Optical coherence tomography angiography parameters in pachychoroid spectrum diseases

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ABSTRACT

Purpose: The aim of this study was to evaluate the findings of optical coherence tomography angiography (OCTA) in patients with pachychoroid spectrum.

Materials and Methods: Thirty eyes of 30 patients diagnosed with pachychoroid spectrum disease and 30 age-gender matched healthy controls, were retrospectively included in the study. The results of the ophthalmological examination and the OCTA measurements of the participants were analyzed retrospectively.

Results: Subretinal fluid was found in all 20 eyes with Central Serous Chorioretinopathy, pigment epithelial detachment (PED) was found in 12 eyes (60%) and choroidal neovascularization (CNV) was found in 3 eyes (15%). The Pachychoroid Pigment Epitheliopathy patients had retinal pigment epithelium changes. Polypoidal multi-lobular PED and subretinal fluid were detected in all cases of Polypoidal Choroidal Vasculopathy and CNV was detected in 3 (50%) cases of PCV. Flat irregular PED and CNV were found in all Pachychoroid Neovasculopathy cases. The subfoveal choroidal thickness of the pachychoroid spectrum group was significantly higher than that of the healthy control group ($p<0.05$). The choriocapillaris flow values in the pachychoroid spectrum disease group were significantly lower than in the healthy control group ($p<0.05$).

Conclusions: OCTA is a noninvasive imaging modality very helpful in the diagnosis and differential diagnosis of pachychoroid spectrum disease.

Keywords: Optical coherence tomography angiography, pachychoroid spectrum disease, pachychoroid pigment epitheliopathy, central serous chorioretinopathy, flow choriocapillaris, choroidal thickness.

INTRODUCTION

The term pachychoroid was defined in 2013 by Warrow et al. Pachychoroidal disease is a spectrum in which there is a focal or diffuse increase in the thickness of the choroid, enlargement of the choroidal vessels in the Haller's layer, and thinning of the choriocapillaris and Sattler's layer. There are also abnormalities in the retinal pigment epithelium (RPE), which is located on top of these dilated vessels.[1]

Pachychoroidal spectrum diseases are classified as follows.

- Pachychoroid Pigment Epitheliopathy (PPE)
- Central Serous Chorioretinopathy (CSC)
- Pachychoroid Neovasculopathy (PNV)
- Polypoidal Choroidal Vasculopathy (PKV)
- Focal Choroidal Excavation (FCE)
- Peripapillary Pachychoroid Spectrum (PPS).[2]

A novel dye-less method for the imaging of the microvascular structures of the retina, called Optical coherence tomography angiography (OCT-A), has been introduced into clinical practice. The movement of red blood cells within the retinal capillaries is used as an intrinsic contrast medium to generate flow imaging.[3]

OCTA can help detect retinal microvascular structures and choriocapillaries. In this study, we sought to compare

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OCTA findings in patients with pachychoroid spectrum disease with healthy controls, taking advantage of the superiority of OCTA in the choroid and retina separately.

MATERIALS AND METHODS

A total of 30 patients diagnosed with pachychoroid spectrum disease and 30 age- and sex-matched healthy control subjects were included in this retrospective study conducted at the Department of Ophthalmology, Faculty of Medicine, Erciyes University. The study was conducted in accordance with the tenets of the Declaration of Helsinki and approved by the Ethics Committee of Erciyes University Faculty of Medicine (number: 2019/797).

The electronic charts of patients evaluated for ophthalmologic examination included best-corrected visual acuity (BCVA), anterior segment examination with slit-lamp, retinal examination, fundus fluorescein angiography, OCT (Spectralis, Heidelberg Engineering Inc., Heidelberg, Germany) and OCT angiography (AngioVue, Optovue Inc., Fremont, California, USA). The BCVA assessment, structural OCT, and OCTA were performed on the same day. OCTA images (6 x 6 mm) were obtained by the Optovue Angiovue System (software RTVue XR, version 2017.1.0.151, Optovue Inc., Fremont, CA, USA). Foveal avascular zone (FAZ) area, FAZ perimeter, acircularity index of the FAZ (AI; the ratio of the circumference of the FAZ and the circumference of an equal area), foveal density 300 (vessel density within 300 µm around FAZ), choriocapillaris flows in a 1 mm radius on the fovea were recorded from the OCT angiography software. The thickness of the subfoveal choroid was measured manually from the outer edge of the retinal pigment epithelium to the inner edge of the sclera in the subfoveal region using the enhanced depth imaging mode. All choroidal thickness measurements were performed at the same time of day (between 10 a.m. and 12 p.m.) to minimize the effect of circadian variation on choroidal circulation.

