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Original Research

Choroidal Thickness Change in Central Serous Chorioretinopathy after Photodynamic Therapy Using Optical Coherence Tomography

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ABSTRACT

Objective: This study aimed to evaluate the change in choroidal thickness and subanalyze Haller's and Sattler' layer in patients with central serous chorioretinopathy (CSC) following low-fluence photodynamic therapy (PDT) using enhanced depth imaging optical coherence tomography (EDI-OCT).

Methods: In this retrospective study, medical records of the patients with CSC were reviewed. Patients with a diagnosis of CSC and a history of decreased visual acuity for more than six months and treated with half-dose PDT with verteporfin were included in the study. Patients who received previous PDT for chronic CSC or had evidence of choroidal neovascular membrane were excluded. Main outcome measures were the change in choroidal thickness and subanalysis of Haller and Sattler layer after treatment.

Results: A total of 13 eyes of 13 patients were included in the study. The mean age of the patients was 49±11 years (range 40–68). The mean subfoveal choroidal thickness decreased significantly from 310.60±89.16 µm at baseline to 308.41±90.03 µm after PDT ($p<0.05$). The mean Haller's layer thickness decreased significantly from 203.40±86.37 µm to 200.20±81.55 µm ($p<0.05$). The thickness of Sattler' layers did not differ significantly after PDT treatment ($p>0.05$).

Conclusion: Half-fluence PDT for CSC resulted in thinner subfoveal choroidal thickness after PDT treatment. Sattler's layer had similar thickness in eyes with active CSC and after PDT. This study finding suggested that subfoveal choroidal thickness changes after half-dose PDT were likely due to the changes in Haller's layer.

Keywords: Central serous chorioretinopathy, choroidal thickness, optical coherence tomography, photodynamic therapy

INTRODUCTION

Central serous chorioretinopathy (CSC) is a sporadic disease that is characterized by serous neurosensory retinal detachment often affecting middle-aged men (1). Although it can heal spontaneously without treatment, it can show recurrent and chronic characteristics and lead to progressive visual loss (2).

A number of theories have been proposed concerning the pathophysiology of CSC, but its mechanism is still not fully understood. Theories related to retinal pigment epithelium (RPE) dysfunction and choroidal vessel abnormalities currently dominate the literature (3). In indocyanine green angiography (ICGA), it is stated that vascular anomalies in choroidal vessels, and increased venous dilation and hyperpermeability in patients with CSS, is more intense compared to RPE leakage (4).

Currently, monitorization, laser photocoagulation, anti-vascular endothelial growth factor (anti-VEGF) inhibitors, mineralocorticoid receptor antagonists, and photodynamic therapy (PDT) are applied for the treatment of CSC (3, 5-7). PDT has been shown to treat subretinal fluid accumulation and increase visual acuity (7). Although the treatment mechanism is unknown, it has been suggested that it reduces choroidal hyperpermeability, causing damage in the choriocapillaris and resulting in resolution of leakage in the RPE (8).

Optical coherence tomography (OCT) is a noninvasive diagnostic imaging technique that provides high-resolution and cross-sectional imaging of the retina and the choroid using light waves. Conventional spectral-domain OCT devices cannot adequately image the choroid layer due to the shadowing effect of the RPE and the choroidal vascular structure. Today, choroidal vascular structure can be visualized with the EDI-OCT technique developed by modification of the spectral-domain OCT technology (9). The choriocapillaris/Sattler's layer, which is known as the choroidal small and medium-sized vessel network just below the Bruch membrane, and the Haller's layers, which are composed of the larger vessels that are located more deeply, can be distinguished by using new technology devices.

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Studies evaluating choroidal thickness with EDI-OCT have reported increased choroidal thickness in patients with CSC and decreased choroidal thickness in patients who spontaneously recovered, and in patients treated with PDT compared to healthy individuals (10, 11). In a study evaluating the choroidal sublayers with EDI-OCT, a significant increase was observed in the subfoveal Haller's layer in patients with CSC compared to healthy subjects, but there was no change in the choriocapillaris/Sattler's layer (12). As far as we know, no study shows the effect of PDT on Haller's and Sattler's layers in patients with CSC.

This study intends to evaluate changes in the choroid layer, choriocapillaris/Sattler's and Haller's layers with EDI-OCT in patients with chronic CSC who have undergone PDT treatment.

