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CORRESPONDENCE

"Choroidal caverns" spectrum lesions

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To the Editor:

Choroidal structures are visualized thoroughly by enhanced depth imaging optical coherence tomography (EDI-OCT) and choroidal OCT angiography (OCTA) with ultra-high resolution as a result of developments in the depth-resolved imaging approach. Recently, "choroidal caverns" lesions, associated with age-related macular degeneration (AMD) and pachychoroid diseases, were demonstrated by EDI-OCT and swept-source OCTA, in accord with histopathological results [1–3].

However, we consider that the term "choroidal caverns" lesions as an entity of the choroidal spectrum lesions, including intrachoroidal cavitation, choroidal cleft, and choroidal lipid globule caverns. In particular, some of the lesions have inherent correlations. The present review investigates the multimodal imaging characteristics of choroidal caverns lesions for similarities and differences to find inherent relationships among these lesions. This study was reviewed and approved by the Institutional Review Board of the First Hospital of China Medical University, and written informed consent was obtained from all patients for publication.

Evidently, the histopathology of retinoschisis involves the congenital or secondary splitting of the neurosensory retina due to varied reasons, including X-linked retinoschisis, optic disk coloboma, and myopia [4]. Especially, retinoschisis is a common sign in patients with high myopia. The age-related elongation of eyes and expansion of staphylomas contributes to macular foveoschisis [5]. Generally speaking, foveoschisis occurs secondary to the inability of the retina to stretch during scleral enlargement.

Freund et al. described the OCT characteristics of peripapillary intrachoroidal cavitation [6], based on which we believe that similar mechanisms might operate in retinoschisis and myopic intrachoroidal cavitation. The choroid is retracted away from the optic nerve margin, because the collagenous limiting tissue of Elschnig between the choroid and the optic nerve is broken during staphyloma [7]. Moreover, the sinkhole in myopic conus and myopic colobomas attribute to the coalescence of peripapillary intrachoroidal cavitation with optic nerve head [8]. With aging, a structurally weak myopic conus may absorb less fluid originating from the vitreous cavity.

Thus, in myopia, the elongation of the ocular axis induces schisis of the choroid. Vitreous liquefaction flows into the intrachoroidal cavitation. So, we contemplate that intrachoroidal cavitation could be named "choroidoshisis", based on the similarities between retinoschisis and intrachoroidal cavitation (Fig. 1).

In OCT, a choroidal cleft in AMD is regarded as a hyporeflective space either under the sub-retinal pigment epithelium (RPE) neovascular tissue [9], or between choroidal neovascularization (CNV) and its Bruch's membrane [10]. Although hyporeflective changes mainly located at RPE level, but hyperreflective changes were predominant in the choriocapillaris, Sattler's and Haller's layers [11]. The choroidal cleft is usually accompanied by a multilayered RPE detachment (PED) [12].

Choroidal cleft is present in 22.2% of eyes with polypoidal choroidal vasculopathy (PCV) [9]. Shin et al. reported that about 61.1% of eyes showing an RPE tear with AMD have fibrovascular PED with underling contractile CNV and a cleft [13]. Herein, we introduce two cases to demonstrate the choroidal cleft in retinal angiomatous proliferation and PCV (Fig. 2). The polypoidal lesion in OCTA showed a round hypoflow structure with a hyperintense

