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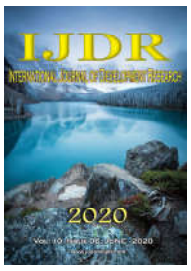

RESEARCH ARTICLE OPEN ACCESS

RESPONSE OF NEOVASCULAR CENTRAL SEROUS CHORIORETINOPATHY TO AN EXTENDED UPLOAD OF ANTI-VEGF AGENTS

***Dan Călugăru and Mihai Călugăru**

Department of Ophthalmology, University of Medicine Cluj-Napoca/Romania

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****Corresponding author: Mihai Călugăru,***

ABSTRACT

The authors are commenting on the study entitled "Response of neovascular central serous chorioretinopathy to an extended upload of anti-VEGF agents" published by Schworm *et al*. in Graefe Arch Clin Exp Ophthalmol 2020;258(5):1013-1021, which retrospectively evaluated the anatomical and functional outcomes of an extended 6-month intravitreal anti-vascular endothelial growth factor upload in choroidal neovascularization secondary to chronic central serous chorioretinopathy. The database analysis included 21 eyes of 21 patients. The authors concluded that a strict injection regimen for neovascular central serous chorioretinopathy can lead to a favorable anatomical and functional treatment response attributable not only to the substantial effect of the anti-vascular endothelial growth factor therapy but also to a modulation of choroidal perfusion. We agree with these findings only after the statistical analyses will encompass all the missing baseline potential predictive factors referred to by us in addition to the baseline characteristics already evaluated in this study, serving to highlight the key metrics of the response of neovascular central serous chorioretinopathy to an extended upload of anti-vascular endothelial growth factor agents.

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INTRODUCTION

The study by Schworm *et al.* (2020) evaluated the anatomical and functional outcomes of an extended 6-month intravitreal anti-vascular endothelial growth factor (anti-VEGF) upload in choroidal neovascularization (CNV) secondary to chronic central serous chorioretinopathy (CSCR). This retrospective database analysis included 21 eyes of 21 patients. At the end of the follow-up, the mean central retinal thickness (CRT) decreased significantly to 275 µm while the mean visual acuity improved significantly to 0.49 logMAR. Significant CNV remodeling was achieved as a decrease in pigment epithelium detachment (PED) vertical and horizontal diameters as well as PED height. The authors concluded that 6 consecutive injections were effective in inducing CNV remodeling and fluid resorption in CNV complicating chronic CSCR. We would like to address several challenges that have arisen from this study, which can be specifically summarized below.

The study was retrospectively conducted and had a relatively small sample size.

There was a selection bias attributable to the fact that 5 patients (23.8%) had treatments prior to developing the CNV, for example, 4 patients had been treated with a half-fluence photodynamic therapy and in 1 patient (4.76%) a recent administration of inhaled steroids was documented. Likewise, 18 eyes (85.71%) featured the type 1 occult CNV originating initially from the choriocapillaris with vascularization limited to the region beneath the retinal pigment epithelium (RPE) and 3 eyes (14.28%) had the type 2 classical CNV arising from the choroid and sprouting of blood vessels through the Bruch's membrane to the subretinal space, causing damage to the outer retina. Taking together, these findings may have confounded the final results.

The CSCR resides within the pachychoroid disease spectrum (Cheung *et al.* 2019) and has been definied as a pachychoroid neovasculopathy. However, the characteristic abnormalities of the pachychoroid disease phenotype (primary choroidopathy) , which is primarily involved in the CSCR and has a contribution in the CSCR pathogenesis, has not been fully documented with the multimodal imaging in subjects of this

study. Specifically, there were no data on the assessment of the following alterations at enrollment and at the end of the follow-up period: the increase permeability of choroidal vasculature with extravascular leakage, one of the hallmark of CSCR imaging which can result from focal or diffuse dilation of large choroidal vessels; the distribution of the pachyvessels in the Haller's layer (in a diffuse or patchy manner) localized within the areas of increased choroidal vascular permeability; 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); and the foveal choroidal excavations.

Regarding the qualitative status of the RPE, which has been compromised by choroidal abnormalities in patients with CSCR, there are no data relating to the multimodal imaging of some alterations of the retinal pigment epithelial band – Bruch membrane complex including: the fluoresce in angiography-based categorization of patients in 2 groups, namely focal CSCR which has a maxiumum 1 hot spot of leakage and diffuse CSCR which has either > 1 hot spot or a larger area of hyperfluorescent leakage (extensive RPE disruptions with the widespread RPE decompensations) not directly linked to 1 point in origin (Chung *et al* 2018); the OCT patterns of some alterations of the RPE such as pigment migration within the neurosensory retina, RPE porosity, microrips or blowouts in the RPE, focal RPE atrophy, RPE hypertrophy, existence or not of the pachydrusen, pigment epithelium detachment (PED) with internal hyporeflectivity (serous PED), if they existed next to the hyperreflective irregular flat, undulating PED with double layer sign; and the diffuse ooze within or adjacent to the decompensated RPE (Călugăru *et al*., 2018)

There were no data referring to the following alterations of the outer retinal microstructures which may suffer progressive and irreversible damages in cases of the CSCR because of the persistence of the subretinal fluid caused by the pronounced dysfunctional RPE outer blood-retinal barrier with severe widespread RPE decompensation. Specifically, these changes include: the thinning of the outer nuclear layer, the discontinuity of the junction between inner and outer segments, the elongation of the photoreceptor outer segments, the interdigitation zone loss, the morphologic alterations in the appearance of the outer border of the photoreceptor layer (smooth, granulated, or as scattered dots attached to external limiting membrane [ELM]), and the hyperreflective deposits frequently accumulated in the subretinal space below the detached neurosensory retina. Likewise, nothing was stated on the ELM band defects allowing fluid to enter the retina, sometimes referred to as "cystoid macular degeneration" (Călugăru *et al*., 2018a) and the OCT location of these intraretinal cystoid spaces without intraretinal leakage on fluorescein angiography (ganglion cell layer or inner/outer retinal layers) was not highlighted.

