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Пахихороидальные состояния

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Pachychoroid Spectrum

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РЕФЕРАТ

«Пахихороидальное состояние» (pachy-[префикс]: полный) – аномальное и необратимое увеличение хориоидальной толщины, часто проявляющееся увеличенными хориоидальными сосудами и другими структурными изменениями в сосудистой архитектуре.

Клинические пахихориоидальные состояния – это группа макулярных заболеваний, при которых проявляются аналогичные хориоидальные изменения, такие как фокальное и диффузное увеличение хориоидальной толщины и наружных хориоидальных сосудов. При таких состояниях описаны застойные явления в хориоидее и их гиперпроницаемость.

Увеличение толщины хориоидального слоя, патологическое увеличение вен в слое Галлера, истончение в слоях Саттлера и хориокапиллярных слоях характерны для таких состояний. Несмотря на отсутствие единого мнения по поводу этой проблемы, данная группа заболеваний включает в себя следующие: плакоидная пигментная эпителиопатия, центральная серозная хориоретинопатия, пахихороидальная неоваскулопатия и полипоидная хориоидальная васкулопатия.

Для диагностики пахихориоидальных заболеваний лучше использовать метод мультимодальной визуализации, так как он позволяет исключить другие состояния, такие как ВМД, узорчатая дистрофия, точечная внутренняя хориопатия, ретинальный пигментный эпителиит. Улучшенная объемная визуализация используется как стандартная техника для визуализации сосудистой оболочки и для измерения хориоидальной толщины. ОСТ-А – новая технология, которая помогает получить высококачественные изображения без внутривенного введения контраста. Данное исследование также полезно для выявления хориоидальной неоваскуляризации в глазах с центральной серозной хориоретинопатией и при пахихориоидальных состояниях. Представлены общие клинические и данные визуализации пациентов с пахихориоидальными состояниями и методы их лечения.

Ключевые слова: *пахихороидальная пигментная эпителиопатия, центральная серозная хориоретинопатия, пахихороидальная неоваскулопатия, полипоидная хориоидальная васкулопатия.* ■

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ABSTRACT

The pachychoroid clinical spectrum is a group of macular diseases that manifest similar choroidal findings such as focal or diffuse increase in choroidal thickness and dilated outer choroidal vessels. Choroidal congestion and hyperpermeability have been frequently described in this spectrum.Increased choroidal thickening, pathologically dilated veins in the Haller's layer (pachy-veins), thinning in Sattler's and choriocapilleris layers. Although there is no consensus on this issue and it is highly controversial, the spectrum comprises the following 4 disease groups: Pachychoroid Pigment Epitheliopathy (PPE), Central Serous Chorioretinopathy (CSCR), Pachychoroid Neovasculopathy (PN) and Polipoidal Choroidal Vasculopathy (PCV). Pachychoroid diseases benefit from a multimodal imaging approach, to avoid misdiagnosis as other conditions including AMD, pattern dystrophy, punctate inner choroidopathy, and retinal pigment epitheliitis.Common clinical and imaging findings in patients with pachychoroid andtheir treament modalities are discussed in detail in this review.

Keywords: *pachychoroid pigment epitheliopathy; central serous chorioretinopathy; pachychoroid neovasculopathy; polipoidal choroidal vasculopathy.* ■

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INTRODUCTION

The term pachychoroid is generally defined as a choroidal thickness greater than 300 μm [1, 2] and comprise a group of chorioretinal disorders which share similar choroidal features in imaging techniques. These choroidal features are focal or diffuse choroidal thicknening in enhanced depth optical coherence tomography (EDI-OCT) *(Fig. 1)*, choroidal hyperpermability and dilated choroidal vessels in indocyanine green angiography (ICGA) *(Fig. 2)* [1, 3]. The choroidal thickening is thought to be the consequence of dilation of large vessels in Haller's layer. Thinning of choriocapillaris and Sattler's layer with or without

overlying retinal pigment epithelium (RPE) abnormalities accompany to this choroidal thickening [1, 4].

