Case Report

COMBINATION OF INTRAVITREAL ANTI VASCULAR ENDOTHELIAL GROWTH FACTOR AND FULL FLUENCE VERTEPORFIN PHOTODYNAMIC THERAPY IN THE MANAGEMENT OF CHOROIDAL HAEMANGIOMA WITH EXUDATIVE RETINAL DETACHMENT: A CASE REPORT

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ABSTRACT

This case report is to review the successful treatment outcome of intravitreal anti vascular endothelial growth factor (anti VEGF) and photodynamic therapy (PDT) with verteporfin for a case of circumscribed choroidal haemangioma associated with exudative retinal detachment (RD). A 48-year-old man presented with a 2-weeks history of decreased right vision. On examination, right visual acuity was 3/60 with evidence of right circumscribed choroidal haemangioma complicated with exudative retinal detachment. He underwent two sessions of verteporfin PDT and twice intravitreal injection of anti VEGF, Ranibizumab. There was resolution of subretinal fluid over a period of 18 months and his visual acuity stabilized at 6/9. Hence, intravitreal anti VEGF and verteporfin PDT are safe and effective therapeutic options for circumscribed choroidal haemangioma associated with exudative retinal detachment (RD).

INTRODUCTION

Choroidal haemangioma is a rare benign vascular tumor with a peak incidence in middle-aged adults although it may be present since birth [1]. Most patients are asymptomatic depending on the location of the tumor. The visual symptoms commonly arise as a result of subretinal fluid, cystoid macular edema, retinal pigment epithelium changes, sub-retinal fibrosis and retinoschisis caused by the tumor. Visual symptoms may include progressive worsening of vision, metamorphopsia, floaters, and even visual field defects.

Choroidal haemangioma, a benign vascular hamartoma can be divided into circumscribed or diffuse type [2]. The circumscribed choroidal hemangioma is an isolated, unilateral and is not associated with systemic associations. On the contrary, the diffuse type is frequently associated with phakomatoses like Sturge-Weber syndrome [1,3]. Diagnosis is made clinically based on the fundus characteristics of the tumor. It is an orange-reddish colored mass with indistinct margins that blend with the surrounding choroidal tissue. It is usually solitary and located at the posterior pole. Most cases are unilateral although bilateral cases have been reported. Its thickness is usually 6 mm or less with some areas of increased pigmentation which can resemble a choroidal melanoma. The base of the tumor can occasionally be pigmented, as a result of compressed choroid.

Ancillary testing such as B scan ultrasound, fundus autofluorescence (FAF), fundus fluorescein angiography (FFA), indocyanine green angiography (ICG), and optical coherence tomography (OCT) are helpful modalities in establishing the diagnosis. Subsequently, once the diagnosis has been made, referral to a medical retinal specialist is warranted.

Various treatment modalities have been advocated. The options available are intravitreal anti-VEGF injections, laser photocoagulation, transpupillary thermotherapy (TTT), photodynamic therapy (PDT), plaque brachytherapy, external beam radiotherapy, proton beam therapy, and stereotactic radiosurgery. Treatment is only indicated in sight threatening cases such as the tumor location at the posterior pole or sub retinal or intra retinal fluid extending to macula. The aim of the treatment is to improve and preserve the visual acuity.

In this article, we report a successful outcome of intravitreal anti VEGF and verteporfin photodynamic

therapy (PDT) in the treatment of the circumscribed choroidal haemangioma associated with exudative retinal detachment.

CASE PRESENTATION

A 48-year-old man presented with complaining of decreased visual acuity over his right eye for the past 2 weeks. He was referred to the Medical Retina Unit, Ophthalmology Department of Shah Alam Hospital to seek a second opinion for choroidal lesion in the right eye. His general and systemic examination was unremarkable. There was no evidence of a cutaneous hemangioma elsewhere noted.

On ocular examination, his best corrected visual acuity 6/6 and 6/9 in the right and left eye respectively. Both anterior segments were unremarkable. The fundus of the right eye revealed a reddish-orange, dome shaped choroidal lesion, measuring about 3-disc diameter, located nasal to optic disc (Figure 1). Minimal pigmentary changes were noted overlying the tumor, with surrounding sub retinal fluid and neurosensory serous retinal detachment, extending from the tumor to the macular area. The left eye fundus was otherwise normal.

