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Acute visual loss and chorioretinal infarction after photodynamic therapy combined with intravitreal triamcinolone

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PURPOSE. *To report acute visual loss associated with dynamic vascular changes after photodynamic therapy (PDT) combined with intravitreal triamcinolone (IVTA) for the treatment of occult choroidal neovascularization (CNV).*

METHODS. *An 86-year-old woman complained of visual loss in her left eye. Angiographic examination showed a serous pigment epithelium detachment complicated by CNV. She underwent combined treatment with IVTA (4 mg) followed by standard verteporfin PDT administered after a 5-day interval.*

RESULTS. *The patient developed vision loss 1 day after PDT. Ophthalmoscopic examination disclosed an acute serous neurosensory retinal detachment. Fluorescein angiography showed a large area of early hypofluorescence in correspondence to and extending beyond the photodynamic spot. Neurosensory retinal vessels involvement with dilation of the retinal arterioles and capillary nonperfusion were also revealed. Indocyanine green angiography showed choroidal infarction within the collateral choroid included in the area of light exposure, with associated nonperfusion of medium and large choroidal vessels being revealed. Five days after PDT, spontaneous severe bleeding with breakthrough into the vitreous occurred, in addition to an RPE tear.*

CONCLUSIONS. *Acute loss of vision associated with vascular changes in retinal and choroidal circulation represents an uncommon but serious complication following combined PDT and IVTA. These risks should be carefully considered in combination therapies. (Eur J Ophthalmol 2008; 18: 652-5)*

KEY WORDS. *Age-related macular degeneration, Choroidal neovascularization, Photodynamic therapy, Triamcinolone*

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INTRODUCTION

Although photodynamic therapy (PDT) improves the prognosis of exudative age-related macular degeneration (AMD), its effectiveness differs among different subtypes of choroidal neovascularization (CNV) (1). In particular, in cases where a serous detachment of the retinal pigment epithelium is associated with CNV, anatomic and functional results are not favorable after PDT (1). Recently, the combination of PDT with intravitreal triamcinolone (IVTA) has been successfully used for the treatment of all types of CNV (2, 3). Several investigations in which verteporfin PDT was combined with IVTA indicate that therapy is more effective in improving visual outcomes, also reducing the rate of retreatment compared to PDT alone. However, despite the potential beneficial effects of combined treatment, the real impact on the retinal pigment epithelium (RPE), neural structures, and choroidal and retinal circulation remains unclear.

We report a case of ocular complications following PDT

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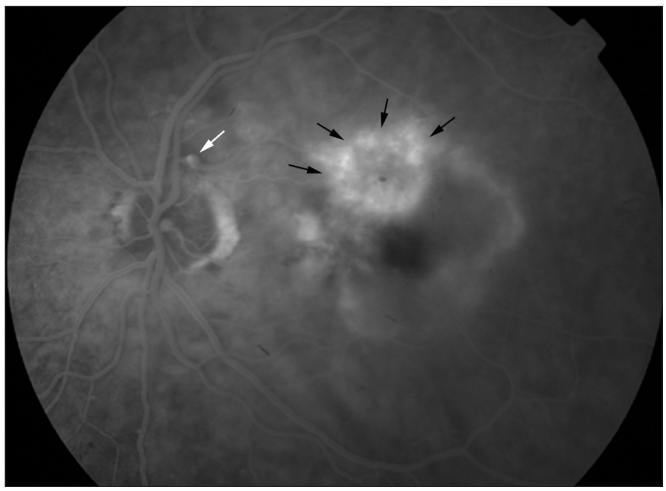


Fig. 1 - *Fluorescein angiography (FA) showing a well-circumscribed area of early hypofluorescence with progressive hyperfluorescence in the later phases, corresponding to elevation of the retinal pigmented epithelium. A notched area is shown (new choroidal vessel beneath pigmented epithelium detachment) along the superior temporal border of the lesion (black arrows). A saccular aneurysmal dilation located closer to the temporal edge of the left disk is also evident (white arrow).*

combined with IVTA for the treatment of CNV with serous pigment epithelium detachment (PED). The data were collected in conformity with national legislation in force and abide by the Helsinki Declaration.

