Preserved retinal sensitivity following spontaneous regression of soft drusen

Soft drusen are the clinical hallmark of intermediate age-related macular degeneration (AMD) and a major risk factor for late-stage disease. Soft drusen usually increase in size, area, and confluence with aging.[1] Their natural life cycle may involve retinal pigment epithelium (RPE) changes, collapse, and macular atrophy or spontaneous regression.[2] Pharmacologic and laser photocoagulation treatments intended to induce drusen regression have yet to show visual benefit.[1,3] Early treatment of intermediate AMD before progression to macular atrophy and/or neovascular complications is an area undergoing intense study and would be a breakthrough. However, whether soft drusen already represent an irreversible loss of retinal structure and function remains a topic of some debate. Confocal microperimetry has been demonstrated to be reliable in evaluating retinal function via threshold retinal sensitivity.[4] Herein we report the multimodal imaging including spectral-domain optical coherence tomography (SD-OCT) and confocal microperimetry of a patient with intermediate AMD with spontaneous drusen regression.

An 82-year-old pseudophakic female with a history of bilateral intermediate AMD presented for follow-up. She denied any recent visual changes. She has been on PreserVision AREDS 2 Eye Vitamin supplementation (Bausch & Lomb Inc, Bridgewater, NJ) and had no history of intravitreal injections or laser treatments. Visual acuity was 20/25 OD and 20/25 OS. Ophthalmoscopic examination disclosed multiple soft drusen, most numerous along the temporal arcades. In the right eye, there was a focal area of irregular RPE mottling within an area of confluent soft drusen. SD-OCT (Spectralis HRA + OCT; Heidelberg Engineering, Heidelberg, Germany) showed preserved outer retina morphology and the absence of deposits below or above the RPE in that region. Review of fundus photography and tracked SD-OCT from the baseline visit 4 years prior revealed that spontaneous regression of soft drusen had occurred in that area (Fig. 1). The patient underwent psychophysical evaluation using confocal microperimetry (Macular Integrity Assessment [MAIA]; CenterVue, Padova, Italy), which uses automated eye tracking to correct for eye movement and display threshold retinal sensitivities mapped to specific retinal locations. After a suprathreshold 10−2 "learning" microperimetry test, the patient underwent a 10−2 protocol on a customized grid that encompassed areas with drusen, with drusen regression, and without any history of drusen based on serial SD-OCT and fundus photography during the follow-up period. Microperimetry was registered with SD-OCT as described previously.[5] Areas with drusen had decreased threshold retinal sensitivity, but there was no difference in the retinal sensitivities between the area of drusen regression and the adjacent area without large soft drusen (Fig. 2).

To the best of our knowledge, this is the first report using confocal microperimetry registered with SD-OCT to evaluate retinal sensitivity after spontaneous regression of soft drusen. We found that retinal sensitivities were similar in areas both with and without soft drusen in a region following soft drusen regression with preserved outer retina morphology. In the Beaver Dam eye study, regression of large soft drusen occurred in 30% of cases over a 10-year follow-up and was accompanied by the appearance of more severe lesions including RPE depigmentation, geographic atrophy, and macular neovascularization in nearly 30% of these eyes.[6] In our experience, regression of soft drusen without