In order to exclude the other differential diagnosis such as choroidal metastasis, further blood investigations were carried out. Renal profile (RP), liver function test (LFT), thyroid function tests (TFT) and serologic tests for tumor markers (CA 19-9, CEA, PSA) were normal. Ultrasound liver was unremarkable and Magnetic Resonance Imaging (MRI) Brain and Orbit was performed and confirmed that the mass was confined within the posterior segment arising from the choroid of the right eye.

On further ocular investigation, optical coherence tomography (OCT) of macula demonstrated presence of sub retinal and intra retinal fluid (Figure 2). A fundus autofluorescence (FAF)

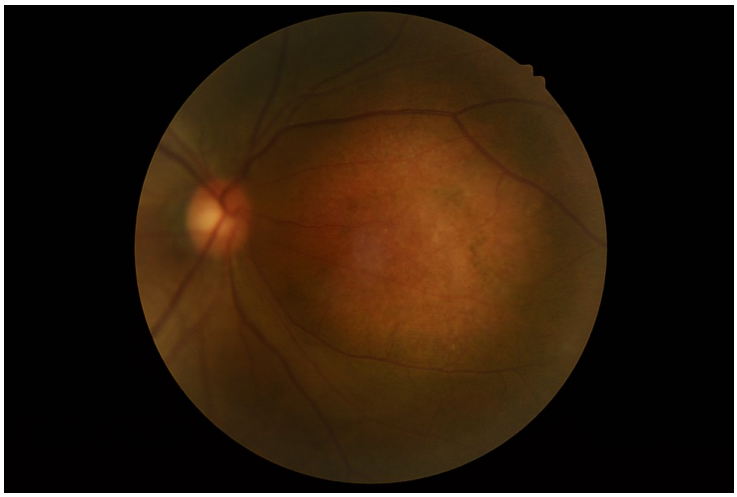

Figure 1: Right eye: choroidal mass nasally with exudative retinal detachment

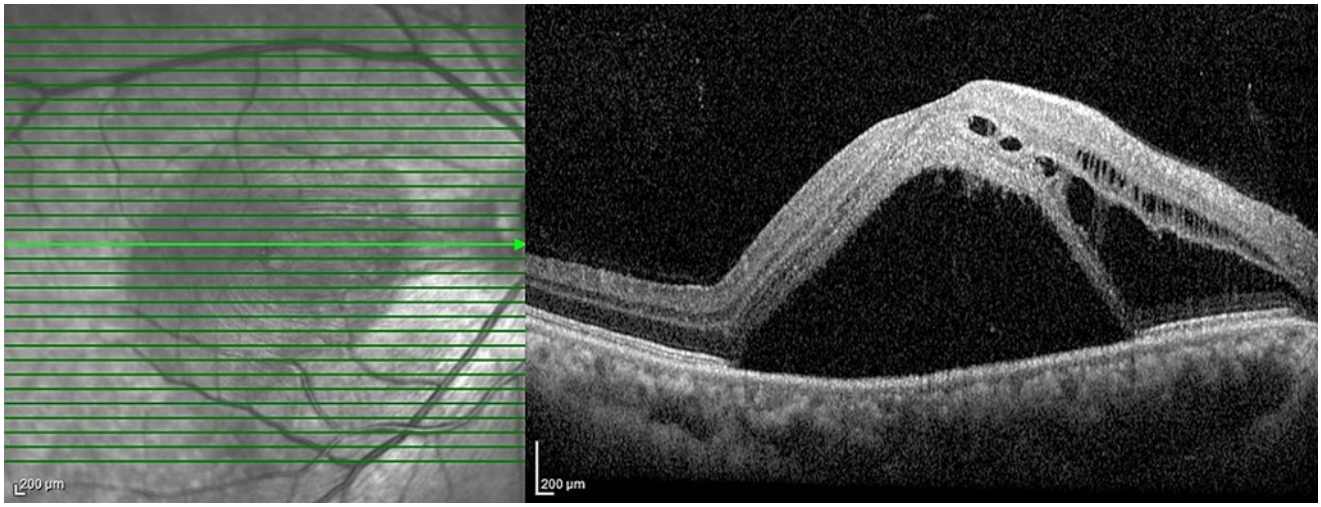

Figure 2: Right macula OCT of the right eye showing subretinal and intraretinal fluid involving fovea.

showed a patchy area of hyper autofluorescence overlying the lesion (Figure 3). B-scan ultrasonography showed a solid dome-shaped choroidal lesion with height of 4.32 mm and high internal reflectivity (Figure 4). He was diagnosed as right eye circumscribed choroidal haemangioma with exudative retinal detachment.