Pachychoroid disease spectrum comprises six different groups;

1. Pachychoroid pigment epitheliopathy (PPE)
2. Central serous chorioretinopathy (CSC)
3. Pachychoroid neovasculopathy (PNV)
4. Polypoidal choroidal vasculopathy (PCV)
5. Focal choroidal excavation (FCE)
6. Peripapillar pachychoroid syndrome (PPS)

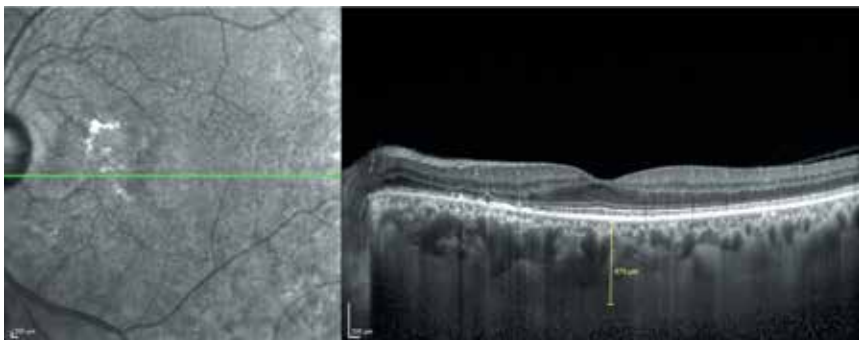

Fig. 1. Enhanced depth imaging-OCT scan of a patient with pachychoroid pigment epitheliopathy (PPE). PPE changes in RPE, thick choroid, pachyveins

Choroidal and retinal morphology and pathogenesis

Choroidal thickness measurements are influenced by age, refractive error, axial length, systemic vascular and metabolic disorders and many other factors. Subfoveal choroidal thickness measurements are reported between 223-590 μm in PCV and 345-505 in CSC [5]. In addition, focal extrafoveal choroidal thickening correlated with the dilated choroidal vessels can be observed in patients who have normal subfoveal choroidal thickness [1].

In pachychoroid spectrum, dilated vessels in Haller's layer accompany to choroidal thickening, which can be detected in OCT [6].

Characteristics of dilated choroidal vessels (pachyvessels);

• In cross-sectional EDI-OCT images, large hyporeflective lumen indicates to dilated choroidal vessels (pachyvessels) [7].

• Pachyvessels can be observed within the deep choroid in en face swept source OCT images [6].

• Pachyvessels can be distinguished from normal choroidal vessels with their course on en face OCT and ICGA. Pachyvessels, unlike normal choroidal vessels, can get very closer to or cross the macula [8].

In PDS, thinning of overlying choriocapillaris and intermediate vessels within the Sattler's layer is a characteristic morphologic feature [2]. In severe cases, only abnormal dilated vessels can be observed and choriocapillaris can not be detected [4]. These patients may have a normal choroidal thickness [4]. Therefore, increased choroidal thickness should not solely be determined as a marker of PDS, morphology of choriocapillaris and Sattler's layer should be evaluated carefully.

Main blood supply of outer retina (outer nuclear layer and RPE) is choroicapillaris. Some outer retinal changes can be observed in PDS [9];

• Motling of RPE
• RPE elevation with microbreak
• Small RPE detachments
• Outer nuclear layer thinning

On ICGA, pachyvessels appear more straight and dilated than normal choroidal vessels. Choroidal hypermeability appears as patchy areas of hyperfluorescence at mid- and late-phase angiograms which is coherent with the staining areas at fluoresceine angiography [3, 10, 11]. Choroidal hyperpermeability rate was reported higher in CSC and PPE than PCV in previous studies [5]. Besides, delayed choroidal filling, choroidal vascular congestion and late punctuate hyperfluorescence can be observed with ICGA *(Fig. 3)*. These ICGA characteristics can be observed at the fellow eyes in PDS [3, 10, 11].

The pathogenesis of choriocapillaris atrophy is stillnot clear, whether choriocapillaris atrophy is a primary condition or a consequence of tissue pressure raised from pachyvessels in Haller's layer [12]. Recent reports indicate that choriocapillaris atrophy might be the primary event, and disturbed perfusion in choriocapillaris may lead to secondary passive overflow into the large choroidal vessels which is represented as pachyvessels in Haller's layer [13-16].

Ischemic milieu due to choriocapillaris atrophy is one of the suggested mechanism for outer retinal abnormality (RPE changes and loss of functional pump capacity and outer retinal thinning) development.