Cases with pachychoroid features with RPE changes but no subretinal fluid and no history of subretinal fluid, no choroidal neovascularization (CNV), no polyps were considered PPE (1). The diagnostic criteria for CSC were subretinal serous fluid and increased choroidal thickness in the enhanced depth imaging mode OCT (subfoveal choroidal thickness ≥300µm). The presence of wide, shallow and irregular PEDs is characteristic of PNV.[4] The presence of pointed PED peaks, PED notches and localized polyp lumens beneath PEDs were diagnostic criteria for PCV.[5]

The exclusion criteria were: (1) previous history of glucocorticoid use during pregnancy; (2) previous ocular surgery; (3) previous treatments, including photodynamic laser therapy, photocoagulation, or intravitreal injections of anti-vascular endothelial growth factor drugs; (4) other ocular diseases that may affect the retinal microvascular flow, such as moderate to mature cataract, age-related macular degeneration, hypertensive retinopathy, diabetic retinopathy, glaucoma, ocular trauma, or macular epiretinal membrane; (5) high diopter > -6 diopter spherical equivalent or long axial legth >26.0 mm; (6) cystic macular degeneration; (7) the quality of the OCTA images is below 7/10.

Statistical analysis

All statistical analyses were performed using SPSS 22 software. Kolmogorov-Smirnov tests were used to test the normality assumption of the variables, and independent t-tests and chi-squared tests were used to determine differences between variables. Data were expressed as mean ± standard deviation. $P < 0.05$ was considered statistically significant in all analyses.

RESULTS

Thirty eyes of 30 patients were included in the study who were followed up at the Ophthalmology Clinic of Erciyes University Medical Faculty Hospital with a diagnosis of pachychoroid spectrum disease. BCVA in the pachychoroid group was significantly ($p < 0.05$) lower than in the control group. The age of the patients in the case and control groups was not significantly different ($p > 0.05$) (Table 1). There was no significant difference between the pachychoroid and control groups for FAZ area, FAZ perimeter, A-circularity index, foveal density 300. The choriocapillaris flow value was found to be lower in the pachychoroid groups than in the healthy control groups (Table 1). The pachychoroid spectrum types in our study are shown in Table 2.

The subfoveal choroidal thickness value measured with OCT - enhanced depth imaging mode in the case group was significantly ($p < 0.05$) higher than in the control group. The choroidal thickness values of the nasal and temporal regions at a distance of 0.5 mm from the fovea, measured with the OCT - enhanced depth imaging mode, were also significantly ($p < 0.05$) higher in the case group than in the control group (Table 3). OCTA images in the pachychoroid groups ; choroidal neovascularization and polypoidal PED were shown in Figure 1. Images of choroidal neovascularization in the choriocapillaris section of OCTA Figure 2. OCT image in a case of CSC; subretinal

Table 1: *Subject Characteristics and Comparison of the FAZ parameters and Choriocapillaris flow area between study groups.*

	n	Controls Mean±Std.Deviation	Pachychoroid Mean±Std.Deviation	p value
FAZ Area (mm^2)	30	0.24±0.08	0.27±0.10	0.185
FAZ Perimeter (mm)	30	1.90±0.33	1.98±0.44	0.464
A-circularity Index	30	1.10±0.03	1.11±0.04	0.305
Foveal Density	30	53.04±9.84	51.38±5.22	0.416
Choriocapillaris Flow	30	2.08±0.14	1.80±0.26	0.001
BCVA (LogMAR)	30	0.00±0.00	0.27±0.34	0.001
Age (years)	30	41.73±6,86	42.86±5.50	0.190
Significant p values are in bold. t-test, p<0.05 significant				

