The Greek root word παχύς, or “pachy,” means “thick,” so the pachychoroid spectrum of diseases share a common feature: a thickened choroid. A number of conditions have been categorized under the pachychoroid spectrum, including uncomplicated pachychoroid, central serous chorioretinopathy, pachychoroid pigment epitheliopathy, pachychoroid neovascularization, aneurysmal type 1 neovascularization / polypoidal choroidal vasculopathy, focal choroidal excavation, and peripapillary pachychoroid syndrome. However, as our understanding of this group of conditions has deepened, the focus has shifted toward elucidating what may represent a common etiopathogenesis.

Improvements in retinal imaging technology over the last decade, particularly in optical coherence tomography, have allowed greater resolution, quantitation, and understanding of the choroid in both healthy and diseased states. Many factors affect choroidal thickness, including age and axial length; therefore, diagnosis of a pachychoroid spectrum condition often relies more now on identifying large pachyvessels in Haller’s layer than the numerical choroidal thickness, as well as other clinical findings such as reduced fundus tessellation and visibly dilated choroidal vessels.

This installment of Practical Retina benefits from the expertise of K. Bailey Freund, MD, from Vitreous Retina Macula Consultants of New York in Manhattan, who has been one of the pioneers in describing this group of conditions and postulating mechanisms for a shared etiology. Dr. Freund updates the retina community on the current understanding of the pachychoroid spectrum of diseases.

Pachychoroid Disease

by K. Bailey Freund, MD

In 2013, the term “pachychoroid” was introduced by Warrow et al. in a description of patients manifesting retinal pigment epithelium (RPE) disturbances over areas of choroidal thickening in eyes lacking objective findings indicative of prior episodes of subretinal fluid (Figure 1). The authors suggested that pachychoroid pigment epitheliopathy (PPE) might be a forme fruste of central serous chorioretinopathy (CSC). They noted that the findings of PPE resembled those often found in the fellow eyes of patients with unilateral CSC, which included dilated choroidal veins and choroidal vascular hyperpermeability (CVH) seen with indocyanine green angiography (ICGA). The majority of eyes had “drusenoid RPE lesions,” which, unlike soft drusen seen in typical AMD, had irregular shapes and were usually found as isolated lesions over large choroidal vessels. Although most of their patients had minimal or no visual symptoms and had findings remaining stable over extended follow-up intervals, they often carried more ominous diagnoses such as age-related macular degeneration (AMD), adult-onset pattern dystrophy, punctate inner choroidopathy, and retinal pigment epitheliitis.

Warrow et al. suggested that PPE was likely part of a broader spectrum of pachychoroid-related entities and predicted that PPE eyes might subsequently develop type 1 (sub-RPE) macular neovascularization (MNV), which could then produce aneurysmal changes commonly known as “polyps.” The authors proposed the term “pachychoroid neovascularization” (PNV) to describe type 1 MNV evolving from PPE. They noted that distinguishing PNV from MNV secondary to prior CSC could be challenging. Subsequent evidence that PNV might evolve from PPE was provided by Pang and Freund.

In the intervening years since the original description of PPE, interest in a pachychoroid disease spectrum has grown quickly. A PubMed search using the term “pachychoroid” showed 144 citations, of which 56 were from 2019. Much of the work in refining this disease mechanism has occurred in Asia, where patients with neovascular AMD often lack the soft drusen defining typical AMD but instead have pigmentary abnormalities and choroidal features that are indistinguishable from those of PPE and PNV. Recognition that the branching vascular network (BVN) giving rise to the aneurysmal lesions of polypoidal choroidal vasculopathy (PCV) is histologically a form of type 1 MNV led Dansingani et al. to propose the term “aneurysmal type 1 MNV” to describe these neovessels (Figures 2 and 3). An obvious conclusion is that many cases of PCV presenting in eyes with pachychoroid disease features evolve from PNV. Given this presumed association, this author currently uses the term “aneurysmal PNV” to describe these findings while using the more generic term “aneurysmal type 1 MNV” to describe...
the occurrence of this neovascular lesion subtype when seen in other diagnoses such as typical AMD, peripheral hemorrhagic chorioretinopathy, and over choroidal nevi. Since approximately 60% of the world’s population is Asian and up to 50% of neovascular AMD patients in Asia present as PCV, determining the etiologic factors contributing to pachychoroid disease expression would have a significant impact on global public health. To this end, greater emphasis on defining pachychoroid-related disorders and determining their underlying causative mechanism has moved beyond the singular finding of increased choroidal thickness. Recently, Cheung et al. proposed that the term “pachychoroid disease” be used to distinguish eyes with pathologic sequelae seen in association with abnormally dilated choroidal vessels from seemingly healthy eyes with thick choroids (“pachychoroid” or “uncomplicated pachychoroid”). Recognition of specific clinical and multimodal imaging findings present in eyes with pachychoroid disease continues to evolve, but many experts have focused on the following features: 