Fig. 2. Pachyvessels are seen in ICGA

Fig. 3. Choroidal vascular congestion and late punctuate hyperfluorescence are seen at late-phase angiograms in ICGA

• In ICGA, RPE changes corresponds to focal choroidal hyperpermeability which is suggested as a functional consequence of choroidal ischemia [10]

• In OCT, spatial distribution of RPE changes, subretinal fluid and neovascularization correlate with areas where pachyvessels and attenuated choriocapillaris localized [5]

• In optical coherence tomography angiography, choricapillaris flow impairment has been shown in eyes without RP epitheliopathy, however, impairment worsened in eyes with RP epitheliopathy [17].

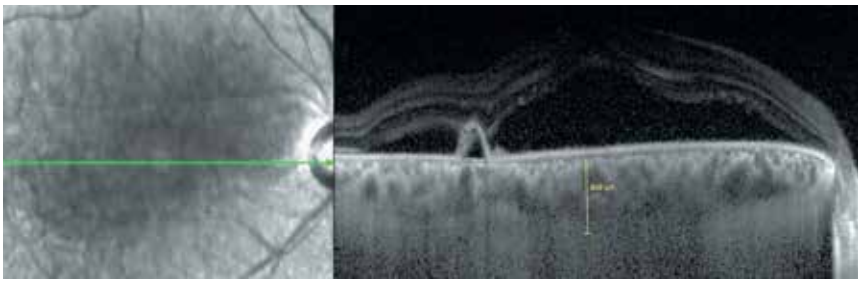

Fig. 4. Subretinal fluid, PED, thick choroid

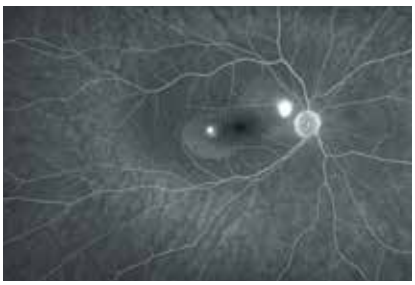

Fig. 5. Dye leakage as ink-blot pattern in fundus angiography

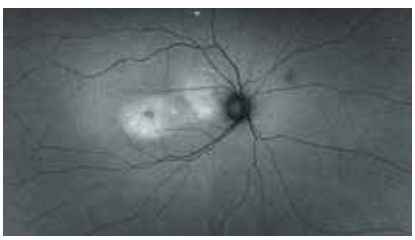

Fig. 6. Fundus autofluorescence (FAF) demonstrates an area of gravitational hyperautofluorescence

Another suggested hypothesis for pachychoroid pigment epitheliopathy(PPE) and central serous chorioretinopathy (CSC) development is increased hydrostatic pressure due to choroidal hyperpermeability [9]. Increased tissue pressure is hypothesized to disrupt gap junctions between RPE cells and cause microbreaks, slight RPE detachment from Bruch's membrane due to fluid leakage and significant RPE detachment (CSR development) if leakage increases. Duration of choroidal hyperpermeability, amount of tissue pressure and alteration of resistance capacity of RPE cells are suggested as possible factors changing the clinical spectrum in this disease group [9].

Pachychoroid pigment epitheliopathy

PPE is regarded as a forme fruste of CSC [2]. Presence of microbreaks at RPE layer is suggested as initial lesions at PPE [9]. Clinical characteristics of PPE are, reduced fundus tesellation, RPE abnormalities including motling of RPE, RPE elevation, small PED, absence of soft drusen, absence of subretinal fluid, absence of subretinal fluid history, and presence of pachychoroid features [3, 18-20]. RPE features may cause misdiagnosis with age-related macular degeneration, retinal pigment epitheliitis and pattern dystrophy [6]. Fundus appearence can be observed at the fellow eyes in other PDS diseases.

The patients with PPE are generally asymptomatic. PPE appear to be a slowly progressive disease. Clnical condition may advance to CSC and these eyes may develop type 1 neovascularization without CSC development [21].