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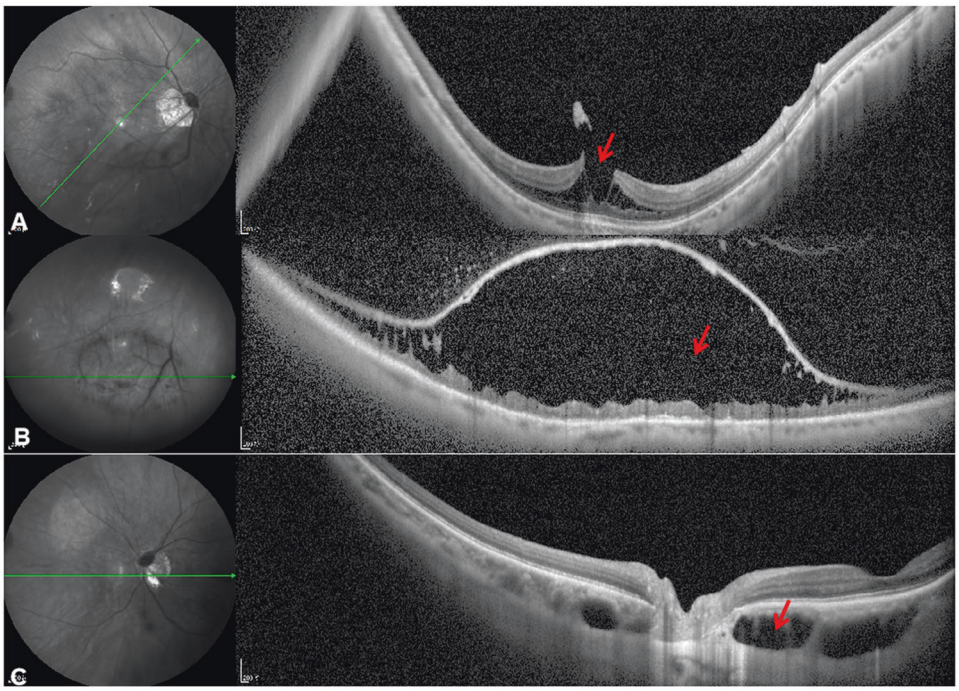

Fig. 1 The comparison between retinoschisis and intrachoroidal cavitation. **a** Widefield structural optical coherence tomography (OCT) showed laminar macular hole and retinoschisis due to elongation of ocular axis in a patient with high myopia. **b** Widefield structural OCT showed a peripheral retinoschisis (red arrow) without any retinal hole in another patient. **c** Widefield structural OCT revealed several peripapillary intrachoroidal cavitations (red arrow) as a result of elongation of ocular axis in another patient with high myopia.