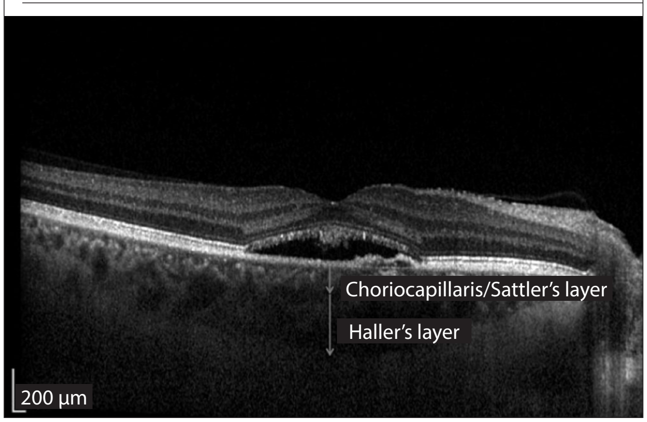
METHODS

Patients admitted to Ankara Atatürk Training and Research Hospital's Retina Clinic between March 2016 and September 2017 with a diagnosis of CSC were retrospectively reviewed on the basis of the file records. Patients who had symptoms of decreased visual acuity for a period of longer than six months receiving PDT treatment were included in the study. Patients with retinal diseases, such as age-related macular degeneration, degenerative myopia, polypoidal choroidal vasculopathy, and diabetic retinopathy, were excluded from the study. Patients with refractive errors of more than 6 diopters and patients with relapsed CSC who had previously undergone PDT and laser photocoagulation or intravitreal injection treatments were also excluded. Patients who did not attend regular follow-ups or have their EDI-OCT measurements were also excluded from the study. The diagnosis of CSC was made on the basis of subretinal fluid in the macular area in the OCT and idiopathic leaks detected via the fundus fluorescein angiography (FFA).

All patients received PDT at low energy levels according to the classical protocol (13). Verteporfin (Visudyne; Novartis, Basel, Switzerland) was calculated according to the body surface area of 6 mg/m^2 and administered intravenously for 10 min. After 15 min of beginning of the injection, the 689 nm diode laser was applied to the lesion site at a dose of 300 mW (half of the conventional dose of 600 mW) for 83 s.

Figure 1. Calculation of choriocapillaris/Sattler's layer and Haller's layer in EDI-OCT

EDI: enhanced depth imaging; OCT: optical coherence tomography;



During all control examinations, a detailed ophthalmologic examination including EDI-OCT measurements was performed on all patients. A visual acuity examination was performed with a Snellen eye chart. An FFA evaluation was performed on the first examination visit. The pre-PDT control examination records of patients and their post-PDT examination records at month 1 were evaluated.

A single technician performed the OCT measurements of the patients in the EDI mode using the Heidelberg spectralis OCT (Heidelberg Engineering, Heidelberg, Germany) device. The same person (Mücella Arıkan Yorgun) manually measured the choroidal thickness in the linear measurement mode of the device over the OCT section across the subfoveal area. After each measurement, the manual additions were deleted and the measurements were repeated three times at different times. The mean values were used for the analysis. Total choroidal, choriocapillaris/Sattler's layer, and Haller's layer measurements were performed at intervals of 500 µm and at a nasal and temporal distance of 1500 µm from the subfoveal point. The distance between the outer border of the retina pigment and the outer border of the choroidal vascular bed was accepted as the "total choroidal thickness". The innermost border of large choroid vessels and the space between the choroid-scleral line were recorded as "Haller's layer". The difference between the total choroidal thickness and Haller's layer was accepted as representing the "choriocapillaris/Sattler's layer" (Figure 1).

This study was conducted in accordance with the principles of the Helsinki Declaration and was approved by the Clinical Trials Ankara Atatürk Training and Research Hospital Ethics Committee Commission on 17.01.2018 with document no. 26379996/16. Written consent was obtained from all patients.