Management options were discussed with the patient. He was given intravitreal anti VEGF *Ranibizumab* and subsequently full fluence verteporfin photodynamic therapy (PDT). At his follow-up visit 6 weeks after verteporfin PDT, his visual acuity improved to 6/9 OD. There was resolution of sub retinal and intra retinal fluid at the fovea as well as serous detachment of the sensory retina (Figure 5) and as evidenced by B-scan ultrasonography with the reduction of the tumor height to 2.53mm (Figure 6).

Unfortunately, patient presented 8 months later with deterioration of his right eye vision and his visual acuity was 2/60 OD. There was presence of sub retinal and intra retinal fluid at fovea (Figure 7) with increasing height of choroidal haemangioma to 4.21 mm (Figure 8). He subsequently underwent intravitreal anti VEGF (*Ranibizumab*) prior to the second full fluence verteporfin PDT. At 6 weeks after the second verteporfin PDT, his right vision improved to 6/9 with complete resolution of sub retinal and intra retinal fluid at fovea (Figure 9) and regression of tumor height to 2.45 mm (Figure 10). He was subsequently followed up every 3 months.

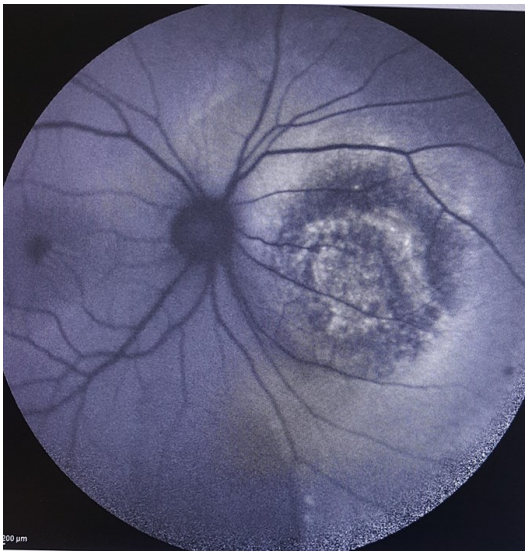

Figure 3: Right fundus: Fundus autofluorescence (FAF) of the choroidal mass showing patchy area of hyper autofluorescence.

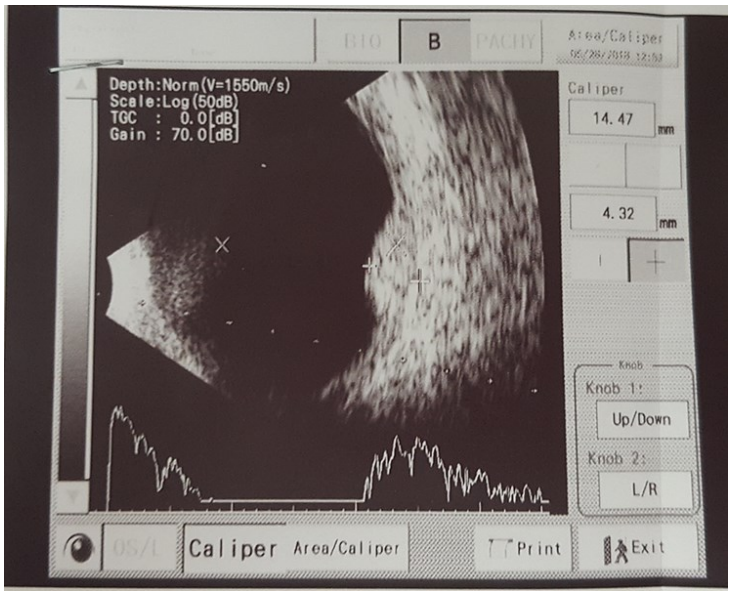

Figure 4: B scan of the right eye: dome shaped mass with high internal reflectivity

