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RESEARCH ARTICLE

A TWO-YEAR STUDY OF DIFFUSED RETINAL PIGMENT EPITHELIOPATHY TREATED WITH HALF-DOSE PHOTODYNAMIC THERAPY GUIDED BY SIMULTANEOUS ANGIOGRAPHY AND OPTICAL COHERENCE TOMOGRAPHY

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ABSTRACT

The authors are commenting on the article entitled "A two-year study of diffused retinal pigment epitheliopathy treated with half-dose photodynamic therapy guided by simultaneous angiography and optical coherence tomography" published by Liu et al. in Eye 2019;33(5):737-745. The authors concluded that the best-corrected visual acuity was inversely significantly correlated with the ellipsoid and interdigitation zone and vision improvement may be attributed to the restoration of the outer retinal microstructures. However, the validation, extrapolation, and generalizability of the excellent outcomes of this study can be made only by regression analyses including all the missing baseline potential predictive factors mentioned by us in addition to the baseline characteristics already assessed.

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INTRODUCTION

We read with great interest the article by Liu *et al.* (2019) which retrospectively evaluated the efficacy and safety of the half-dose photodynamic therapy (PDT) in treating patients with diffused retinal pigment epitheliopathy (DRPE). Fort-eight consecutive patients (48 eyes) with DRPE treated with half-dose PDT were followed for 24 months after the initial treatment. The outcomes of this study were excellent, namely, 100% of eyes achieved complete resolution of fluid at 24 months and the best-corrected visual acuity (BCVA) improved significantly from 0.51 logarithm of the minimum angle of resolution (logMAR) at baseline to 0.19 at 24 months. The integrities of the ellipsoid zone (EZ) and interdigitation zone (IZ) improved throughout, the recurrence rate was 6.3%, and no severe complications were witnessed. We would like to address several challenges that have arisen from this study which can be specifically summarized below.

1. The DRPE, thoroughly investigated in this series, met the conditions to be categorized as diffuse chronic Central Serous Chorioretinopathy (CSC) according to a previously described categorization (Chung *et al*. 2018). Unlike the focal chronic CSC, which has a maximum of 1 hot spot of leakage detected by fluorescein angiography, the diffuse chronic CSC has either > 1 hot spot of leakage or a larger area of hyperfluorescent leakage (extensive retinal pigment epithelium [RPE] disruptions with widespread RPE decompensations), not directly linked to 1 point in origin. The study by van Rijssen *et al.* (2019) reported in detail the efficacy and safety of the half-dose PDT in focal and diffuse chronic CSC.
2. The following relevant data regarding the abnormalities in the pachychoroid phenotype and retinal pigment epithelial band – Bruch's membrane complex, which are primarily involved in the chronic CSC and have a contribution in its pathogenesis, have not been fully documented in this study using multimodal imaging at presentation and at the completion of the study: the choroidal thickening and vascular hyperpermeability which can result from focal or diffuse dilatation of large choroidal vessels, commonly localized with in areas of increased vascular permeability on indocyanine green angiography (ICGA); the distribution of the pachyvessels in the Haller's layer (in a diffuse or patchy manner); the focal or diffuse attenuation of the inner choroid layer (thinning/absence of the choriocapillaris and intermediate caliber vessels within the Sattler's layer in areas overlying abnormally dilated Haller's layer vessels); the foveal choroidal excavations; the calculation of the perfusion indices (density of blood vessels and flow index) for the choriocapillaris zone on the optical coherence tomography (OCT) angiography;

the OCT patterns of some alterations of the RPE (pigment migration within the neurosensory retina, RPE porosity, microrips or blowouts in the RPE, focal RPE atrophy, RPE thickening, existence or not of the pachydrusen that correspond to punctate hyper fluorescent spots on ICGA, and type of only one of the persistent pigment epithelial detachment identified [with internal hypo or hyper reflectivity]) (Călugăru *et al.* 2019, 2019a).

3. There were no data at presentation and at the end of the study referring to the following alterations of the outer retinal microstructures, which may suffer progressive and irreversible damages in cases of chronic CSC because of the persistence of the subretinal fluid caused by the pronounced dysfunctional RPE outer blood-retinal barrier with severe widespread RPE decompensation: the thinning of the outer nuclear layer, the elongation of the photoreceptor outer segments, the hyper reflective deposits frequently accumulated in the sub retinal space below the detached neurosensory retina, and the location of the intraretinal fluid in the 3 cases identified (ganglion cell layer or inner/outer retinal layers). Moreover, the perfusion indices for the outer retinal zone (photoreceptor) were not calculated on the OCT angiography. Of note, although the outer retina does not have vessels, the perfusion indices can be still determined (Călugăru *et al*. 2018, 2018a, 2019a).
4. Noting was stated regarding the assessment of the findings existing in fellow eyes in patients with unilateral DRPE. Importantly, the OCT angiography, which allows detection of choroidal neovascularization (CNV) secondary to chronic CSC not visible with other imaging techniques (neovascular chronic CSC) and which seems to be helpful to show an abnormal blood flow corresponding to CNV complicating the chronic CSC, has not been used. Of note, Ersoz *et al.* (2018) reported that the fellow eye had thickened choroid and pigmentary changes (pachychoroid pigment epitheliopathy) in 91.8% of cases with unilateral chronic CSC. Mandadi *et al.* (2019) found in patients with neovascular chronic CSC that 25 out of 40 (62.5%) fellow eyes had flat irregular pigment epithelial detachments on OCT out of which 21 had internal hyper reflectivity. Likewise, a definite vascular network was picked up by OCT angiography in 9 of these 40 fellow eyes (22.5%) suggesting a subclinical neovascularization.

Altogether, the authors of this study concluded that the BCVA in logMAR was inversely significantly correlated with the EZ and IZ and vision improvement may be attributed to the restoration of the outer retinal microstructures.

However, the validation, extrapolation, and generalizability of the excellent outcomes of this study can be made only by regression analyses including all the missing baseline potential predictive factors mentioned by us in addition to the baseline characteristics already assessed, serving the identification of the significant putative biomarkers of long-term visual outcomes (Călugăru *et al*., 2018b, 2019a).

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