There were no data referring to the baseline serum potassium levels, the renal function, the level of endogenous and exogenous corticosteroids, the type personality of the patients, and the testing of patients with regard to the Helicobacter pylori infection.

The final outcomes of this series were unsatisfactory although the means CRT and subfoveal choroidal thickness decreased significantly to 257 µm and 302 µm, respectively, and the visual acuity improved significantly to 0.49 logMAR. Specifically the PEDs have persisted despite their diameters (horizontal and vertical) and heights that have significantly decreased and the proportion of the wet maculae have remained relatively high (47.6%). These findings certified the unresolved macular edema owing to insufficient macular deturgescence and indicated that the disease process was still active and progressive requiring further treatment with antiangiogenic agents. Two facts can explain the quality of these elicited results. First of all the study included elderly patients with an average of 65 years, an age well above the middle age of the CSCR patients whose peak lies between 40 and 50 years. Of note, the elderly group patients are associated with a lower resolution of the PED, increased impairment of the RPE layers, foveal thinning, and worse vision outcomes compared with the young group suggesting a chronic insult to the choroidal vessels involving more severe damages to the outer retinal layers (Bae *et al.* 2019). Secondary, the study encompassed patients with 2 types of CNV, that respond completely different to anti-VEGF treatment, for example, while the type 1 occult CNV (arteriogenesis) is refractory to anti-VEGF therapy as it contains more mature vessels requiring adjunctive therapy (photodynamic therapy), the type 2 classic CNV (angiogenesis) responds well to antiangiogenic agents (Murali *et al.* 2020).

The authors of this series found a significant reduction of the mean subfoveal choroidal thickness and choroidal hyperpermeability after an extended upload of 6 injections. They reasonably consider that these changes may lead to less subretinal fluid and thus to a reduced CRT. Importantly, the prolonged inhibition of VEGF using anti-VEGF therapy may affect the integrity of the choriocapillaris, considering the key role of the VEGF-A in the normal function of the retina and in the regulation of the survival and permeability of the choriocapillaris. Thus, the significant subfoveal choroidal thickness thinning may affect the integrity of the RPE and outer retina favoring the development of the fovea-involving macular atrophy and subretinal fibrosis with subsequent visual deleterious effects because the choroid is involved in maintaining the perfusion of the outer retinal layers and is the sole source of metabolic exchange (nourishment and oxygen) for the fovea.

Altogether, the authors concluded (Schworm *et al*. 2020) that a strict injection regimen for neovascular CSCR can lead to a favorable anatomical and functional treatment response attributable not only to the substantial effect of anti-VEGF therapy but also to a modulation of choroidal perfusion. We agree with these findings only after the statistical analyses will encompass all the missing baseline potential predictive factors referred to above by us in addition to the baseline characteristics already evaluated in this study, serving to emphasize the key metrics of the response of neovascular CSCR to an extended upload of anti-VEGF agents.

Acknowledgments/Disclosure

All authors have completed and submitted the ICMJE form for disclosure of potential conflicts of interest. No financial disclosures. Both authors (D.C and M.C) were involved in the design and conduct of the study; collection, management, analysis and interpretation of the data; and preparation, review or approval of the manuscript. The authors have full control over the primary data and they agree to allow the International

Journal of Development Research to review their data if requested.

REFERENCES

Bae K, Nam SW, Kang SW, et al. Central serous chorioretinopathy in elderly subjects: angiographic and tomographic characteristics. *Graefes Arch Clin Exp Ophthalmol* 2019; 257(2):279-288.

Călugăru D, Călugăru M. Clinical features of central serous chorioretinopathy with type 1 choroidal neovascularization. *Am J Ophthalmol* 2018; 195 (November): 245-246.

Cheung CMG, Lee WKI, Koizumi H, et al. Pachychoroid disease. *Eye* 2019;33(1):14-33.

Chung CY, Chan YY, Li KKW. Angiographic and tomographic prognostic factors of chronic central serous chorioretinopathy treated with half-dose photodynamic therapy. *Ophthalmologica* 2018; 240(1):37-44.

Murali A, Krishnakumar S, Subramanian A, Parameswaran S. Bruch's membrane pathology: a mechanistic perspective. *Eur J Ophthalmol.* Epub ahead of print 28 April 2020. DOI:10.1177/112067212120919337.

Schworm B, Luft N, Keidel LF, et al. Response of neovascular central serous chorioretinopathy to an extended upload of anti-VEGF agents. *Graefes Arch Clin Exp Ophthalmol* 2020; 258(5):1013-1021.

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