Tablo 2: *Types of pachychoroid spectrum disorders in the study.*

		N	(%)
Pachychoroid Spectrum Disease	PPE	2	6,7%
	CSC	20	66,7%
	PNV	2	6,7%
	PCV	6	20,0%
PPE: Pachychoroid Pigment Epitheliopathy; CSC: Central Serous Chorioretinopathy; PNV: Pachychoroid Neovasculopathy; PCV: Polypoidal Choroidal Vasculopathy			

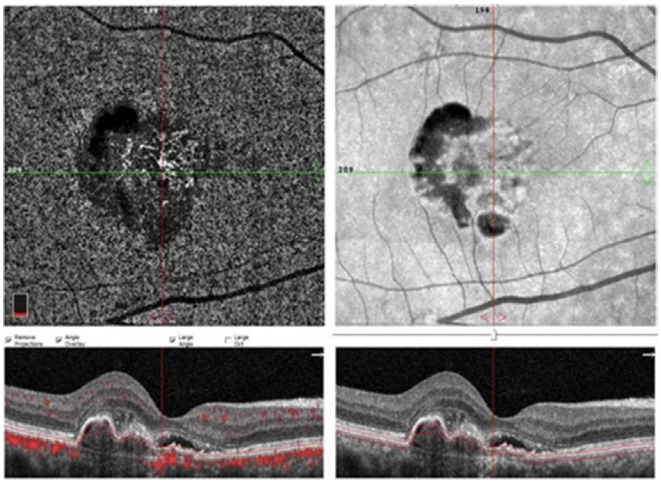

Figure 1: *OCT angiography of the patient with a diagnosis of PCV, type 1 choroidal neovascularisation seen on the choriocapillaris section and the corresponding M-shaped hemorrhagic giant polypoidal PED on the B-scan image.*

fluid in the subfoveal region; multilobular PED in a case of PCV Figure 3.

In our study, CNV was detected in 8 (26.6%) of 30 eyes with pachychoroid spectrum by OCTA. PED was found in 20 (66.6%) of the 30 eyes with a pachychoroid spectrum, and CNV was found in 8 (40%) of the 20 patients with PED. Subretinal fluid was found in 28 (93.3%) of 30 eyes with pachychoroid spectrum.

Central serous chorioretinopathy was present in 20 (66.7%) of 30 eyes with pachychoroid. Subretinal fluid was present in all 20 eyes with CSC. CNV was present in 3 (15%) eyes, brush border in 3 (15%) eyes and dipping

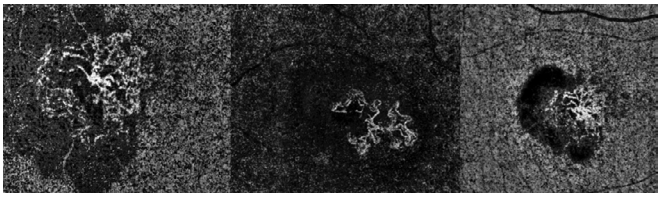

Figure 2: *Choroidal neovascularisation observed in the choriocapillaris section by OCT angiography.*

Table 3: *Subfoveal choroidal thickness (µm).*

	n	Controls Mean±Std.Deviation	Pachychoroid Mean±Std.Deviation	p value
Subfoveal	30	280.46±18.98	421.60±50.81	0.001
Nazal-foveal	30	270.63±18.11	390.03±45.95	0.001
Temporal-foveal	30	273.70±18.59	392.70±42.89	0.001
Significant p values are in bold. t-test, p<0.05 significant				

