of the follow-up. A total of 9 out of the 14 patients (64.3%) had improved BCVA, which was greater than two lines testing on the Snellen chart. Among these cases, a male patient aged 50 years showed a visual recovery from decimal BCVA 0.15 before treatment to 0.6 at three months post-treatment and improved to 1.0 at 16 months post-treatment (Figure 1). Another case showed visual recovery from 0.04 to 0.15 at one month post-treatment and 0.6 at five months post-treatment. The remaining five patients had stable BCVA; macular degeneration was observed in four of the five cases.

In the single-spot group, the mean BCVA increased from 0.09±0.12 (0.02 to 0.5) to 0.29±0.34 (0.04 to 1.0). Two patients (25.0%) had improved vision of over two lines testing on the Snellen chart. The remaining 6 cases kept stable visual acuity. The difference in the changes in BCVA between the two groups was not statistically significant according to the Fisher's exact probabilities in a 2×2 table (P=0.183).

Anatomic Outcomes In the overlapping-spot group, the lesions of 9 cases located in the temporal retina involving the macula, and the tumors of the other 5 cases located in the nasal retina. In the single-spot group, the lesions of 6 cases located in the temporal retina involving the macula, and the lesions of the other 2 cases located in the nasal retina adjacent to the optic disc. All of the patients had evidence of exudative retinal detachment at pretreatment, and some patients had associated cystoid macular edema and macular pigment alterations. The abnormal, large tumor vessels were visualized in the early phase on fluorescein angiography, while diffuse and intense hyperfluorescence in the late phase of each case. The macula was partially or completely