METHODS

An 86-year-old woman presented with a 1-month history of blurred vision and metamorphopsia in her left eye. Visual acuity (VA) was 20/20 in the right eye and 20/100 in the left. Her medical history was significant for systemic hypertension. She did not take anticoagulant or antiplatelet drugs. Anterior segment evaluation and intraocular pressure were normal. Funduscopic examination disclosed a sharply circumscribed, dome-shaped detachment of the macular retinal pigmented epithelium in the left eye. Fluorescein angiography (FA) showed a serous PED and some classic CNV in the left eye (Fig. 1), both confirmed by indocyanine green angiography (ICG). FA and ICG angiographic study of the fellow eye excluded any retinal and choroidal vascular involvement. On the basis of the angiographic features and the CNV (our patient had serous RPE detachment and some classic CNV - a clear nonindication for PDT according to TAP [the neovascular component covered less than half of the lesion area]), it was proposed that the patient undergo combined therapy. Standard verteporfin PDT was performed 5 days after intravitreal injection (4 mg in 0.1 mL of saline solution) of triamcinolone (Kenalog, Bristol-Myers Squibb, New York, NY, USA).

RESULTS

One day after PDT, VA decreased to 20/400 in the left eye. Ophthalmoscopic examination revealed a serous neurosensory retinal detachment (Fig. 2A). FA revealed a large area of hypofluorescence corresponding to and partially extending over the area of the photodynamic spot during the early phases. Neurosensory retinal vessel dilation of retinal arterioles was also disclosed, together with nonperfusion of the perifoveal capillary network and chorioretinal folds, due to a contraction of the neovascular tissue (Fig. 2, B and C). Early ICG showed hypofluorescence within the collateral choroid included in the area of light exposure, due to choriocapillaris infarction, with absence of choroidal filling and complete nonperfusion of the medium and large choroidal vessels (Fig. 2D). A late-phase frame showed persistence of the relatively less central hypofluorescent area seen in the early phase, with some additional hyperfluorescent areas of staining surrounding the hypofluorescence (Fig. 2E). About 5 days after PDT, spontaneous severe bleeding occurred with breakthrough into the vitreous and an RPE tear (Fig. 3).

DISCUSSION

In our patient a severe loss of vision associated with a sudden, short-term sequence of vascular events occurred in both retinal and choroidal vasculature. After PDT, 1) endothelial damage of the retinal vessels occurred within the area of the spot with breakdown of the blood–retinal barrier and perifoveal capillary nonperfusion, and 2) complete occlusion of the choriocapillaris lumina and medium/large choroidal vessels were observed. These findings are in contrast with previous studies which documented excellent preservation of the retinal and choroidal vasculature after PDT. Schmidt-Erfurth et al (4) described complete occlusion of the choriocapillaris lumina caused by damage to the endothelial cells 1 week after PDT. In this study, histopathologic examination demonstrated the

