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BRIEF COMMUNICATION

Remodeling of the choroidal vasculature and the role of choriocapillaris perfusion drop in pachychoroid diseases: a global rheological approach

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Key messages

What is known

- Pachychoroid, either diffuse or focal, is observed in various different diseases, that remains uncompletely explained and a need for a global approach of comprehension has been emphasized.

What is knew

- Universal adaptative rheology laws suggest that choriocapillaris flow drop may be both the cause and the consequence of venous stasis.
- Choroidal venous congestion and anastomosis may be viewed as adaptative modifications of the venous wall tone of mere rheological nature, in related diseases having in common hypoxia and inflammation as mechanistic causative factors.

The relationship between diffuse pachychoroid, focal pachyvessels, delayed choroidal arterial filling, and pachyvein hyperpermeability is incompletely illuminated, and a need for a global approach to comprehension has been emphasized.

Rheology laws apply allover. According to the Fahraeus-Lindqvist effects, the venous system is capacitative, at slow velocity, high viscosity, low pressure and shear stress [1]. According to the Hagen–Poiseuille law, vessel diameter is one component of flow regulation [2]. The veno-arteriolar reflex (VAR) is adaptative to arterial/capillaris supply deficiency: venous dilation, nitrite oxide (hypoxia-induced), and orthosympathetic-dependent, generates a pressional slope that aims to restore efficient capillary flow, tissular arterial oxygen and nutrients supplies [3]. In case pressure and volume perfusion flow drops overwhelm the venous parietal compliance, tissular hypoxia develops, itself an additional stimulus for venous dilation that generates inflammation, which itself worsens hypoxia [4].

The choriocapillaris is an open system in total continuum without glomi: venous networks originate at low pressure and follow a progressive natural percolation from small to larger vessels. The choroidal venous drainage is segmented but "heavily anastomotic" [5], an overlooked anatomical feature that explains physiological choroidal veno-venous anastomosis. This is illustrated by step-by-step analysis of

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dynamic indocyanine green cine video angiography. Venous flow fills in a simultaneous and homogeneous way, including in the areas of arterial watershed zones. Veno-venous anastomosis is visible after the choriocapillaris flooding perfusion. In case of delayed/nonhomogeneous ciliary arterial supply, which generates ischemia, venous diameter is nonhomogeneous in territories of capillary closures, i.e., increased due to the operational VAR to improve their volume and pressure filling within the limits of its resilience capacity. In case it is overwhelmed, ischemia/hypoxia are no longer compensated, and areas of capillary non perfusion persist. Ultra-wide and flattened corresponding drainage veins indicate terminal exhausting of the VAR. In physiological conditions, venous pulsation is damped by the resistive capillary filter, and the gradient pressure between systolic and diastolic venous pressures drives the flow orientation (Poiseuille law) [2]. Within the endocular milieu, the choroidal venous circulation must overcome the intraocular pressure. Pulsatile choroidal drainage and retrograde flow may become visible in case of capillary bypass, venous anastomosis with a vein of higher pressure, or arterio-venous anastomosis, and/or when the systolic venous pressure raises above the intraocular pressure and the gradient venous pressure raises above 1 mmHg or more.

Choriocapillaris perfusion drop may reflect upstream arterial supply deficiency but also downstream postcapillary venules and veins dysfunctioning. Downwards flow blockade/slowing down may originate either from outside the venous walls (pathophysiology emphasized in the pachychoroid literature) and/or from the wall components and/or within the venous lumen (postcapillary "leucocyte block"). Persistent infections are under intense scrutinization in the pandemic era and in neurodegenerative diseases: they impair epithelial apoptosis and autophagy, drive innate, adaptive, and autoimmunity activations with inflammatory infiltration, increase resistances, generate microvascular occlusions, and venous hyperpermeability. Chronic damage of the postcapillary endothelial glycocalyx, e.g., by immune complexes, would be coherent with the long-reported infection-related putative etiopathogeny of central serous choroidopathy. In some age macular degeneration cases with focal pachyvessels, it might add itself to individual causes of choriocapillaris perfusion drop, either upstream systemic (e.g., atherosclerosis, hypertension, carotid stenosis, and sleep apnea) and/or senescence-related upstream and downstream impairment of all players of the choroidal vascular system, i.e., from endothelial cells (via glycocalyx shedding and hematopoietic stem exhaustion), to immune system aging and inflammaging, smooth vascular muscles innervation, pericytes loss, increased choroidal extracellular matrix and scleral stiffness, and perivascular spaces modifications.

Altogether, we suggest that in related diseases having in common hypoxia and inflammation as mechanistic causative factors, diffuse and focal venous choroidal remodelings are adaptative modifications of mere rheological nature.

Author contribution Richard Luscan and Claude Boscher equally participated to the conceptualization and writing of the present letter. Ozlem Erol performed the clinical investigations, and contributed to the letter's formatting.

Declarations

Conflict of interest The authors declare no competing interests.

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