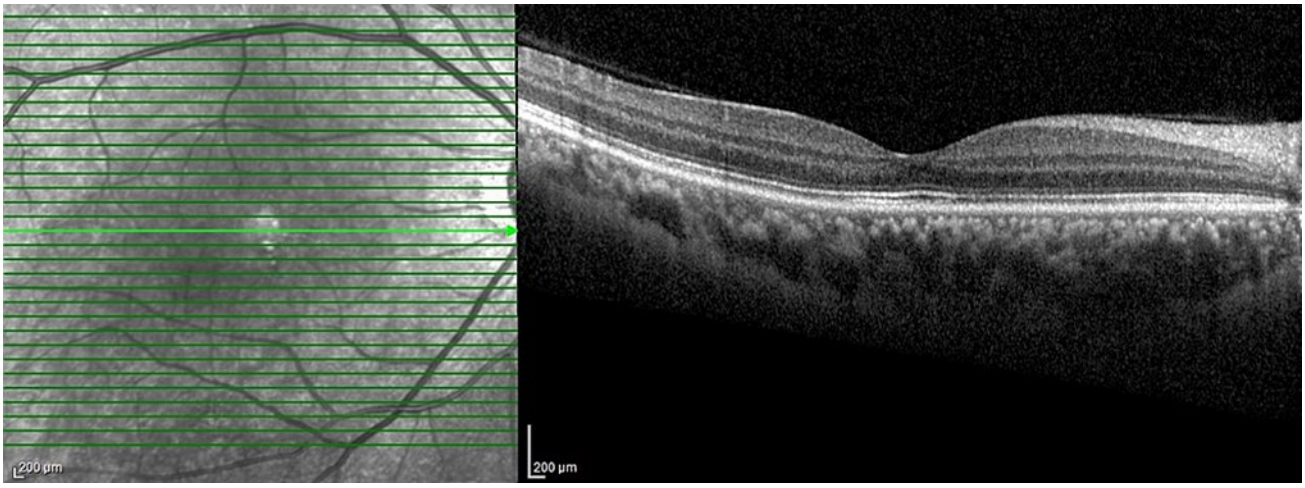

Figure 5: Macular OCT showing resolution of sub retinal and intra retinal fluid.

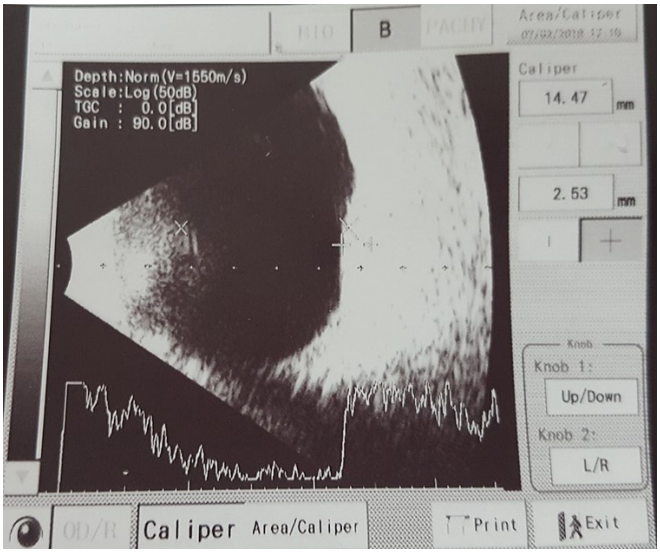

Figure 6: B-scan of the right eye: Reduction in size of the choroidal mass with and resolution of exudative retinal detachment.