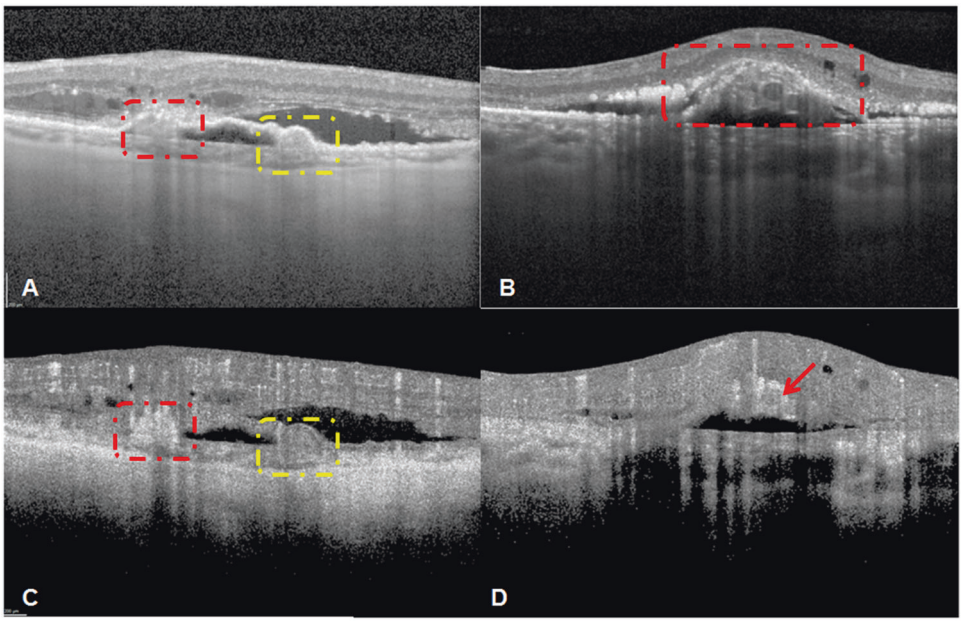

Fig. 2 The choroidal cleft in RAP and PCV. a Structural OCT in a patient with RAP showed intra-retinal neovascularization (red dots box), sub-RPE fibrosis (yellow dots box), and choroidal cleft in between. **b** Structural OCT in a patient with PCV showed RPE detachment; a fusiform complex of highly organized, layered, hyper-reflective material; a polypoidal lesion, and an underlying spindle-shaped hyporeflective space (red dots box). **c** Cross-sectional OCTA of **a** revealed the blood signal of intra-retinal neovascularization (red dots box), and no vascular signal in both the choroidal cleft and sub-RPE fibrosis lesion (yellow dots box). **d** Cross-sectional OCTA of **b** showed no vascular signal in the choroidal cleft as well. Interestingly, the polypoidal lesion appeared to be a round hypoflow structure surrounded by a hyperintense halo (red arrow). RAP retinal angiomatous proliferation, PCV polypoidal choroidal vasculopathy, OCT optical coherence tomography; OCTA OCT angiography, RPE retinal pigment epithelium.

halo, as a result of blood circulation only at the aneurysmal wall, the turbulent blood flow inside the polyp, or fringe washout artefact [14].

Two distinct factors might contribute to cleft development. First is the accumulation of fluid originating from the active CNV components among the PED materials, forming

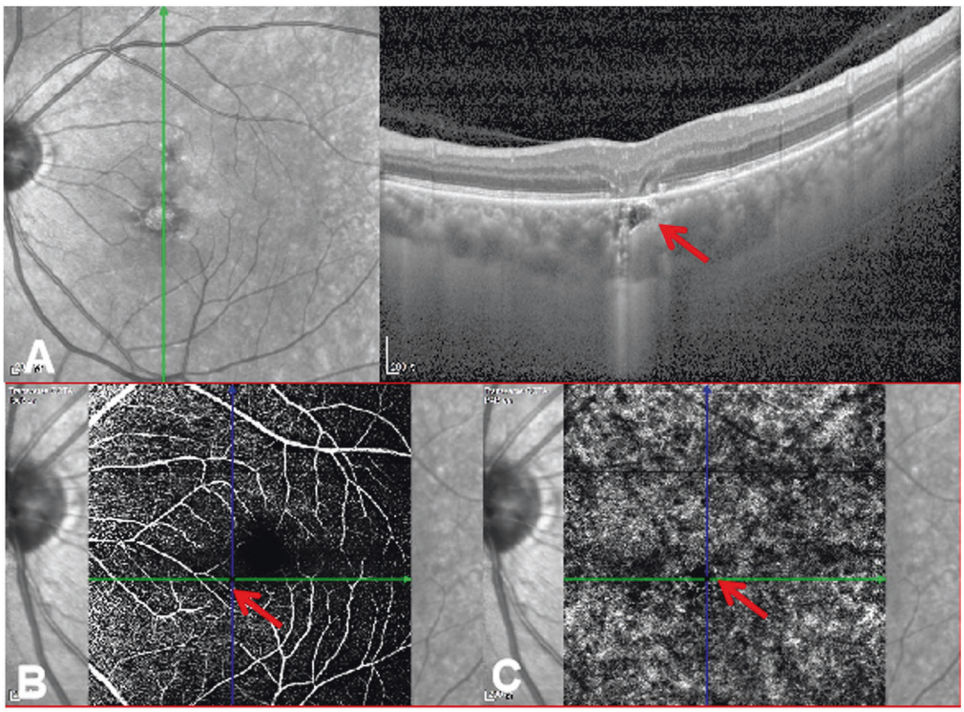

Fig. 3 Optical coherence tomography angiography of choroidal lipid globule caverns in dry age-related macular degeneration. a EDI-OCT showed parafoveal geographic atrophy and underlying choroidal lipid globule caverns (red arrow) with posterior tail of hypertransmission. **b** En face OCTA revealed normal flow signal with superficial segmentation (red arrow). **c** En face OCTA visualized no flow signal choroidal lipid globule caverns in choroidal segmentation (red arrow). EDI-OCT enhanced depth imaging optical coherence tomography, OCTA optical coherence tomography angiography.