Statistical Analysis

The Statistical Package for the Social Sciences 21.0 Windows version package program (SPSS IBM Corp.; Armonk, NY, USA) was used for the statistical analysis. The mean and standard deviation values of the data were calculated. The best corrected visual acuity (BCVA), measured with a Snellen eye chart, was converted to log MAR. The normal distribution of the data was tested with the Kolmogorov–Smirnov Test. The Student t test was used to compare quantitative data and Pearson's chi-square test was used to compare qualitative data. The p value of <0.05 was accepted as statistically significant. Thickness variations in the total choroid layer and Haller's and Sattler's layers after the photodynamic treatment were accepted as the evaluation criteria.

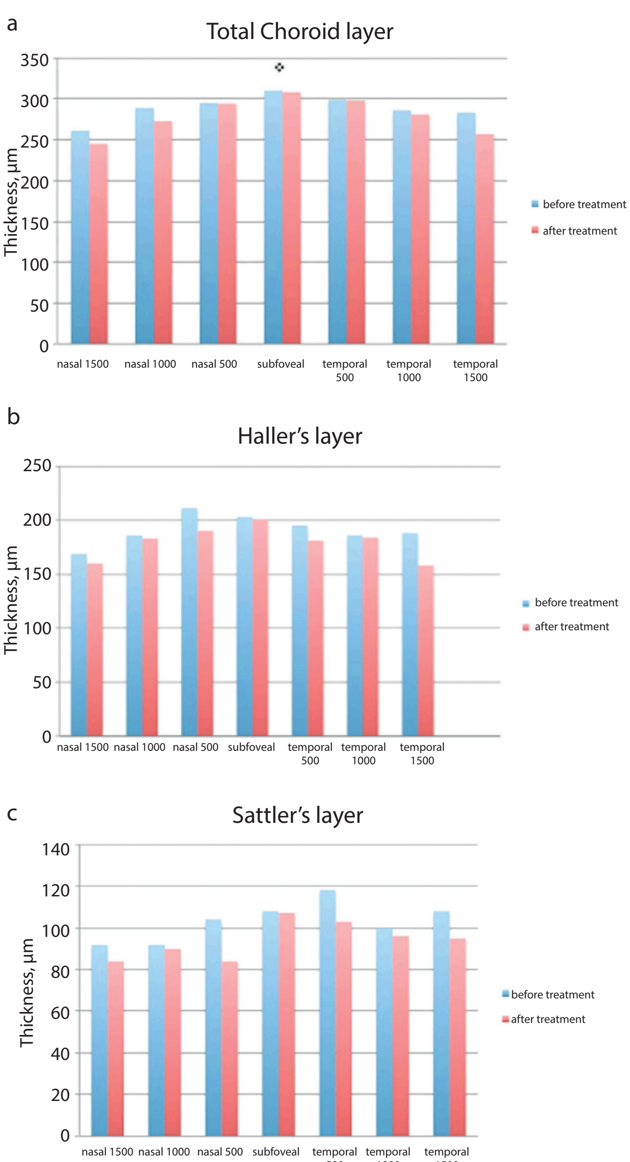
RESULTS

A total of 13 eyes of 13 patients who met the study criteria were included in the study. The average age was 49±11 years (range 40–68). The number of female cases was 5 (38%) and the number of male cases was 8 (62%). The mean symptom duration was 21.6±5.6 months. Complete relief of serous retinal detachment was observed in all patients following the first month post PDT treatment. The mean BCVA was 0.17±0.13 log MAR before treatment and 0.18±0.13 log MAR after treatment (p=0.16). The subfoveal total choroidal thickness before PDT was

310.60±89.16 (range 214–454), and 308.41±90.03 µm after PDT (range 183–411) (p=0.048). The subfoveal Haller's layer thickness was 203.40±86.37 µm before PDT and 200.20±81.55 µm after the treatment (p=0.032). The Sattler's layer was 108.20±33.75 µm before PDT and 107.2±17.03 µm after the treatment (p=0.147). No significant differences were found in the mean values before and after PDT in the total choroidal thickness of the nasal and temporal areas, the thickness of the Haller's layer, and the thickness of the Sattler's layer (p>0.05). Total choroidal thicknesses, choriocapillaris/Sattler's layer thicknesses, and Haller's layer thickness values before treatment and one month after treatment are shown in Figure 2.