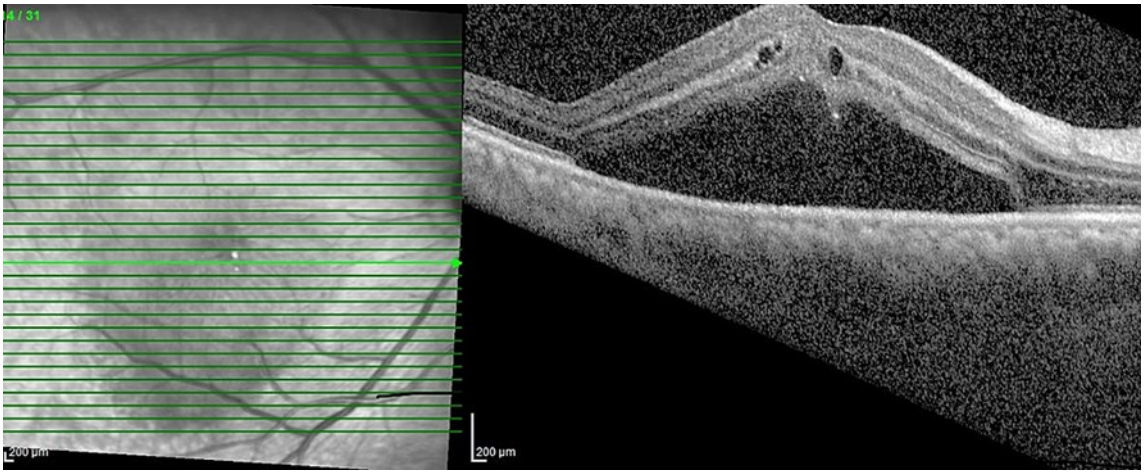

Figure 7: Macular OCT prior to the second verteporfin PDT demonstrating increased sub retinal fluid with overlying small intra retinal fluid.

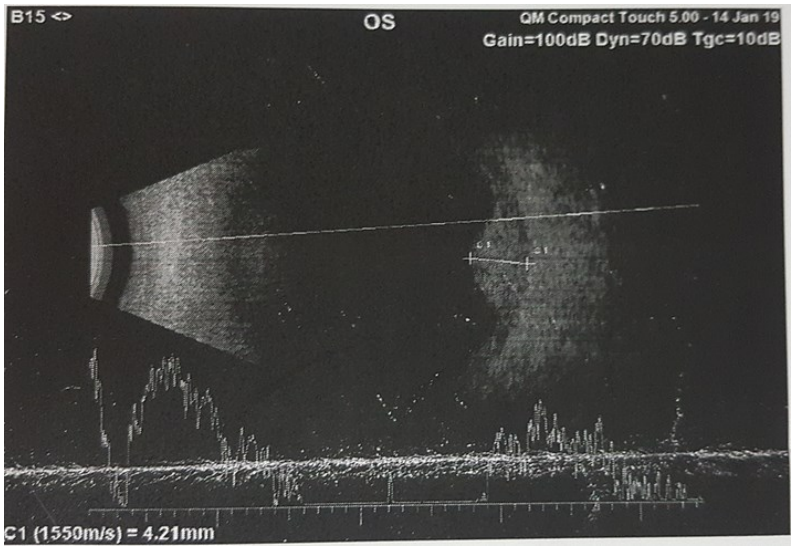

Figure 8: B-scan of the right eye prior to the second verteporfin PDT showing increased choroidal mass thickness

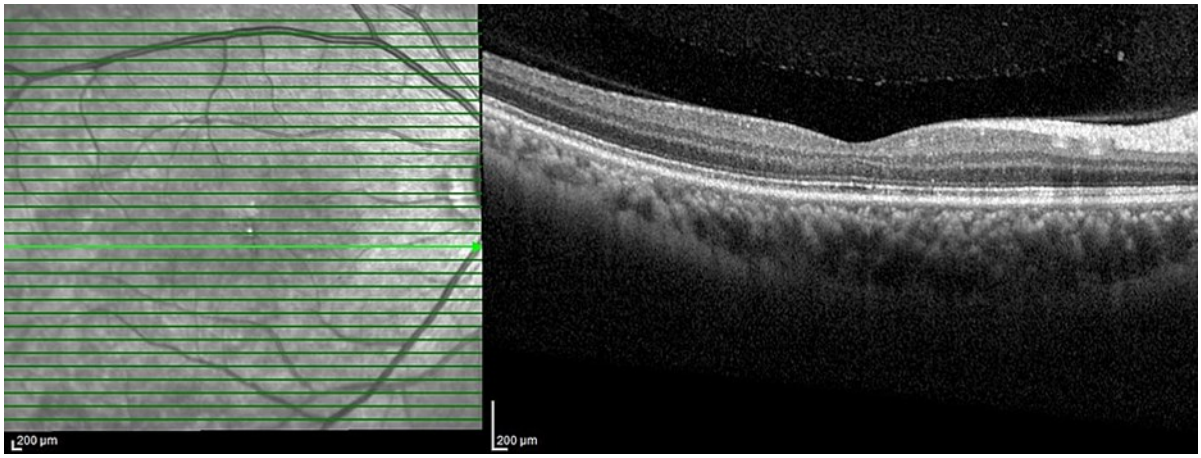

Figure 9: Macula OCT after the second verteporfin PDT showing resolution of the fluid at fovea