a space resulting in a cleft [9]. Second is the contraction of sub-PED materials, that occurs spontaneously or after anti-vascular endothelial growth factor treatment or photo-dynamic therapy (PDT) [15]. A histopathological study of occult AMD specimens reported a cleft between the Bruch's membrane and underling CNV [16].

OCTA provides precise signals of true blood flow based on red cell motion, especially in high-risk cases and those with inconclusive fluorescein angiography and OCT findings [17]. Cross-sectional OCTA images show no blood in the choroidal clefts and the location of CNV with fibrosis, comparable with previous histopathological findings.

Moreover, an elaborate and sizable vessel complex in OCTA possibly supports the overlying photoreceptors and RPE, resulting in a lower incidence of geographic atrophy [18, 19], ensuring the viability of the photoreceptor population through RPE preservation, as well as maintaining good visual acuity [20].

Friedman and Smith [21] firstly described the extracellular lipids globules in postmortem eyes. These similar sizable globules in similar tissue locations in healthy individuals and patients with AMD were perhaps a lipid depot related to photoreceptor metabolism [1]. So choroidal lipid globule caverns and choroidal clefts share similar contents in AMD cases. Moreover, 52% of pachychoroid eyes showed choroidal lipid globule caverns, with increased choroidal thickness and dilated Haller's layer veins [3]. These extracellular and extravascular globules [1] could represent deposition of lipid droplets in the choroidal stroma.

OCT characteristics of choroidal lipid globules as caverns include the presence of a focal oval hyporeflective region located mainly in the choroidal Sattler's and Haller's layers, and the posterior tail of hypertransmission and none flow signal on OCTA. Querques et al. also reported that choroidal lipid globule caverns was a relatively rare and unique lesion in geographic atrophy eyes, appearing as angular hyporeflective cavities, often with internal punctate or linear hyperreflectivity [2]. Furthermore, we demonstrated a case of geographic atrophy with choroidal lipid lesions and failed to visualize any flow signal in OCTA (Fig. 3).

Some authors insist on differentiating choroidal lipid globule caverns from choroidal clefts, for that the former are choroidal origin, while the latter are only hyporeflective spaces secondary to CNV [15]. However, we consider that choroidal lipid globule caverns and choroidal clefts have inherent correlations based on similar mechanisms and lipid content. For example, in some cases, the choroidal cleft can be partitioned into irregularly curve-shaped hyporeflective spaces by fibrovascular hyperreflective septi, resembling choroidal lipid globule caverns [22].

The vascular degeneration of choroidal lipid globule caverns remains controversial. Some authors believe that choroidal lipid globule caverns correspond to hypoperfused or regressed vessels. Choroidal caverns may originated from nonperfused vessels, and the persistent stromal pillars could represent the original location of the vessels [2]. Similarly and interestingly, we observed the regression of choroidal lipid globule caverns after PDT in a patient with