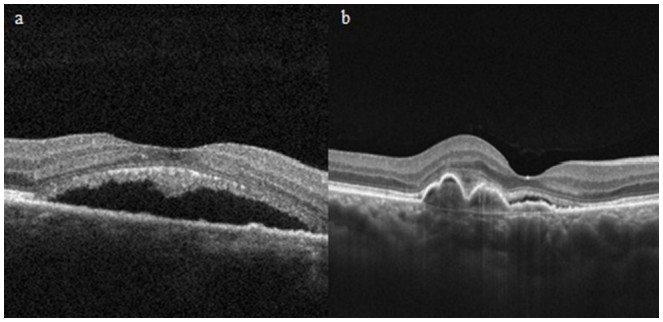

Figure 3: *a) Subretinal fluid and brush border pattern appearing in CSC. b) M-shaped multilobular PEDs are seen in PCV.*

pattern in 1 (5%) of 20 eyes with CSC. Pachychoroid pigment epitheliopathy was present in two (6.7%) of 30 eyes with pachychoroid spectrum. Subretinal fluid was not observed in any of the patients with PPE. Retinal pigment epitheliopathy abnormalities were present in all 2 patients. Polypoidal choroidal vasculopathy was found in 6 (20%) of the 30 eyes with a pachychoroid spectrum. In all 6 eyes polypoidal multilobular PED and subretinal fluid were found. Pachychoroid neovasculopathy was found in two (6.7%) of the 30 eyes with a pachychoroid spectrum. Flat irregular PED and CNV were found in all patients with PNV.

DISCUSSION

Pachychoroid spectrum disease has marked changes in the choroid, including increased choroidal thickness and a compressed choriocapillaris layer. Therefore, detailed information on the anatomy and functional characteristics of the choroidal vasculature may help to better understand the pathogenesis of the disease. Optical coherence tomography (OCT) angiography is a non-invasive imaging modality that does not require the use of dyes. It enables the imaging of blood vessels based on flow characteristics and provides improved information about the retinal and choridal microvasculature compared to conventional fluorescein angiography.[6,7]

In the current study, we compared the changes in choriocapillaris flow, choroidal layer thickness and retinal morphology in pachychoroid spectrum disease with the normal group using OCTA.

This was a cross-sectional case-control study. We assessed and compared the parameters in OCTA, structural OCT and BCVA between patients with pachychoroid spectrum disease and healthy controls. The major findings of this study are as follows: (1) The choriocapillaris flow of patients with pachychoroid spectrum disease was found to be lower than that of healthy control eyes; (2) The subfoveal choroidal thickness of patients with pachychoroid spectrum disease was found to be thicker than that of the healthy control eyes; (3) The visual acuity of patients with pachychoroid spectrum disease was found to be lower than that of healthy control group; (4) There were no significant differences between the patients with pachychoroid spectrum disease and controls in; Faz area, Faz perimeter, A-circularity index and foveal density.

Although there is agreement that the pathology of pachychoroid disease is choroidal in origin, the main mechanism is still not fully understood. It is thought that the hyperpermeability of the choriocapillaris disrupts the architecture of the choroid and leads to other pachychoroidal features and pachychoroidal complications.[2,8] In our study, PED was detected in 20 eyes and subretinal fluid in 28 of 30 eyes.

It is thought that increased secretion of vascular endothelial growth factor, due to the ischaemic environment present in eyes with pachychoroids, leads to the development of CNV.[9,10] In our study, CNV was found in 8 out of 30 eyes with pachychoroid. Bousquet et al. found CNV with OCTA in one-third of cases with flat irregular PED appearance. In our study, we found CNV with OCTA in 40% of pachychoroid patients with PED appearance.[11] In our study, we found chorioretinal changes such as PED, subretinal fluid and CNV in patients with pachychoroid spectrum. These changes are thought to develop secondary to choriocapillary damage, choroidal hyperpermeability and choroidal ischemia.

Enhanced depth imaging technology improves visualisation of the choroidal-scleral interface and can be applied to OCT. It allows for more accurate visualisation of the choroid. The most commonly studied choroidal parameter is subfoveal choroidal thickness. It is measured manually as the distance between the outer edge of the hyperreflective line of the retinal pigment epithelium and the inner edge of the hyperreflective interface of the choroid and the sclera. Subfoveal choroidal thickness is reported to be normal between 190 µm and 350 µm, although values vary depending on factors such as gender, age, imaging time, refractive error and axial ocular length.[12,13] Choroidal thickness is considered to be a marker of ocular and systemic health, with several studies indicating that choroidal thickness changes are related to abnormalities of choroidal circulation and inflammation.[14,15]

In our study, the thickness of the subfoveal choroid was significantly greater in the pachychoroid spectrum disease group than in healthy controls. These findings show us that morphological changes occur not only in the retinal layer but also in the choroidal layer in patients diagnosed with pachychoroid spectrum disease.

