Evolution of focal choroidal excavation in ABCA4-related retinopathy

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ABSTRACT

Purpose: To report long-term evolution of unilateral focal choroidal excavation in a patient with ABCA4-related retinopathy.

Observations: A 51-year-old female with ABCA4-related retinopathy developed a small juxtafoveal defect in Bruch’s membrane in a region of macular atrophy in her left eye. In follow-up, the defect widened and subsequently developed into a focal choroidal excavation. Over the next 8 years, serial optical coherence tomography imaging illustrated the conversion of the focal choroidal excavation from conforming subtype into non-conforming subtype with eventual macular hole formation.

Conclusions and importance: The long-term follow-up of a patient with serial imaging highlights the potential dynamic nature of focal choroidal excavation in ABCA4-related retinopathy. Progressive retinal degeneration may influence focal choroidal excavation morphology and may promote macular hole formation.

1. Introduction

The detection of choroidal excavation by optical coherence tomography (OCT) in the absence of posterior staphyloma or scleral ectasia was first reported by Jampol et al. in 2006.1 The lesion was later classified as a focal choroidal excavation (FCE) and was divided into conforming and non-conforming types.2 A conforming FCE maintains apposition between the photoreceptor outer segments and retinal pigment epithelium (RPE) in the area of retinal protrusion. In contrast, the photoreceptor outer segments and RPE are separated by hypo-reflective spaces on OCT in non-conforming FCE. These lesions have been identified both in otherwise normal eyes and in eyes with pathologies such as age-related macular degeneration, polypoidal choroidal vasculopathy, and central serous chorioretinopathy.3-4 The underlying pathomechanism of FCE is not yet fully understood.

Several occurrences of FCE in the setting of chorioretinal degeneration have been described, including in patients with Best disease, Stargardt disease, pattern dystrophy, and cone dystrophy.5–7 They have also been described in patients with choroideremia.5 The majority of these cases have not depicted significant progression or expansion of the FCE over time; however, many of these reports are of limited follow-up duration.6,11 We report a case of unilateral FCE with progressive changes in a patient with molecularly confirmed ABCA4-related retinopathy. Serial spectral domain OCT (SD-OCT) images recorded over 8 years capture the lesion’s evolution, expansion, and eventual macular hole formation, highlighting the potential dynamic characteristics of FCE in retinal degeneration.

2. Case report

A 51-year-old lady with ABCA4-related retinopathy presented for routine evaluation. She had developed bilateral reduced vision, dyschromatopsia, and glare symptoms in her early 20s. Subsequently, she received a clinical diagnosis of Stargardt disease. Molecular confirmation was undertaken initially through Sanger sequencing the ABCA4 gene and more recently through a next-generation sequencing inherited retinal degeneration panel approach. This resulted in the identification of biallelic ABCA4 pathogenic variants: c.5882G>T (p.Gly1961Glu), c.3758C>T (p.Thr1253Met), and c.3050+5G>A. Segregation analysis confirmed the c.5882G>T variant as maternally inherited. The c.3758C>T variant has almost always been reported in cis with c.5882G>T and the combination has been associated with disease in multiple publications.11,12 The intronic splice variant c.3050+5G>A has also been reported as disease causing.13,14 No variants were identified in other genes that are associated with macular dystrophy. She had consented to the “Natural History of Eye Diseases Related to ABCA4 Mutations” study (NCT01736293), a National Eye Institute (NEI) clinical research protocol approved by the National Institutes of Health.

Abbreviations: FCE, focal choroidal excavation.

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Her past medical history was significant for celiac disease, anxiety, depression, and obstructive sleep apnea. Her current medications included oxcarbazepine, quetiapine, clonazepam, venlafaxine, prophylactic valacyclovir, aspirin, and multivitamins.

In 2013, a small defect in Bruch’s membrane, immediately supranasal to the fovea, was identified on SD-OCT imaging. It was located within a larger area of macular atrophy and surrounding yellow pisciform flecks. The subtle defect in Bruch’s membrane identified on SD-OCT is not overtly apparent (arrow). A focal defect in Bruch’s membrane is evident (arrows). This lesion was not readily apparent on fundus examination and there was no evidence of choroidal neovascularization (CNV) or subretinal fluid (Fig. 1A and B). It was not apparent on SD-OCT at a prior examination in 2011. The right eye demonstrated confluent macular atrophy with areas of intraretinal pigment migration in the absence of a similar defect in Bruch’s membrane. At this time, she denied any recent vision changes and her best-

(NIH) institutional review board. Her past medical history was significant for celiac disease, anxiety, depression, and obstructive sleep apnea. Her current medications included oxcarbazepine, quetiapine, clonazepam, venlafaxine, prophylactic valacyclovir, aspirin, and multivitamins.

In 2013, a small defect in Bruch’s membrane, immediately supranasal to the fovea, was identified on SD-OCT imaging. It was located within a larger area of macular atrophy and surrounding yellow pisciform flecks in the left eye. This lesion was not readily apparent on fundus examination and there was no evidence of choroidal neovascularization (CNV) or subretinal fluid (Fig. 1A and B). It was not apparent on SD-OCT at a prior examination in 2011. The right eye demonstrated confluent macular atrophy with areas of intraretinal pigment migration in the absence of a similar defect in Bruch’s membrane. At this time, she denied any recent vision changes and her best-