Central serous chorioretinopathy

CSC is characterized with subretinal fluid with or without PED *(Fig. 4)*. Major predisposing factors are systemic corticosteroid and sympathomimetic use, Cushing syndrome, type A personality, hypochondria and hysteria [5, 8]. Acute form occurs generally in young to middle aged men and involves one eye. Typical imaging characteristics are dye leakage as ink-blot or smoke-stack pattern in fundus angiography *(Fig. 5)*. Choroidal hyperpermeability (presented as hyperfluorescent patches), delayed choroidal filling and venous dilation. Increased choroidal thickness and prominent pachyvessels with choriocapillaris attenuation can be observed with OCT [22]. Acute form resolves within 4 to 6 months. Chronic CSC is defined as subretinal fluid persistence greater than 6 months. Granular hypoautofluorescence with a hyperautofluorescence margin which extends towards inferior can be seen with fundus autofluorescence *(Fig.6)*. In addition, elongation of photoreceptor outer segments and outer retinal attenuations can be detected with OCT.

Treatment of CSC

- Subretinal fluid usually resolves spontaneously in acute CSC, depending on symptoms and amount of subretinal fluid some cases may not need treatment
- If the patients are symptomatic or demand rapid visual gain or have poor visual acuity in the fellow eye, subthreshold micropulse laser photocoagulation, verteporfin photodynamic therapy (PDT) and systemic mineralocorticoid antagonists are recent treatment options
- Subthreshold micropulse photocoagulation (577 nm)
- effective in eyes with focal leaks [5]
- can be an option for closing leaks close to fovea [5]
- is not appear to be effective in eyes with diffuse RPE leaks [23]
- has limited effect on reducing choroidal thickness [24]
- Verteporfin PDT
- is generally used in chronic CSC
- effective for reducing the choroidal thickness [25]
- can alter intrachoroidal structures [26]
- full-dose treatment may have some adverse effects such as transient visual loss, RPE atrophy, secondary neovascularization and choroidal ischemia or infarction [5]
- therefore half-dose PDT is recently used and provides good safety and efficacy in the treatment [27-30]
- Systemic mineralocorticoid antagonists (spirinolactone-eplerenone)
- No definite effect has been demonstrated. Some randomized controlled studies have shown beneficial effects on visual gain and subretinal fluid reduction, however, it is still a debate whether visual gain and anatomic improvement are the result of treament or natural course of the disease [31-32].

Pachychoroid neovasculopathy

This entity is described as type 1 neovascularization associated with in-

creased choroidal thickness and dilated pachyvessels in Haller's layer in the absence of age-related macular degeneration features [33]. PNV can develop in PPE and chronic CSC and may progress to PCV in some cases [34].

Type 1 neovascularization is demonstrated as shallow irregular vascularized PEDs (double-layer sign) in OCT *(Fig. 7)* and late leakage from undetermined source [35]. PNV areas corresponds to areas displaying pachychoroid features.

Detection rate of type 1 neovascularization within shallow PEDs appear to be low (29%) with dye-angiography, which means diagnosis rate of PNV appear to be underestimated with classical dye-angiography [37]. OCT angiography appear to be better than dye angiography in detecting type 1 neovascularization *(Fig. 8)*. Type 1 neovascularizations can be visualized with OCT angiography as tangled networks beneath shallow PEDs [36].

Anti-VEGF agents are the standart treatment of active neovascularization [37, 38]. Treatment free interval appear to be longer in this group compared to AMD [39, 40]. Verteporfin PDT may be combined with anti-VEGF agents in refractory cases [41].

