Acta Scientific Ophthalmology (ISSN: 2582-3191)

Volume 4 Issue 12 December 2021

Short Communication

Pachychoroid: A Phenotype Not Yet Understood

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Received: September 23, 2021

Published: November 09, 2021

The term "pachychoroid" is a familiar term in retinal parlance and describes a unique disease phenotype characterized by functional and structural changes in the choroid. This phenotype is thought to play a key role in the pathogenesis of a spectrum of related retinal disorders, referred to as the "pachychoroid spectrum" [1]. The Pachychoroid spectrum predominantly include four disease conditions sharing common features - pachychoroid pigment epitheliopathy (PPE), central serous chorioretinopathy (CSCR), pachychoroid neovasculopathy (PNV), and polypoidal choroidal vasculopathy (PCV). These spectrums of diseases represent a distinct entity that has to be differentiated from typical age-related macular degeneration and other inflammatory and infilterative entities with thickened choroids. The common characteristics of this spectrum include the presence of pachyvessels represented by the dilated Hallers layer of the choroid, with overlying attenuation of the sattlers layer and choriocapillaris with or without increased thickness of the choroid [1]. The location and the overlying retinal manifestations may differ according to the clinical type of presentation.

When examined clinically, eyes with pachychoroid typically exhibit reduced fundus tessellation at the posterior pole and altered normal hue of the fundus. These changes may be evident on routine color, multicolor or red-free photography [2]. Retinal pigment abnormalities may be visible on examination. Some of these eyes may have large drusens overlying dilated choroidal vessels which are recently described as pachydrusens by some authors. ICGA has remained the standard investigation to study the choroidal circulation and it serves to delineate and demonstrate pachyvessels better [3]. Eyes with pachychoroid on ICGA may reveal delayed arterial filling in the early phase of ICGA while mid phases and late phases show punctate or patchy hyperfluorescence representing choroidal vascular hyperpermeability [3,4]. Though the phenotype is typically bilateral, sometimes the other eye may appear seemingly normal but will demonstrate similar ICGA findings. Choroidal vascular hyperpermeability is the hallmark finding on angiography and is believed to be a resultant of leaky dysfunctional outer choroidal vessels or choriocapillaris. Even though choroidal vascular hyperpermeability generally correspond to areas with increased choroidal thickening, the opposite may not always be true [5].

The advent of commercial OCT has enabled us to study choroidal thickening and morphology in great detail. Choroidal evaluation is best studied either using the enhanced depth imaging (EDI) mode of spectral domain optical coherence tomography or the swept-source optical coherence tomography which evaluates the choroidal anatomy better by virtue of its deeper penetrance [6]. The choroidal thickening may be a localized phenomenon or may be diffuse involving the fovea and adjacent regions. Although there could be variations in the estimation of the choroidal thickness due to various factors including age, diurnal variations, refractive error, axial length and differences in imaging systems, the normal subfoveal choroidal thickness (SFCT) is reported to be in the range of 299.1 ± 131.2 µm in the Indian population [7]. 'Pachy' is actually a greek word which means 'thick' and 'pachychoroid' essentially was meant to represent thick choroid. Though there is no consensus

on a particular threshold value for thick choroid, most researchers agree that a SFCT of more than 300um is suggestive of pachychoroid [1,8]. In case of extrafoveal thickening of the choroid where the SFCT may be normal, the thickness of the concerned area of interest may be at least 50um thicker compared to SFCT [8]. However estimation of the thickness is still not standardized as evaluation of the choroido-scleral interface is often unclear especially in the setting of gross thickening and pathology. Cross sectional OCT imaging and enface studies vividly reveal the pathologically dilated Haller vessels [1]. Another important characteristic is the presence of focal or diffuse attenuation of the overlying choriocapillaris and the Sattler's layer corresponding to the area of pachyvessels [8]. Even though there are pachyvessels and outer choroidal thickening, the inner layers may be sometime so attenuated that the overall choroidal thickness may be near normal. This highlights the importance of giving more focus on the altered choroidal vessel morphology rather than the mere demonstration of choroidal thickening in making a diagnosis of pachychoroid [9]. Nevertheless the documentation of an increased choroidal thickening in the setting of abnormal choroidal vascular pattern is diagnostic of 'Pachychoroid' phenotype. Evaluation of the choroidal vascular index using newer software tools specifically quantifying the luminal areas in the choroid could serve as a more reliable surrogate marker [10]. In addition to the described choroidal morphological changes, outer nuclear layer thinning and RPE layer attenuation have also been reported in pachychoroid diseases [11].