In our study, there was no significant difference in FAZ area between controls and pachychoroid spectrum disease groups (Table 1). Using OCTA, Samara et al. detected 70 healthy eyes and obtained a mean FAZ area of 0.266 ± 0.097 mm2 in the superficial plexus, which was very similar to our pachychoroid eyes (0.27 ± 0.10 mm2).[16] In our opinion, changes in the choroidal and RPE segments are more pronounced in pachychoroidal disease and the most damaged and affected segment is in the choriocapillary layers.

Takahashi K. et al. investigated the relationship between OCT and histopathological findings in pachychoroid spectrum disease. They found that the pathological condition involved dilation of the choroidal veins and loss of the choriocapillaris.[17] An ischaemic environment is created as a result of choriocapillaris atrophy in pachychoroid eyes. OCTA has shown a decrease in choriocapillaris flow in these eyes.[18,19] The choriocapillaris flow abnormalities were found to precede retinal pigment epithelial changes in eyes with pachychoroid, suggesting that choriocapillaris flow abnormalities may be an antecedent event before further development of pachychoroid pigment epitheliopathy, central serous chorioretinopathy or pachychoroid neo-vasculopathy.[20] It is useful for researchers and clinicians to evaluate the earliest changes that occur in choriocapillaris flow. This can be used to assess disease activity and progression.[21] And in our study, we found low choriocapillaris flow on OCTA in patients with the pachychoroid spectrum of disease, which we believe may be an indicator of reduced choroidal blood flow in this area.

In pachychoroid spectrum diseases, the mechanism underlying internal choroidal thinning and choroidal ischaemia is unknown. Saito et al. hypothesized that in eyes with acute CSC, disturbances in choroid blood flow due to increased sympathetic activity and arteriolar vasoconstriction result in impaired capillary perfusion.[22] Gal-Or et al. identified zones of decreased choriocapillaris flow in eyes with chronic CSC and PPE, with anatomic correlations to pachyvessels and structural sequelae in the RPE and retina.[18] The area of impaired choriocapillaris flow was increased in eyes with pachychoroid. It was even greater in the presence of epitheliopathy. Pachychoroid was associated with reduced choriocapillaris flow according to location and size.[20] These results, together with those from previous studies, suggest that choriocapillaris flow defects may be associated with thick vessels and the space narrowing caused by these thick vessels. Further studies are needed to elucidate the pathogenic mechanisms underlying the pachychoroid diseases.

Given the limited number of studies using OCTA, we believe this study will contribute to the clarification of microvascular abnormalities in patients with pachychoroid spectrum disease, and that OCTA detection of choroidal flow area changes with different treatment modalities could be evaluated in future studies.

Study Limitations

Limitations of our study include the retrospective single-center nature of the study, the small number of subjects, and the potential for slight errors in optical coherence tomography measurements of choriocapillary flow area due to projection of large vessels and retinal pigment epithelium. However, this artifact was common to both study and control eyes and may not affect the comparison.

In conclusion, we found that there are vascular changes in the retina of patients with pachychoroid spectrum disease. Our results showed significantly increased subfoveal choroidal thickness and significantly lower values for the choriocapillaris flow in the group with pachychoroid spectrum disease compared to the control group. OCTA may therefore be considered an easy-to-use, non-invasive screening method to assess microvascular morphology in these patients.

Ethics

Ethics Committee Approval: Erciyes University Ethics Committee (No: 2019/797). Authorship Contributions

Concept: Z.C., C.K., Design: Z.C., C.K., Data Collection or Processing: Z.C., C.K., Analysis or Interpretation: Z.C., Literature Search: Z.C., Writing: Z.C.

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