Reticular Pseudodrusen: A Common Pathogenic Mechanism Affecting the Choroid–Bruch’s Membrane Complex and Retinal Pigment Epithelium for Different Retinal and Macular Diseases

I read with great interest the article by Gliem et al. on the novel phenotypic characteristics of Sorsby’s fundus dystrophy (SFD), which included drusen-like deposits. From the multimodal imaging provided with the cases description, I noted that what the authors reported as “drusen-like” deposits should be better classified as “reticular pseudodrusen-like” deposits. Particularly, spectral-domain optical coherence tomography (SD-OCT) shows discrete collections of hyporeflective material located not under (as do typical drusen), but above the RPE. This material (see figs. 2 and 4 in the article of Gliem et al.) appears as well-defined round or triangular hyporeflective deposits localized between, externally, the RPE and, internally, the external limiting membrane (ELM) or the outer plexiform layer (OPL). Moreover, despite the authors having performed multimodal imaging, they did not note the typical reticular fundus autofluorescence pattern in several of their images, which is consistent with reticular pseudodrusen deposits (also known as subretinal drusenoid deposits [SDD]), not typical soft drusen.

It is noteworthy that the same group and others have recently reported on the association between reticular pseudodrusen and Pseudoxanthoma elasticum (PXE). In SFD and PXE, Gliem et al. hypothesize similar pathogenic mechanisms affecting the choroid–Bruch’s membrane complex. The formation of reticular pseudodrusen, or better “pseudodrusen-like” deposits, might eventually result from such impaired physiologic mechanisms ultimately affecting the RPE. Impaired choroid–Bruch’s membrane complex and RPE might disturb various physiologic processes, including the removal of waste products of photoreceptors, the supply of the RPE and outer retina with nutrients and oxygen, and the recycling or degradation of shed outer segments (OS) and retinoids. Interestingly, hyporeflective deposits localized above the RPE, and very similar to reticular pseudodrusen on OCT (personal observation), have been reported recently in fundus albipunctatus, a disease associated with mutations in RDH5 which is abundant in the smooth endoplasmic reticulum of the RPE.

All these data suggest that reticular pseudodrusen and pseudodrusen-like deposits are not simply “drusenoid deposits” located above instead of under the RPE, due to a misdirection of transport into the subretinal space. Histologic descriptions indicate a material in some deposits that resembles outer segments, but lacking disks (called “outer segment condensate”). Moreover, the pseudodrusen material appears to show some autofluorescence, implying presence of retinoids.

Mrejen and Spaide, by comparing the “physiological” choroidal thinning in myopic eyes with the “pathological” choroidal thinning in age-related macular degeneration (AMD) eyes, recently suggested that pseudodrusen are not primarily due to a dysfunction of the level of the choroid. It is pointless to compare AMD and myopia in the first place, because they are such different conditions. Here and elsewhere, by investigating pathologic eyes with different retinal and macular diseases, the authors have nicely demonstrated how formation of “reticular pseudodrusen-like” deposits might result from impaired physiologic mechanisms affecting the choroid–Bruch’s membrane complex (including disturbed homeostasis in Bruch’s membrane extracellular matrix remodeling and calcification) and RPE. Similarly in AMD, the fibrotic replacement of the choroid may imbalance the RPE functions and finally cause shed of unphagocytized photoreceptor OS and retinoids to accumulate above the RPE.

Whether the deposits in SFD (as well as PXE and fundus albipunctatus) are the reticular pseudodrusen/SDD specifically characterized histologically and biochemically in AMD eyes by Curcio et al. remains to be determined. Therefore, until a convincing clinicopathologic correlation is published the terminology “reticular pseudodrusen-like” seems to add more unreality to this nomenclature. Nonetheless, it is clear that reticular pseudodrusen/SDD are a more general feature of some degenerations of the outer retina, RPE, and Bruch’s membrane, particularly those with abnormalities in the visual cycle or an impaired choroid–Bruch’s membrane complex.

I congratulate the authors for their excellent observations and pathophysiologic considerations.

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