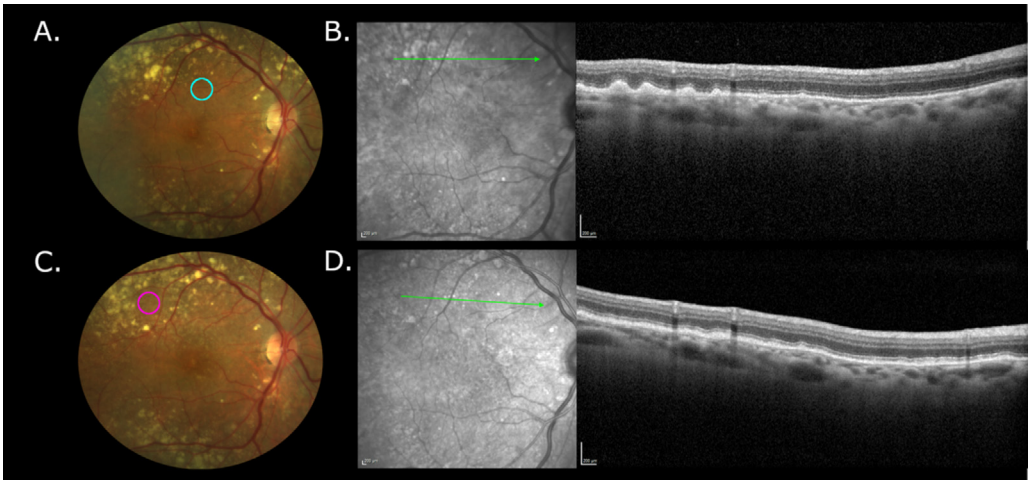

Fig. 1—Colour fundus photographs (A) and tracked spectral-domain optical coherence tomography (B) of the right eye at baseline show soft drusen along the superior arcade as well as an adjacent area without drusen (cyan circle). Four years later, there is an area where spontaneous drusen regression has occurred (C, magenta circle) in which spectral-domain optical coherence tomography shows preserved outer retinal bands (D).

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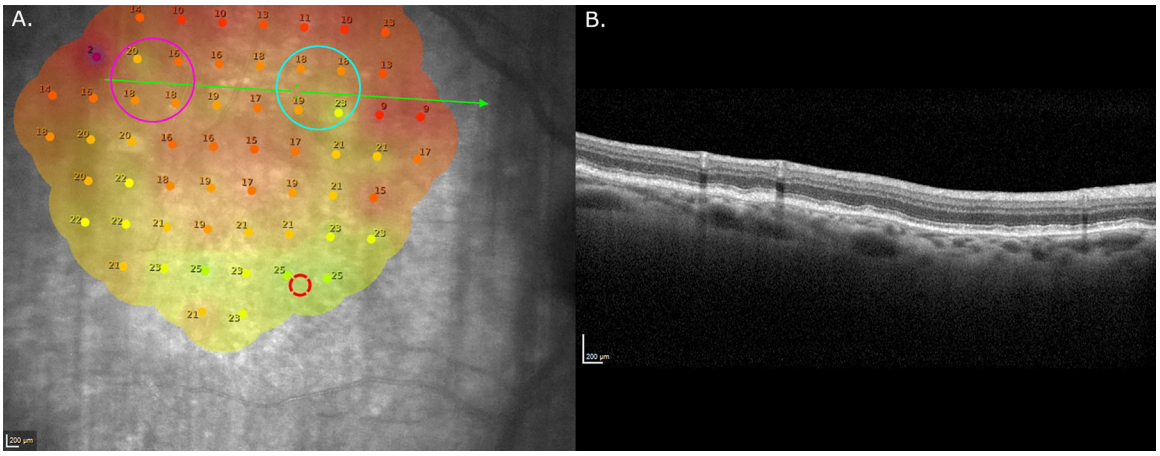

Fig. 2—Confocal microperimetry (A) of the right eye using a customized grid registered with the horizontal raster spectral-domain optical coherence tomography (B) that morphologically correlates with the area of soft drusen along the superior arcade, including the area of spontaneous drusen regression (magenta circle) and the adjacent area without drusen (cyan circle). The area of spontaneous drusen regression showed threshold retinal sensitivities similar to nearby unaffected areas.

subsequent geographic atrophy is more likely to occur in eyes with concomitant cuticular drusen than in those lacking this finding. We hypothesize that the presence of a thick basal laminar deposit in eyes with cuticular drusen provides structural support to the overlying and adjacent RPE and photoreceptors during the process of drusen resorption.

A limitation of our approach is that baseline retinal sensitivity was not established at the initial visit for a longitudinal assessment of retinal function in the area of drusen regression. Instead, adjacent areas without soft drusen were used for comparison. While we cannot be certain that those locations had comparable retinal sensitivities at baseline, previous normative MAIA microperimetry data sets have reported similar retinal sensitivities in those same regions.[7]

Our results agree with a previous psychophysical study in patients with soft drusen regression using fine matrix mapping.[8] The authors demonstrated no significant difference in local sensitivities between areas with drusen regression and unaffected neighbouring areas on colour fundus photography. They also observed that after drusen regression, retinal mean sensitivity was inferior to that of age-matched control individuals without AMD. Our work agrees with this observation. Compared with fine matrix mapping, microperimetry enables direct measurements of focal retinal sensitivity that is precisely mapped to an eye-tracked near-infrared fundus image. Registration of SD-OCT and MAIA microperimetry eye tracked to near infrared shows preserved outer retinal morphology correlating with preserved visual function.

While soft drusen are well recognized as a major ocular risk factor for progression to advanced AMD, their presence may not always signal irreversible loss of retinal function, thus supporting the potential benefit of targeting the disease at this stage.

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Footnotes and Disclosure

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