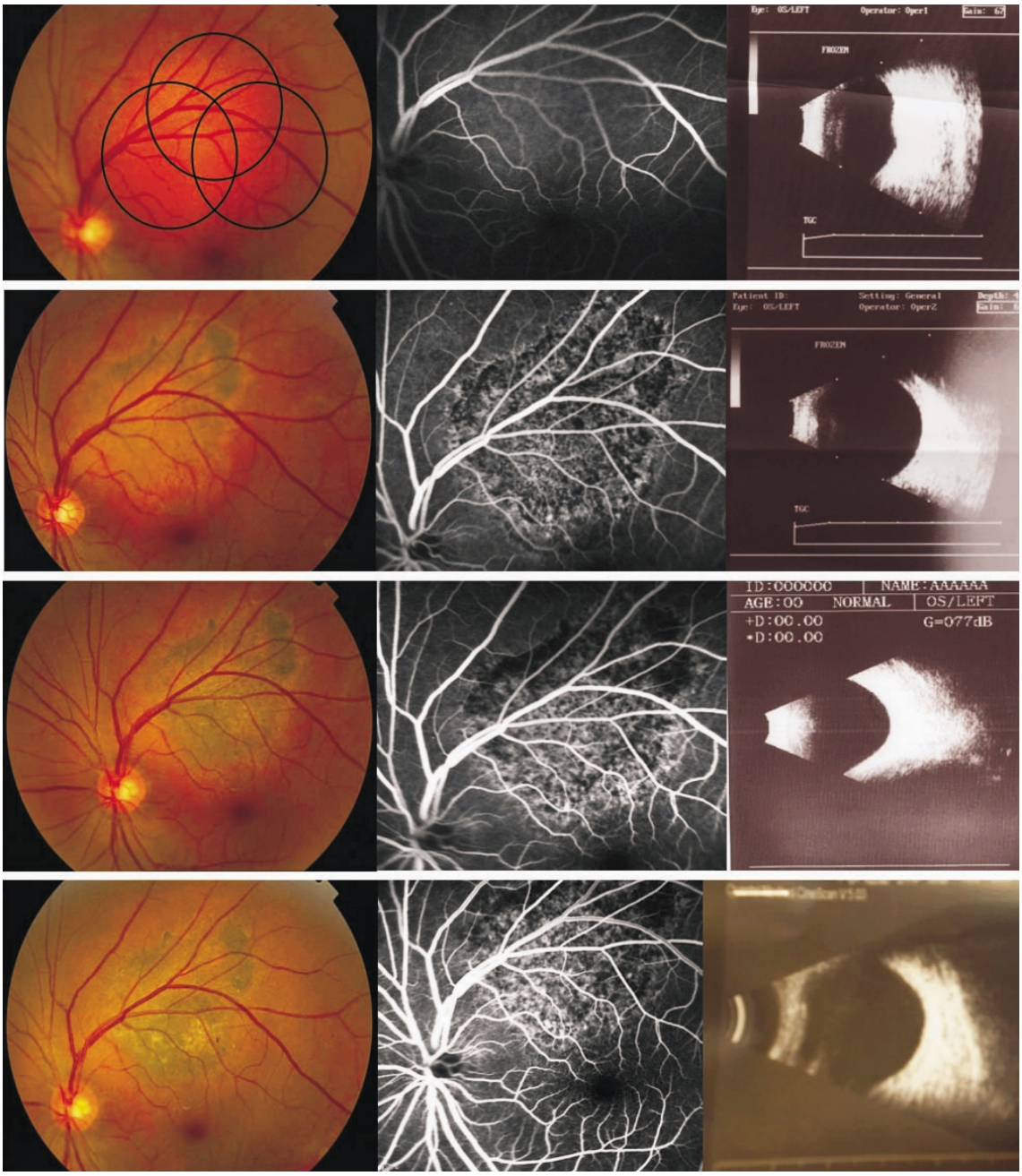

Figure 1 Images from the left eye of a 50-year-old man with macular circumscribed choroidal hemangioma who received the overlapping-spot PDT The top row images show the clinical features of the lesion at baseline. (Top left) A color fundus photograph illustrates the extent of the choroidal hemangioma with three 5mm spots with 2mm partial overlap was applied. (Top middle) Fluorescein angiography illustrates an extensive vascular leakage. (Top right) B-scan ultrasonography demonstrates that the tumor is 2.0mm thick and 7.6mm in the greatest linear dimension. The images in line 2 illustrate the clinical manifestations of the case two months after the overlapping-spot PDT (parameters: 50J/cm^2 and 83s). Color fundus photography (line 2, left) shows disturbances of the retinal pigment epithelium. Fluorescein angiography (line 2, middle) illustrates partial resolution of dye leakage. B-scan ultrasonography (line 2, right) demonstrates that the tumor is undetectable. The images in lines 3 and 4 illustrate the clinical manifestations of the case 16 months and 38 months after treatment, respectively. Color fundus photography images in lines 3 and 4 (left) show tumor regression and disturbances of the retinal pigment epithelium. Fluorescein angiography (line 3 and 4, middle) illustrates vascular network shrinkage and disappearance of dye leakage. B-scan ultrasonography (line 3 and 4, right) demonstrates that the tumor is undetectable.

involved; some cases even demonstrated cystoid edema. After the treatment, the tumor showed shrinkage with disturbances of the retinal pigment epithelium. No obvious retinal detachment and choroidal atrophy was observed through ophthalmoscopy in all of the cases in both groups. Fluorescein angiography demonstrated the abnormal tumor vascular network shrinkage with disappeared or reduced fluorescence leakage, macular edema, and exudative detachment.

In the overlapping-spot PDT group, B-scan ultrasonography

showed that the mean thickness of tumor decreased from 2.7±0.8mm (1.4 to 3.8mm) to 1.2±0.9mm (0 to 3.0mm) and the mean greatest linear dimension decreased from 7.4 ± 1.5mm (5.2 to 9.9mm) to 4.5 ±3.5mm (0 to 8.6mm) at post-treatment. At the final follow-up, the tumor was undetectable in four cases (25.9%) and the lesion of the other 10 cases all showed shrinkage. B-scan ultrasonography also demonstrated large reduction in subretinal fluid with complete retinal reattachment in six cases (42.9%).