Figure 2. a-c. (a) Change of total choroidal thickness before PDT and at month 1 after PDT, (b) change of Haller's layer before PDT and at month 1 after PDT, (c) change of choriocapillaris/Sattler's layer before PDT and at month 1 after PDT

PDT: photodynamic therapy



DISCUSSION

Today, developments in OCT technologies enable noninvasive measurement of choroidal thickness and indirect evaluation of choroidal vascular hyperpermeability, as well as investigation of the pathogenesis of diseases by distinguishing layers such as Haller's and Sattler's. In this study, in which subanalyzes of choroids and layers were performed with EDI-OCT, there was no significant change in the Sattler's layer, while a decrease in the thickness of the total choroid in the subfoveal area and the Haller's layer was detected during controls at month 1 in patients treated with PDT.

Two main theories have been proposed in the etiology of CSC: choroidal dysfunction and RPE dysfunction. In indocyanine green angiography studies, choroidal vascular anomalies causing choroidal hyperpermeability have been demonstrated (14). Choroidal hyperpermeability can be evaluated non-invasively by measuring the choroidal thickness in EDI-OCT studies. Imamura et al. (11) showed in their studies evaluating choroidal thickness with EDI-OCT that there was an increase in subfoveal choroidal thickness in patients with CSC compared to healthy individuals. Studies have reported that choroidal thickness is reduced in patients who recovered without treatment (11, 15). It is reported that there is no change in choroidal thickness in patients treated with laser, while the choroidal thickness decreases with PDT treatment (16). Maruko et al. (15) showed a reduction in the choroidal thickness with OCT in one month and a decrease in choroidal hyperpermeability with ICG in their study in which they followed up their patients with CSC who were administered a half-dose PDT for one year. Similarly, our study showed a decrease in the subfoveal choroidal thickening at month 1 after PDT treatment. Based on the results of these studies, it can be assumed that treatment with PDT causes a decrease in permeability by acting on the choroid, resulting in thinning of the choroid.

Dilatation in the choroidal vessels in the Haller's layer has been accepted as a descriptive feature of CSC disease agreed in the current literature as belonging to the group of "pachychoroid spectrum diseases" (17). Studies in which choroid layers have been evaluated by EDI-OCT showed dilation and increase in thickness of the impacted eye's vessels in the Haller's layer in CSC cases compared to the other eye and healthy subjects. It has been shown that the increase in choroidal thickness may be due to the enlargement of large choroidal vessels in the Haller's layer (8, 12, 18). No other study in the literature evaluates the choroidal lower layers using OCT after PDT treatment. However, in a study by Chan et al. (19) in which the choroidal layer was assessed through ICGA, a 32% reduction in the size of the dilated choroidal vessels was reported post-PDT in patients with CSC. In our study, a thinning of the subfoveal Haller's layer was observed after PDT treatment, but no change in the parafoveal choroidal thickness was detected. The smooth muscle cells present in the choroidal vessels are more dense in the area under the fovea and are affected by sympathetic and parasympathetic innervation, causing narrowing of the choroidal vessel wall. In the PDT protocol, the laser beam also acts on the parafoveal area circularly, as well as the subfoveal area. The lack of impact on the parafoveal area while reduction was seen in the choroidal thickness of the subfoveal area may be due to differences in the innervation and vessel network, which are more intense in the foveal area, rather than the direct effect of the laser beam.

The retrospective nature of our study, the small number of cases, and the short follow-up periods are the main limitations of the study. At the same time, even though the OCT device used contains an EDI mode, which provides high-resolution deep-screening, factors such as optical obstructions in front of the choroid layer, eye movements, and manual segmentation may have prevented optimal choroidal stratification. Although it has been used in some experimental studies with OCT devices that provide high penetration with a wavelength of >1000 nm (20), OCT devices, which we also use at our clinic, that enable penetration at an 840 nm laser wavelength are available. Finally, although the change in the choroidal thickness was statistically significant in our study, this change in choroidal thickness may not be clinically significant.

CONCLUSION

This study demonstrates that a decrease was observed in the subfoveal choroidal thickness and Haller's layer thickness with half-dose PDT treatment in patients with CSC. We think that the results of this study will shed light on the application of PDT mechanism on patients with CSC, whose etiopathogenesis is inadequately understood. Based on our current knowledge, no study in the literature shows the effect of PDT on Haller's and Sattler's layers in patients with CSC. In this regard, studies with a wide case series and a long follow-up period are needed.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Ankara Atatürk Training and Research Hospital (date: 17.01.2018, no. 26379996/16).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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