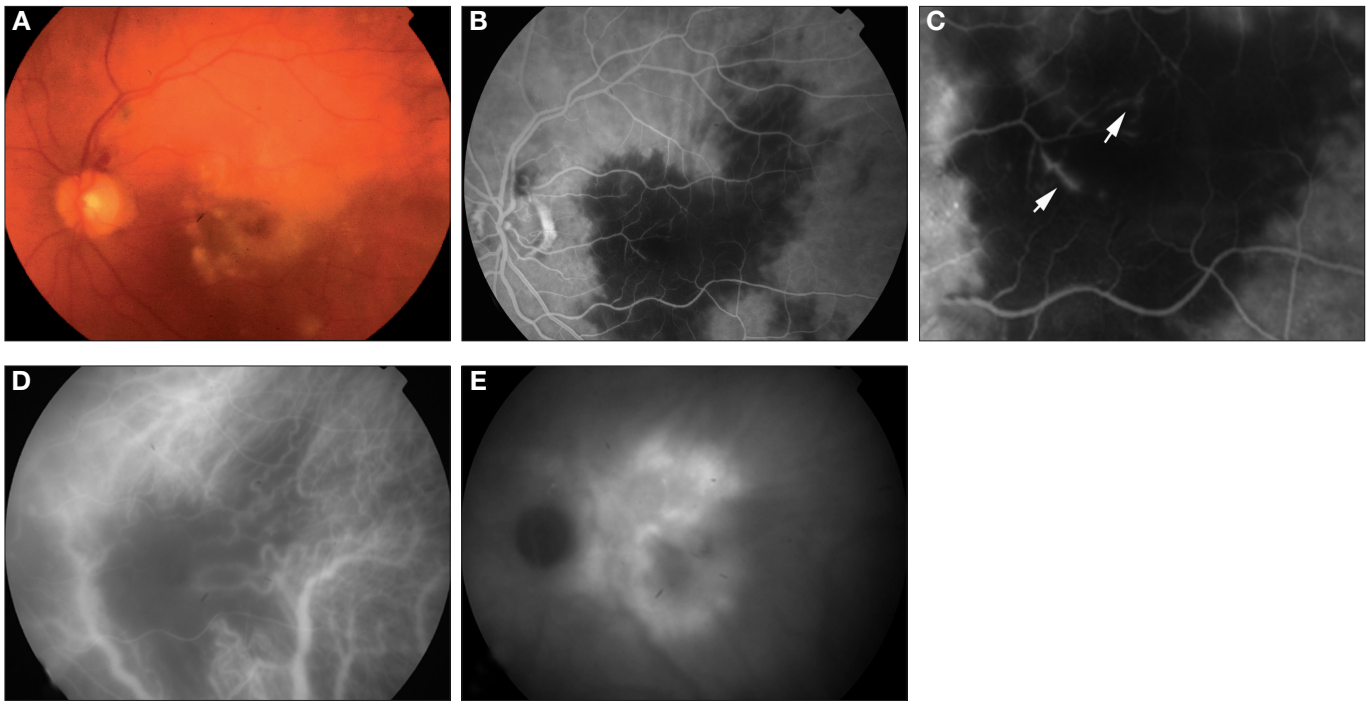
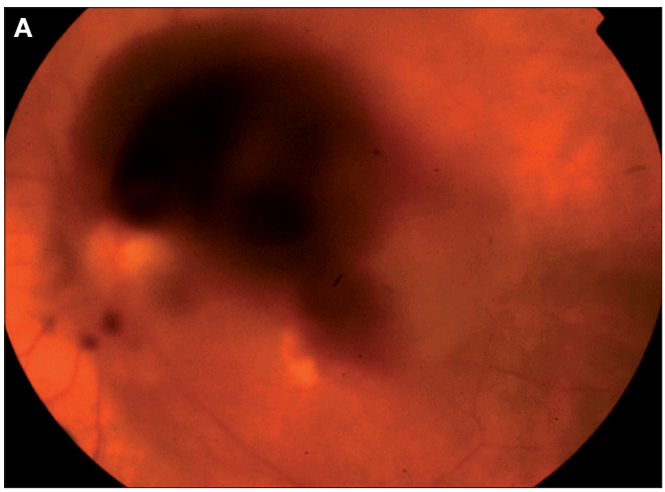


Fig. 2 - (A) *A color photograph shows an irregular whitening involving the posterior pole with serous neurosensory detachment which occurred 1 day after photodynamic therapy.* **(B)** *Fluorescein angiography (FA) shows a black spot of hypofluorescence corresponding to and also extending over the area of treatment during the early phases. Chorioretinal folds secondary to contraction of the neovascular tissue on FA are also evident.* **(C)** *FA magnification corresponding to the fovea showing dilation of the precapillary retinal arterioles with progressive fluorescein leakage (white arrows) and perifoveal capillary dropout along superior, nasal, and temporal border of the foveal avascular zone.* **(D)** *An early phase indocyanine green angiogram showing occlusion of both medium and large choroidal vessels within the area of the spot.* **(E)** *A late-phase frame showing persistence of the relatively less hypofluorescent area seen in the early phase, with some additional hyperfluorescent areas of staining surrounding the hypofluorescence.*