In the single-spot PDT group, the mean thickness of the tumor before the treatment was 2.5±0.7mm (1.3 to 3.5mm) and decreased to 1.4±1.0mm (0 to 2.8mm) after treatment. The mean greatest linear dimension decreased from 7.2 ± 1.3mm (5.0 to 9.4mm) to 4.5±3.5mm (0 to 8.8mm). Complete regression of tumor was observed in one case (12.5%), and two patients (25.0%) showed retinal reattachment. No significant difference in tumor regression was observed between the two groups (P=0.613).

DISCUSSION

Madreperla *et al* [19] and Robertson [20] reported that PDT induces tumor shrinkage, sub-retinal fluid resolution, and visual improvement among patients with circumscribed choroidal hemangioma. Several studies have reported that PDT is not only effective but also safe to use in the treatment of circumscribed choroidal hemangioma located in the macula[10-15]. In our study, 22 patients (22 eyes) with macular or peripapillary symptomatic circumscribed choroidal hemangioma received PDT. Fourteen patients received overlapping-spot PDT, whereas eight patients received single-spot PDT. All of the patients had improved or stable vision function after the treatment, and no significant difference in visual change was found between the two groups. In the overlapping-spot group, nine patients (64.3%) had their vision improved over two lines on the Snellen chart and the other five cases had unchanged stable BCVA at the end of the follow-ups. In the single-spot group, two patients (25%) showed improved vision of over two lines on the Snellen chart and six patients showed stable BCVA remained. Additionally, tumor regression was observed in all of the cases in both groups evidenced by the decrease in the thickness and greatest linear dimension of tumor, shrinkage of abnormal tumor vascular network, as well as disappearance or obvious reduction of fluorescence leakage and macular edema. Since the limitation of a retrospective study, we didn't have optical coherence tomography that time to document the anatomical changes before and after PDT. However, B-scan ultrasonography showed the anatomical outcomes in both groups. In the single-spot group, one case (12.5%) showed complete regression of tumor and two cases (25.0%) showed retinal reattachment. In the overlapping-spot group, tumor was undetectable in four cases (25.9%) and complete retinal reattachment was observed in six cases (42.9%). The differences in the changes of the mean thickness and mean greatest linear dimension between two groups were also not significant (P>0.05). Our study confirmed that PDT, with overlapping-spot or single-spot pattern, is effective for the treatment of symptomatic circumscribed choroidal hemangioma.

In our study, no ocular or systemic adverse reaction was observed during or after the treatment. Given that PDT induces selective destruction of choroidal vascular network of the tumor through photochemical reactions without damage to normal retinal vessels and never fibers, PDT is now regarded as the primary treatment for circumscribed choroidal hemangioma [21]. The treatment parameters and strategies vary in the previous studies. Laser parameters of 50J/cm^2 to 100J/cm^2 with exposure time of 83s to 186s, and single spot or multiple spots with overlapping or non-overlapping patterns were all used in these studies[11-15]. Overlapping spots were avoided in some studies to prevent the potential risk of choroidal atrophy [16-18]. In fact, overlapping-spot PDT using conventional energy dose in our study induced no complications. Given that the center of a tumor is much thicker than its peripheral part and the maximum diameter of tumor often exceeds the maximum treatment spot diameter of the laser equipment, we also performed overlapping-spot PDT in the present study.

In addition, our study involves only Chinese patients, a patient population with relatively high pigmentation, which often reacts more strongly to laser treatment. To address this issue, specialized treatment parameter and strategy were employed for the overlapping-spot PDT. Laser was used at 50J/cm^2 for 83s and the partially overlapping part was located to the most prominent area of the tumor. Our results demonstrated that no obvious retinal and choroidal damage occurred in the overlapping area compared with the non-overlapping area. The overlapping part induced more intensive treatment to the thickest part of the tumor, which may ensure the efficacy of the treatment.

In conclusion, the overlapping-spot PDT with appropriate treatment parameters and strategies is as effective and safe as the single-spot PDT in treating symptomatic circumscribed choroidal hemangioma. Overlapping-spot PDT is specifically suitable for large-sized tumors. Treatment with overlapping-spot PDT resulted in tumor regression, subretinal fluid elimination, and improvement or stabilization of visual acuity.

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