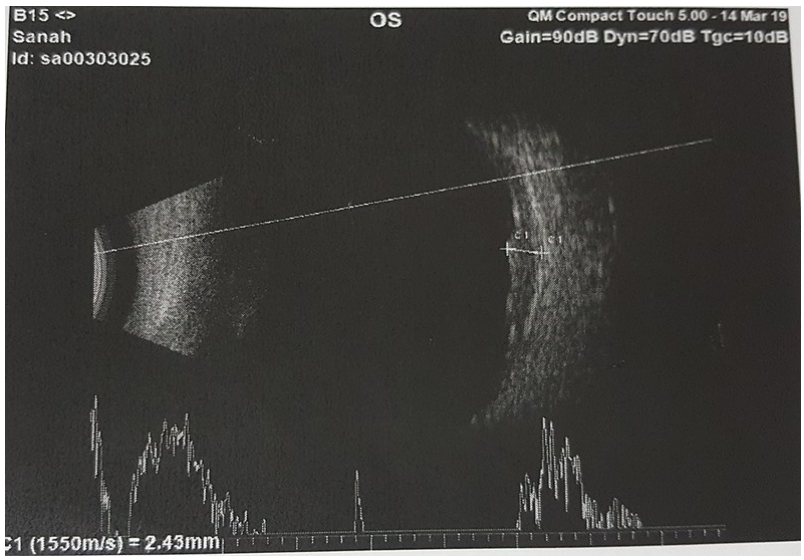

Figure 10: B-scan of the right eye after the second verteporfin PDT showing a decrease in the choroidal mass thickness.

His ocular condition was currently stable with no evidence of recurrent sub retinal fluid or exudative retinal detachment at his follow-up visit 18 months later. The recent B-scan ultrasonography showed the tumor height maintained at 2.64 mm. His vision stabilized at 6/9 OD.

DISCUSSION

Photodynamic therapy (PDT) with verteporfin (Visudyne) is an excellent treatment modality in treating various retinal and choroidal lesions such as choroidal neovascularization in age related macular degeneration, pathological myopia, presumed ocular histoplasmosis syndrome, and even in idiopathic causes cases. Photodynamic therapy selectively occlude the choroidal neovascularization and minimize the damage to the healthy neurosensory retinal layers and Bruch's membrane layer. Currently, PDT has been advocated as one of treatment options for subretinal vascularization and exudative lesion such as choroidal haemangioma [1,4]. Photodynamic therapy is proven a safe, fast and indisputably easily performed outpatient procedure which can be done under topical anaesthesia. The procedure is started with administration of intravenous verteporfin, a photochemical sensitizer. It is then followed by a targeted low power and long duration infrared laser beam application. Laser beam will activate verteporfin and free radicals formation will then occur, which subsequently leads to the closure of the leaking blood vessels and resorption of fluid [2,5].

There are two mechanism of action of PDT in causing intraocular tumor regression. First, the photochemical sensitizer is attached to low density lipoproteins in the tumor cells endothelium and subsequently destroys the tumor cells by cytotoxic activity. Second mechanism is via the promotion of intraluminal photo thrombosis in the vessels supplying the tumor. Finally, the tumor size will regress and resorption of subretinal fluid will occur [2,6].

Excellent outcomes have been reported in several studies with complete tumor regression with rapid resorption of subretinal fluid, and favorable visual outcomes. Barbazetto et al reported successful treatment of choroidal haemangioma with PDT [2]. Singh et al report revealed that verteporfin PDT is a safe modality in the choroidal hemangioma treatment as verteporfin targets a specific tumor destruction location, thus sparing the overlying healthy retina and retinal vasculature will be left unharmed [7].

The advantage of PDT is that it causes regression of the haemangioma through the photochemical effect rather than thermal effect, thus minimizing the damage to the retina and nerve fiber bundles in contrast to the other treatment modalities such as argon photocoagulation or transpupillary thermotherapy (TTT) [8]. This is a very important point to consider especially in cases of tumor abutting the optic nerve where loss of optic nerve fibers can result in considerable loss of peripheral field.