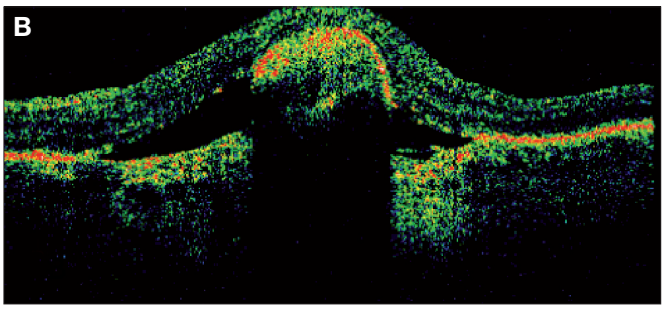


Fig. 3 - (A) *Funduscopic picture, showing a massive intraretinal and intravitreal hemorrhage 5 days after photodynamic therapy.* **(B)** *Optical coherence tomography showing a retinal pigment epithelium tear.*

larger choroidal vessels to be fully patent with intact, nondeformed endothelial cells; neural structures, photoreceptors, retinal capillaries, and the RPE also remained intact. In a recent study, Klais et al (5) also reported some choroidal infarction after therapy combining PDT and IVTA in a small number of patients, without involvement of the retinal circulation. In our case we are unable to precisely interpret and explain such retinal and choroidal involvement, but we cannot rule out that the combined treatment had a causal effect. Since we checked the accuracy of

the calculations of PDT spot size and verteporfin dosage, we excluded excessive PDT exposure as a potential cause of this phenomenon. We hypothesize that an exaggerated response to treatments could have been triggered by a combination of two possible mechanisms: first, a possible deposit of fibrin beneath the PED, and second, an enhanced photothrombotic effect of PDT induced by IVTA, resulting in increased sensitivity to the photochemical effect of PDT, with the alteration and collapse of retinal and choroidal vessels (it may also be that this eye possessed lower tolerance, and increased vascular sensitivity in both retinal and choroidal circulation secondary to combined treatment). In addition, the RPE tear in our patient occurred despite adding IVTA to PDT. RPE tear is a complication that may occur following PDT, particularly when the PDT is applied to an occult subfoveal CNV with PED. In our case, combination therapy was thought to potentially reduce the exudative/inflammatory response associated with PDT, but administration of triamcinolone within 1 week before PDT may not be sufficient.

Photodynamic therapy is a proven method for the prevention of vision loss in patients with CNV. However, there have been reported cases of ocular complications associated with the use of standard PDT (5). Recent data show that combination treatment with PDT and intraocular antiangiogenic and/or antiinflammatory therapies (e.g., triamcinolone acetonide) may be more efficacious than PDT alone (3, 6). The theoretical basis for combination therapy resides in the data documenting inflammation and VEGF release following PDT administration (4). By suppressing VEGF release or by abolishing secondary mediators involved in inflammatory signaling, it may potentially be possible to reduce the exudative/inflammatory response associated with PDT (2, 3). However, the risk of some collateral side effects due to an exaggerated response combining intraocular drugs with PDT may strongly compromise the concept of selectivity and efficacy (5). The concept of modified parameters in combination therapy should be of particular interest (7). Indeed, an increased selectivity with a decreased effect on the surrounding vasculature should be of advantage also in combination strategies. If a lower amount of light (e.g., PDT at low fluence rate) is used, the availability and concentration of oxygen and verteporfin molecules is less likely to be depleted in the photodynamic reaction. As a result, there may be a better selectivity for CNV, causing less damage to the normal choroidal vessels, and possibly to the RPE.

In conclusion, a vascular event in the retinal and choroidal circulation seems to be an uncommon but very serious complication after combined PDT with IVTA. These risks should be carefully considered in combination strategies.

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