Pachychoroid pigment epitheliopathy is a pachychoroid phenotype first described by Warrow et al with characteristic but subtle RPE changes overlying pachychoroid areas [12]. In the presence of subretinal fluid and RPE abnormalities, the pachychoroid disease could be part of central serous chorioretinopathy (CSCR). Subsequently RPE-Bruch's disruption along with chronic inflammation and ischemia may predispose to local release of angiogenic factors and lead to type 1 choroidal neovascularization referred to as pachychoroid neovasculopathy (PNV) [13]. PCV is now an established pachychoroid variant characterized by multiple recurrent bilateral PEDs with exudation and hemorrhage. It is now described as aneurysmal type 1 CNV as abnormal branching vascular networks or interconnecting channels occur in the sub RPE region with the typical appearance of polypoidal changes on ICGA [14]. Treatment of pachychoroid entities are required in certain phenotypes including some cases of chronic CSCR, PNV and active PCV lesions. While pachychoroid entities with no overlying retinal fluid changes including pachychoroid epitheliopathy [12] and acute cases of CSCR are managed conservatively, chronic CSCR with diffuse epitheliopathy often require photodynamic therapy or focal laser photocoagulation [16,17]. Recently mineralocorticoid receptor antagonists have been found to be useful to manage pachychoroid manifestations. Pachychoroid neovasculopathy eyes respond well to intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections [18]. Active PCV variants with foveal threatening exudation or hemorrhage are treated with photodynamic therapy monotherapy or in combination with anti-VEGF therapy. Recently the role of Aflibercept antiVEGF monotherapy has been established in these eyes [19,20].

In addition to age related macular degeneration, other diseases that manifest thickening of the choroid should be considered in the differential diagnosis of pachychoroid disorders. Uveitic entities like Vogt-Koyanagi Haradas disease, posterior scleritis and granulomatous disease entities such as tuberculosis, sarcoidosis and intraocular tumors including intraocular lymphoma, choroidal hemangioma and choroidal metastases should be ruled out by relevant investigations. However, the presence of typical imaging features suggestive of pachychoroid pathology and the absence of systemic conditions and signs of intraocular inflammation would support the diagnosis of pachychoroid disease.

Pachychoroid thus represents a variable phenotype representing specific choroidal changes of clinical significance. Although our understanding of these disorders has expanded, there are still many concerns regarding the nomenclature, definition, pathophysiology and management of these disorders. A review of literature on this entity will reveal that there is no unifying definition and different studies have used various parameters to describe this entity [21]. A consensus on pachychoroid terms is therefore the need of the hour. What is currently understood is that variable pathogenic mechanisms may be at play including resistance of the RPE to fluid/hydrostatic pressure imbalance, variable degrees of associated ischemia and/or inflammation and neovascularization which lead to the various manifestations of this unique spectrum of diseases. Whether the primary pathology is in the inner choroid with choriocapillary attenuation and secondary compensatory outer choroidal vascular dilatation, choroidal congestion and hyperpermeability or is the primary event predominantly involving the outer choroidal

blood vessels with consequent overlying choriocapillaris atrophy remains poorly understood. The heterogeneity in presentation, overlapping structural and functional choroidal changes and the possible transition from one type to the other has however drawn investigators and clinicians towards this enigmatic spectrum of disorders. Recently Focal choroidal excavation (FCE) and Peripapillary pachychoroid syndrome (PPPS) have been added to the spectrum of pachychoroid diseases [22,23]. The current treatment paradigm to manage these disorders however aims at addressing the exudative manifestations and abnormal vasculature. Newer imaging modalities and software advancements will possibly provide more information about the structure and function of the choroid, better understand blood flow and help us define, classify and treat these diseases better.

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