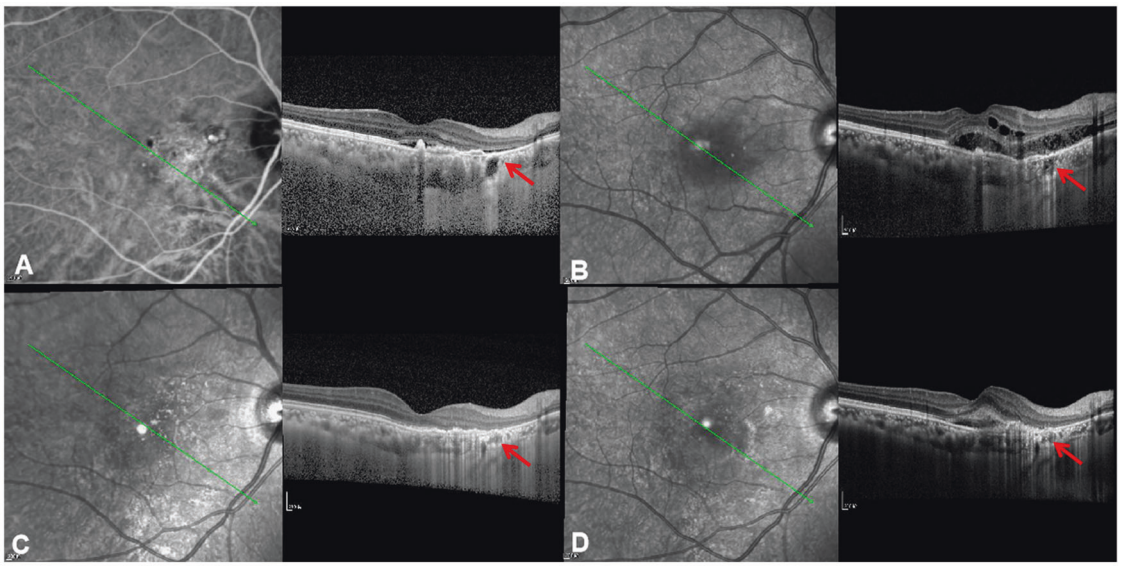

Fig. 4 The regression of choroidal lipid globule caverns after photodynamic therapy in polypoidal choroidal vasculopathy. **a** ICGA and EDI-OCT confirmed the diagnosis of PCV with choroidal lipid globule caverns (red arrow). **b** The globule caverns collapsed 1 day after PDT (red arrow). **c** The globule caverns appeared to be atrophic at 1 week (red arrow). **d** The globule caverns relapsed. ICGA indocyanine green angiography, EDI-OCT enhanced depth imaging optical coherence tomography, PCV polypoidal choroidal vasculopathy, PDT photodynamic therapy.

PCV. The globule caverns collapsed immediately after PDT, atrophied at 1 week, and finally relapsed (Fig. 4). To our knowledge, the changes in the globule caverns after PDT were identified with abnormal choroidal vessels, supporting the vascular degeneration theory.

However, Querques et al. [2] debated that there were significant differences between choroidal lipid globule caverns and choroidal vessels, for example, blood flow and vessels made the choroidal vessels slightly intraluminal hyperreflective with a characteristic hyperreflective border. In contrast, choroidal lipid globule caverns failed to visualize perfused choroidal vessels in both indocyanine green angiography and OCTA [2]. If vessels were to involute, occlusive fibro intimal thickening with collagenous proliferation should be detectable histologically, with mild hyperreflectivity on OCT images. We speculate that the nonreflectivity observed in lipid globule caverns may represent the tiny hyperreflective border beyond the limitation of current OCT devices, and a possible blurring by media opacities. Whether choroidal vessels appear to be thin and hyporeflective by regression, occlusion, haemostasis, or some combination requires further investigation.

Based on similar morphology, we propose to classify choroidoshisis, choroidal cleft, and lipid globule caverns into the choroidal caverns spectrum lesions. We consider that ocular axis elongation is the common aetiology for both myopic retinoschisis and choroidoshisis. In addition, we also speculate that choroidal lipid globule caverns could converge into choroidal cleft in patients with AMD. EDI-OCT and OCTA are useful tools to identify these lesions. Even so, the vascular degeneration of choroidal lipid globule caverns remains controversial.

Data availability

The imaging data used to support the findings of this study are included within the article.

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Author contributions All authors contributed equally in this work. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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