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COMMENT

Vortex vein anastomosis and pachychoroid—an evolving understanding

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The pachychoroid spectrum of diseases including central serous chorioretinopathy (CSC), pachychoroid neovasculopathy (PNV), and polypoidal choroidal vasculopathy (PCV) constitute key areas of interest in the recent past [1, 2]. However, the pathophysiology of pachychoroid remains an enigma. Diffusely thickened choroid and pachyvessels are the predominant characteristics of this spectrum of disease with the exception of some cases of PCV that have a thin choroid [1, 3–5]. The terms thick choroid and pachyvessels have been difficult to define because of physiological variability. Nonetheless, it has been proposed that a choroid thicker than 300 µm and the presence of pachyvessels, which can be seen on enhanced depth spectral domain optical coherence tomography along with engorged vascular profiles observed on indocyanine green angiography (ICG) can be used by clinicians to make this diagnosis [1, 2, 6]. Several researchers have suggested that congestion of the vortex veins, leading to choroidal congestion can result in pachychoroid disease [6–9]. Alternative pathophysiological reasons include obstruction at the level of ampulla of the vortex veins [6]. To date, there is no clear understanding as to why neovascularization occurs predominantly at the peripapillary area in pachychoroid disease. Study of the veno-venous anastomosis between the vortex veins located in different quadrants of the choroid may help in understanding the pathophysiology of the pachychoroid spectrum of diseases.

Recently, Spaide et al. described choroidal flow as analogous to that of the cerebral venous circulation and highlighted the potential role of vortex vein as a resistor in the eye [10]. Vortex veins serve as choroidal drainage routes passing through the sclera. Horizontal and vertical watersheds divide the choroidal vasculature into four quadrants. Each quadrant is served by a different set of vortex veins. Vortex veins typically range from 3 to 8 in number, with 65% of people having 4 or 5 [11, 12]. In the past, researchers have tried to understand the relationship and impact of vortex vein occlusion using experimental animal studies [13]. Recent advances in multimodal imaging and ultrawidefield ICG angiography has allowed for better visualization and detailed assessment of vortex veins in defining their patterns, extent, and coverage from the center of the macula to the ampulla [6]. It has been shown that there is an asymmetry in choroidal venous outflow and asymmetric dilation of vortex veins in different quadrants in cases of CSC and PNV [7, 14].

Anastomosis between vortex veins in different sectors may act as a decongestive mechanism within the choroid and this observation may serve to explain the wide range of findings in the pachychoroid spectrum. Matsumoto et al., have demonstrated that the normal horizontal water shed between the superior and inferior vortex vein disappeared in 90% cases of PNV and was replaced by anastomosis [15]. Later, the same group has reconfirmed this finding in CSC and PCV in addition to PNV [16]. They also demonstrated anastomosis between the superior and inferior vortex veins in 90.2% of CSC, 95.1% of PNV, and 100% of PCV [16]. They have proposed that this could be the result of remodeling in the vortex veins due to longstanding asymmetric congestion of the choroid. Similarly, Spaide et al., found

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intervortex anastomosis in superonasal, superotemporal, and inferotemporal sectors in patients who had CSC, peripapillary pachychoroid syndrome, pachychoroid associated neovascularization, and pachychoroid [17]. However, the two groups of authors used different methods of assessment. Matsumoto et al., used en face OCT images (12 × 12 mm), OCT angiography (3 × 3 mm), and posterior pole ICG whereas, Spaide et al., used widefield ICG angiography which covers a wider area and has the ability to show peripheral anastomosis. This latter method allowed Spaide et al., to remark on all four choroidal quadrants whereas, the findings of vascular connections described by Matsumoto et al., only in the superotemporal and inferotemporal regions may be related to the fact that imaging was restricted to the central retina. Nonetheless, both groups emphasize the importance of venous anastomosis within the choroid at the macula and the peripapillary area as one of the pathophysiological factors for the development of pachychoroid associated neovasculopathy and PCV.

This emerging understanding on vortex vein dilation and anastomosis provides evidence to support the view that progression can occur from CSC to PCV. Matsumoto et al., have demonstrated that central choroidal thickness (CCT) was highest in CSC followed by PNV and PCV [18]. Furthermore, they also showed that in CSC, the mean diameter of the vortex veins is significantly larger and the CCT correlates with the mean diameter of the vortex veins [18]. These observations suggest that the initial stage of CSC occurs as a consequence of congestion of vortex vessels which in turn leads to a thick choroid. Over time, due to overwhelming congestion, veno-venous anastomoses are formed amongst different vortex veins as a decongestive mechanism and leads to a reduction in the choroidal congestion and hence the thickness. Chronic congestion and formation of pachyvessels cause compression of choriocapillaris which results in ischemia of the outer retina, which in turn can trigger the development of neovasculopathy. Over a long period of time, PNV vessels mature and develop aneurysmal dilations resulting in PCV. The above hypothesis explains why CSC is common in the young and PCV in the older population.

Although, the concept of intervortex venous anastomosis is exciting, there are additional areas to be explored to strengthen the concept. Control groups derived from normal age-matched populations need to be studied well in large numbers. Matsumoto et al., showed that 40% of the normal population also had anastomosis between superior and inferior vortex veins [16]. Similarly, Spaide et al., had 22% cases in the control group who had anastomosis [17]. Furthermore, the vortex veins of the nasal sector require additional study to determine why connections in this sector are not common [17].

We propose that, going forward, the sclera too must be evaluated as it is the site where the veins are likely to encounter resistance to flow. Studying flow through the sclera might shed light on why only some people develop choroidal congestion leading to the anastomosis, why don't all cases of CSR progress to PCV, and why normal eyes can also exhibit anastomosis without any clinical disease manifestation.

To summarize, intervortex anastomosis opens up a new research avenue to further evolve our understanding about the pathophysiology of pachychoroid spectrum of diseases.

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Compliance with ethical standards

Conflict of interest AS—consultant: Novartis India, Allergan Global, Intas India, Bayer India. NP: none. NK: none. FB—consultant: Allergan, Bayer, BoehringerIngelheim, FidiaSooft, Hoffmann-La Roche, Novartis, NTC Pharma, Sifi, ThromboGenics, Zeiss. BDK—clinical research: Alcon, Alimera, Allegro, Allergan, Apellis, Clearside, Genentech, GSK, Ionis, jCyte, Novartis, Regeneron, ThromboGenics; consultant: Alimera, Allegro, Allergan, Cell Care, Dose, Eyedaptic, Galimedix, Genentech, Glaukos, Interface Biologics, jCyte, Novartis, Ophthotech, Regeneron, Revana, TheravanceBiopharma, AL—consultant: Allergan, Novartis, Roche, Notal Vision, FiorSightsLabs, Beyeonics, Bayer Healthcare. CR—consultant: Allergan, Chengdu Kanghong, Genentech/Roche, Novartis, Kodiak, Notal, Merck, Shire-Takeda, Adverum, Graybug, Eyepoint; research support: Allergan, Chengdu Kanghong, Genentech/Roche, Novartis, Kodiak, Iveric, Adverum. UC—personal fees from Allergan, Bayer, Novartis, and Roche; and is a data safety and monitoring board member for Bayer.

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