1. Increased choroidal thickness co-localizing with areas of fundus abnormalities, which may be focal or diffuse.
2. Clinically visible dilated choroidal vessels or reduced fundus tessellation in eyes with diffuse choroid thickening.
3. Attenuation of the inner choroid in areas of fundus pathology.
4. ICGA choroidal hyperpermeability and reduced inner choroidal flow signal shown with optical coherence tomography angiography.
5. Pachyvessels (dilated veins of Haller’s layer) often co-localizing with overlying disease manifestations.
6. Drusenoid RPE lesions (recently renamed “pachydrusen” by Spaide). The etiology of pachychoroid disease remains poorly understood. Many experts believe CVH precedes many of the other disease manifestations and that, over time, eyes develop reduced inner choroidal blood flow, producing RPE changes, outer retinal ischemia, and, if genetically predisposed, type 1 MNV. There are likely mechanical effects from pachyvessels, which further compromise choriocapillaris blood flow, although the etiology of the pachyvessels themselves is poorly understood. Downstream resistance to venous outflow at the vortex veins has also been hypothesized to be contributing to choroidal congestion. As older patients with pachychoroid disease may show additional findings of typical AMD such as soft drusen, cuticular drusen, and reticular pseudodrusen (subretinal drusenoid deposits) there is, at times, additional complexity to the presentation.

Figure 1. Multimodal imaging of pachychoroid pigment epitheliopathy in the right eye of a 64-year-old white male. Confocal color photograph (A) shows central areas of hypo- and hyperpigmentation, which correspond to areas of hypo- and hyperfluorescence on fundus autofluorescence (B). Early phase (C) and mid-phase (D) indocyanine green angiography (ICGA) show dilated choroidal veins (pachyvessels) within the macula and choroidal vascular hyperpermeability. Horizontal swept-source optical coherence tomography (SS-OCT) B-scan through the fovea and optic nerve shows attenuation of the inner choroid over pachyvessels (E). There are focal disruptions of the outer retinal bands and intraretinal pigment migration overlying the pachyvessels. En face structural SS-OCT (F) of the choroid demonstrates an abnormal vascular pattern in which the large veins fail to taper as they approach the central macula. En face SS-OCT angiography (G) showing reduced central choriocapillaris flow signal.
Figure 2. Progression of pachychoroid neovasculopathy to aneurysmal pachychoroid neovasculopathy (polypoidal choroidal vasculopathy) in the left eye of a 65-year-old Asian female. Color photograph (A) shows a central retinal pigment epithelium (RPE) disturbance with scattered drusenoid RPE lesions (pachydrusen). En face swept-source optical coherence tomography (SS-OCT) angiography (B, C) corresponding to the red square in A shows an aneurysmal lesion (white arrow) evolving from a branching vascular network that is composed of type 1 (sub-RPE) macular neovascularization. The magenta lines in the corresponding SS-OCT B-scans (D, E) show the segmentation boundaries used to create B and C. The yellow arrow in E indicates the aneurysmal lesion. The green arrow in A indicates the location and direction of the SS-OCT B-scans.

Figure 3. Aneurysmal pachychoroid neovasculopathy (polypoidal choroidal vasculopathy) in the right eye of a 58-year-old white female. Color photograph (A) shows mild retinal pigment epithelium (RPE) changes and large choroidal vessels. Early phase indocyanine green angiography (ICGA) (B) shows dilated choroidal veins (pachyvessels) and a hyperfluorescent aneurysm (black arrow). Late-phase ICGA (C) shows choroidal vascular hyperpermeability surrounding pachyvessels. Spectral-domain optical coherence tomography B-scan (D) corresponding to the green line in A demonstrates attenuation of the inner choroid over pachyvessels with splitting of the overlying retinal pigment epithelium-Bruch's membrane complex by type 1 macular neovascularization (double layer sign). There is a temporal aneurysm (red arrow) with overlying subretinal fluid.
Although some progress has occurred in our understanding of the pachychoroid disease spectrum, there are many questions that remain unanswered, such as why some eyes with very thick choroids show no evidence of RPE alterations or SRF (uncomplicated pachychoroid). Genetic, behavioral, and environmental mechanisms that influence the characteristic choroidal findings of the pachychoroid disease phenotype remain to be clarified, as does the reason why only some eyes with non-neovascular pachychoroid disease entities, PPE and CSC, progress to the neovascular variants (PNV and aneurysmal PNV). Answers to these questions could lead to therapies aimed at modulating pathologic choroidal changes across the entire pachychoroid disease spectrum.

In summary, advances in retinal imaging have enabled the recognition that choroidal changes first identified in eyes with CSC seem to influence a much broader range of retinal disease. Since the first description of PPE in 2013, investigators have identified specific changes in choroidal structure which seem to distinguish diseased eyes from those with a benign increase in choroidal thickness. Clinicians should consider the possibility of pachychoroid disease in any patient with RPE changes of unclear origin or in older patients with presumed degenerative macular changes appearing atypical for AMD. Identifying areas of reduced inner choroidal perfusion marked by choroidal vascular hyperpermeability on ICGA and pachyvessels on OCT appear to be key findings which can assist clinicians in identifying this disease mechanism in their patients.

REFERENCES

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