Fig. 7. Type 1 neovascularization, thick choroid in OCT

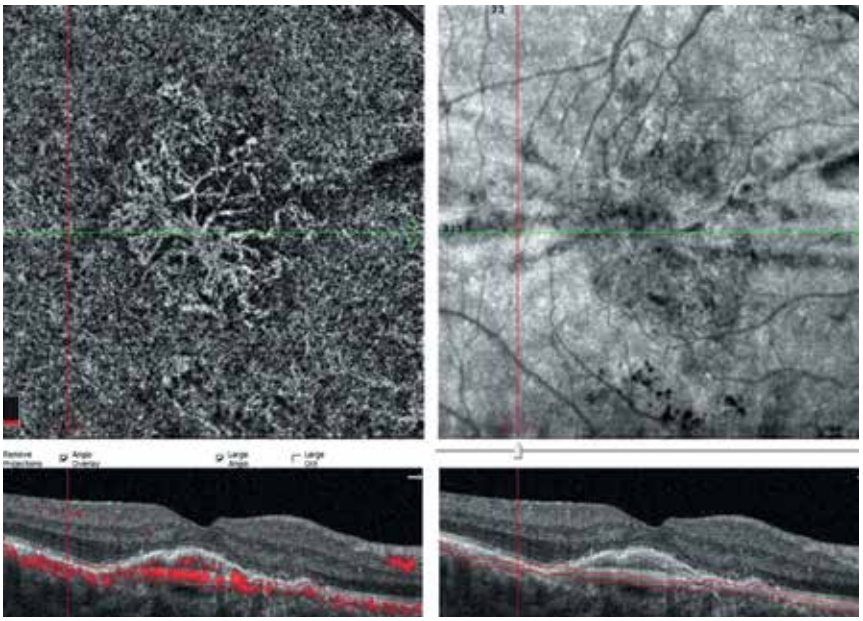

Fig. 8. Type 1 neovascularization in OCTA

Polypoidal choroidal vasculopathy

PCV is characterized with exudative maculopathy and orange nodules with PEDs clinically [42, 43]. ICGA features were described as choroidal branching networks with polypoidal dilatations by Spaide [44]. PCV was considered as a subtype of neovascular AMD. However, eyes with PCV differentiated from classical AMD because several characteristic features of AMD such as drusen, pigmentary changes and atrophy are not common in PCV. Furthermore, EDI-OCT provided new information that these eyes have thick choroid in contrast to AMD [46]. Branching networks and polyps are identified between elevated RPE and Bruch's mebrane (indicated as a variant of type 1 neovascularization) and are correlate with the areas of pachyvessels and attenuated choriocapillaris [12, 45]. Those findings suggest that PCV is a disease in pachychoroid spectrum [45].

The role of VEGF in the pathogenesis is not fully determined. Some studies have found strong VEGF expression in endothelial and RPE cells [46, 47]. The VEGF concentration has been found lower compared to AMD, but higher than normal controls [48, 49]. In addition, elevated proinflammatory cytokine levels indicate the role of inflammation in PCV [50, 51].

Atherosclerosis and other vascular wall altreations, excess endoluminal stress due to high flow rates, high blood pressure that exceeds neovascularization capacity are suggested as pathophysiological mechanisms of polypoidal lesion development [34, 52]. Polyps are the reason of fluid exudation and hemorrhage rather than branching networks [5].

Treatment of PCV with polypoidal neovascularization

- Verteporfin PDT monotheraphy
- Has favourable visual otcomes and polyp regreression at 1 year [53, 54].
- However, 50% eyes had recurrent exudation [55].
- Intravitreal anti-VEGF monotherapy
- Ranibizumab monotherapy has lower rates of visual acuity gain and polyp regression than ranibizumab combined with verteporfin PDT [56].,
- Visual acuity gain and polyp regression rates are similar between aflibercept monotherapy and aflibercept combined with verteprofin PDT [57, 58].
- Today, intravitreal anti-VEGF therapy with/without verteporfin combination is the standart treatment reg-

imen of PCV with polypoidal type 1 neovascularization.

Focal choroidal excavation

FCE is a choroidal concavity without a psoterior staphyloma or scleral ectasia. Clinical characteristics are good or mildly decreased visual acuity with near-normal overlying retinal structures [59]. FCE is divided into two patterns; conforming FCE described as no seperation between photoreceptors and RPE and preservation of ellipsoid zone and RPE within the lesion. Non-confirming FCE is described as detachment of photoreceptors from RPE and a hyporeflective space presumed as subretinal fluid. Increased choroidal thickness and FCE localization close to areas of choroidal hyperpermeability may suggest the association of FCE with PDS [59].

Peripapillar pachychoroid syndrome

PPS is a novel variant of PDS, which is described as pachychoroid features surround the optic nerve and associated with intra/subretinal fluid overlying pachyvessels and optic nerve edema in some patients [60]. Maximal choroidal thickness is around the optic disk rather than subfoveal localization. Most of the eyes present with serous PEDs or gravitational tracks. ICGA demonstrates dilated peripapillary pachyvessels and choroidal hyperpermeability [60].

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