Fig. 1. A. Color fundus image (Topcon Medical Systems, Oakland, New Jersey, USA) of the left eye of a patient with ABCA4-related retinopathy in December 2013 demonstrates macular atrophy and surrounding yellow pisciform flecks. The subtle defect in Bruch’s membrane identified on SD-OCT is not overtly apparent (arrow). B. Corresponding SD-OCT (Heidelberg Engineering, Heidelberg, Germany) image of the left eye demonstrates outer retinal thinning and macular atrophy. A focal defect in Bruch’s membrane is evident (arrows). C. Color fundus image of the left eye in February 2022 demonstrates an enlarged area of macular atrophy with evidence of centrifugal migration of the yellow flecks. Focal choroidal excavation is apparent with underlying bare sclera visible (arrow). D. Corresponding SD-OCT image of the left eye demonstrates a non-conforming focal choroidal excavation with interruption of the overlying inner retinal layers and resultant full-thickness macular hole formation. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Fig. 2. Eight serial SD-OCT (Heidelberg Engineering, Heidelberg, Germany) images demonstrate the development, progression, and evolution of FCE over an 8-year time period in a patient with ABCA4-related retinopathy.
corrected visual acuity had remained stable at 20/160 OD and 20/200 OS. On a follow-up examination approximately 6 months later, the focal defect in Bruch’s membrane in her left eye had widened considerably on SD-OCT. This was accompanied by prolapse of the outer retinal layers into the superficial choroidal space. On fundus examination, there was subtle thinning of the retina in the area of the lesion with more visible underlying choroidal vasculature. The appearance of the lesion was consistent with a focal choroidal excavation (FCE) of the conforming subtype. There was no evidence of CNV, and her visual acuity remained unchanged.

The ensuing 7 years of follow-up demonstrated further deepening of the FCE with associated thinning of the choroid. Prominent cystic spaces developed within the lesion, consistent with a transformation from conforming to non-conforming FCE subtype. Clinically, the juxtafoveal defect became more apparent over time. As the FCE deepened and the choroid thinned, bare sclera became visible on fundus examination. There was no CNV detected throughout the follow-up period.

At the time of writing this report, her best-corrected visual acuity was 20/320 OU with a refractive error of −0.75D sphere OD and −0.25D sphere OS. Her intraocular pressure measured 18 mmHg OD and 19 mmHg OS with applanation. Anterior segment examination revealed clear corneas and trace nuclear sclerosis OU. The anterior chamber was deep and quiet OU. There were no anterior vitreous cells present. Fundus examination demonstrated bilateral confluent macular atrophy with intraretinal pigment migration and surrounding yellow flecks. The FCE was apparent in her left eye with underlying bare sclera. On SD-OCT, there was an interruption of the inner retinal layers above the non-conforming FCE, resulting in a full-thickness retinal hole (Fig. 1C and D). Given the lack of new symptoms and the absence of subretinal fluid or neurosensory detachment, the lesion was observed. Fig. 2 highlights the evolution of the focal choroidal excavation in the left macula on 8 registered serial SD-OCT images from 2013 to 2022.

3. Discussion

Focal choroidal excavation is a relatively uncommon finding in patients with retinal degeneration, reportedly occurring in 4.3% of eyes of patients with macular dystrophy. While the precise etiology is unknown, relative choroidal hypoperfusion and degenerative changes of the outer retina, RPE, and adjacent choroid have been proposed to facilitate the formation of choroidal excavation. Recently, Capellan et al. (2021) proposed classifying FCE into three types (myopic, congenital, and acquired) according to choroidal thickness and the presence or absence of associated chorioretinal pathology. Based on their criteria, our patient with ABCA4-related retinopathy would be classified as type 3 (acquired). Type 3 lesions are hypothesized to originate from degenerative or inflammatory processes that disrupt the Bruch’s membrane and RPE complex. Our case provides evidence in support of this since the earliest indication of abnormality that we identified was a juxtafoveal defect in Bruch’s membrane that developed prior to FCE formation (Fig. 1A and B).

Several studies that identified choroidal excavation in patients with chorioretinal degeneration did not document significant changes in lesion appearance over time. In contrast, our patient demonstrated progressive FCE deepening in association with choroidal thinning. We suspect that the length of follow-up combined with structured serial SD-OCT imaging facilitated the detection of FCE evolution in our patient (Fig. 2). Although the choroidal excavation began as a conforming type, it transformed into a non-conforming type with prominent hypo-reflective cystic spaces that progressively expanded over time and eventually formed a macular hole (Fig. 1C and D). This is consistent with the hypothesis that both conforming and non-conforming FCE types exist along a spectrum of severity. Similar to our case, non-conforming FCE and macular hole formation has been reported in a patient with advanced retinitis pigmentosa and macular atrophy. Given the progression of ABCA4-related retinopathy in our patient, evident by the expansion of macular atrophy in the en face SD-OCT images, we propose structural chorioretinal changes in progressive retinal degenerations may influence FCE morphology. Note is made of evolution of vitreomacular traction evident on the most recent OCTs in our patient. It is possible that patients with FCE and concurrent vitreomacular traction in the setting of an inherited retinal degeneration are at higher risk of developing macular hole (as compared to either pathology alone).

From the time the FCE was first identified to the most recent follow-up visit, we did not detect any evidence of CNV. We did not perform fluorescein angiography, indocyanine green angiography or OCT angiography given the low suspicion for CNV; however, these modalities may be helpful if the suspicion is higher. Up to 40% of patients with type 3 FCE develop CNV, and this is generally responsive to anti-VEGF agents. Given the dynamic nature of FCE in our case and the possibility of developing CNV, regular follow-up is prudent so that early treatment may be implemented if indicated.

4. Conclusions

In summary, we report a patient with ABCA4-related retinopathy and unilateral FCE and highlight its evolution from a focal defect in Bruch’s membrane to a non-conforming lesion with macular hole formation. Our case emphasizes the potential dynamic nature of FCE in retinal degeneration and thus supports the need for ongoing surveillance.

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Patient consent

The patient consented to the publication of the case in writing.

Declaration of competing interest

The authors confirm that they have no relevant conflicts of interest to disclose.

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