The successful outcome with complete resolution of subretinal fluid and regression of choroidal hemangioma size in our case suggest that verteporfin PDT may be beneficial and as an option to consider in the treatment of choroidal haemangioma along with the other treatment modalities available. Several published reports also revealed that PDT with verteporfin can be used as a therapeutic option for exudative retinal detachment associated with circumscribed choroidal haemangioma with good visual outcome [2,9].

Barbazetto et al suggested verteporfin PDT was a favorable primary treatment for circumscribed choroidal haemangioma complicated by exudative detachment involving macula. Study by Jurklies et al showed that verteporfin PDT was safe and efficacious for the treatment of subfoveal choroidal haemangioma [9]. The verteporfin applied in both studies were using 6 mg/m2 body surface area concentration and light dose of diode laser at 100 J/cm2 of 692 nm wavelength. The mean performed treatment sessions was 2.15 (range 1-5) in Jurklies et al study meanwhile in Barbazetto et al administered 2 sessions in 2 isolated cases of circumscribed choroidal haemangioma and retreatment up to 4 sessions in a case of subfoveal choroidal haemangioma with persistent tumor height in order to achieve completely flattened tumour [2,9].

Shields et al reported that the verteporfin PDT usage in the management of choroidal haemangioma significantly resulted in a better visual outcome compared to the era before PDT treatment. The report showed that the mean patients' final visual acuity improved to 20/400 compared to 20/63 in the 458 eyes of circumscribed choroidal haemangioma. Pre-PDT era treatment included argon laser photocoagulation, transpupillary thermotherapy (TTT), plaque radiotherapy, external beam radiotherapy, enucleation and observation. They also noted the difference in size of the tumor regression in the verteporfin PDT treated patients as compared with eyes treated by other treatment modalities, as evidence by the reduced mean tumor thickness of verteporfin PDT treated patients was 2.49 mm as compared with 2.95 mm in patients treated in the pre-PDT era ($P < 0.001$) [10].

Anti-vascular endothelial growth factor (Anti VEGF) agents have been used in multiple ophthalmic pathologies. Anti VEGF has the ability to reduce vascular permeability and is thus very effective for resolution of sub retinal and intra retinal fluid. Han Kim et al reported the PDT effectiveness and safety with the synergistic response of anti VEGF with repeated PDT, and potential reduction of PDT treatments by adding anti VEGF to the treatment [11]. Sagong et al reported the reduction of subretinal fluid following the use of anti VEGF prior to PDT, and subsequently maximized the effect of PDT [12]. Furthermore, no serious side effects of verteporfin PDT were observed in our case and

other studies [2,8,9]. In comparison, other treatment modalities such as radiation therapy can cause serious side effects. Radiation therapy includes plaque brachytherapy and external beam radiotherapy can result in radiation retinopathy, optic neuropathy, macula ischemia, and subretinal fibrosis. Meanwhile the other treatment option such as laser photocoagulation can result in retinal scarring and retinal pigmented epithelium (RPE) atrophy which may jeopardize the vision due to the side effect of scotoma. Laser photocoagulation is also not a suitable treatment modality for sub foveal lesions. Some reports revealed that the recurrence of sub- retinal fluid was common in this laser group, and up to 40% of patients later required additional treatment [13].

Khetan et al reported the similar visual outcomes between PDT and TTT, although PDT was more favorable in subfoveal lesions due to its safety profile. However, patients in the TTT group required more treatment sessions in contrast to PDT although TTT was a cheaper treatment option compared to these two [8].

CONCLUSION

Intravitreal anti VEGF and verteporfin PDT are effective treatment options to consider while treating sight threatening choroidal haemangioma associated with exudative retinal detachment threatening or involving macula. Intravitreal anti VEGF prior to verteporfin PDT is beneficial to reduce the exudation caused by the tumor and will enhance the efficacy of verteporfin PDT. Photodynamic dynamic treatment is useful in the regression of tumor size, even complete resolution of tumor has been observed in few studies. Tumor recurrence is also rare after verteporfin PDT together with intravitreal anti VEGF. However, this patient will still require lifelong follow up for possible tumor recurrences in the future.

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