Hyperreflective Intraretinal Foci as an OCT Biomarker of Retinal Inflammation in Diabetic Macular Edema

We read with great interest the article titled "Association Between Soluble CD14 in the Aqueous Humor and Hyperreflective Foci on Optical Coherence Tomography in Patients with Diabetic Macular Edema" by Lee et al.[1] The authors investigated the expression of soluble CD14 (sCD14) in aqueous humor (AH) samples of patients with diabetic macular edema (DME), and the presence of hyperreflective foci (HF) on spectral-domain optical coherence tomography (SD-OCT) in these eyes. The authors found both higher levels of sCD14, and increased number of HF in the inner retina compared to controls, and concluded that, since sCD14 is released by retinal microglia, HF might represent aggregates of activated microglial cells in DME eyes.[1] The presence of and changes in OCT HF, also called hyperreflective spots, have been previously described in detail in diabetic eyes and reported to depend on activated microglia.[2–5] DME-affected eyes treated with intravitreal anti-VEGF and steroids have also been investigated, demonstrating a reduction of HF number with both treatments—confirming HF as a retinal inflammatory biomarker.[3,4] To improve this observation, we also investigated diabetic eyes in a large population to identify HF-specific characteristics,[5] a topic not sufficiently addressed by Lee et al. In particular, we disagree with the statement that HF, as aggregates of retinal microglial cells, have the same reflectivity as the retinal pigment epithelium (RPE), whereas it is more similar to that of the retinal nerve fiber layer (RNFL). Other clinical characteristics (size < 30 µm, absence of back-shadowing, presence in both inner and outer retinal layers in DME)[5] allow differentiation of HF, as an inflammatory biomarker, from hard exudates, small intraretinal hemorrhages, microaneurysms, and tiny capillaries, which also appear as OCT hyperreflective foci (spots). The correct identification of inflammation-driven HF from other forms of hyperreflective material is relevant when using this new biomarker in the follow-up of any DME treatment. As consequence, any investigation of HF on OCT in diabetic eyes should be more precise to avoid inconsistent results.

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References

1. Lee H, Jang H, Choi YA, Kim HC, Chung H. Association between soluble CD14 in the aqueous humor and hyperreflective foci on optical coherence tomography in patients with diabetic macular edema. *Invest Ophthalmol Vis Sci*. 2018;59:715–721.
2. Vujosevic S, Bini S, Midena G, Berton M, Pilotto E, Midena E. Hyperreflective intraretinal spots in diabetics without and with nonproliferative diabetic retinopathy: an in vivo study using spectral domain OCT. *J Diabetes Res*. 2013;2013:491835.
3. Vujosevic S, Torresin T, Bini S, et al. Imaging retinal inflammatory biomarkers after intravitreal steroid and anti-VEGF treatment in diabetic macular oedema. *Acta Ophthalmol*. 2017;95:464–471.
4. Vujosevic S, Berton M, Bini S, Casciano M, Cavarzeran F, Midena E. Hyperreflective retinal spots and visual function after anti-vascular endothelial growth factor treatment in center-involving diabetic macular edema. *Retina*. 2016;36:1298–1308.
5. Vujosevic S, Bini S, Torresin T, et al. Hyperreflective retinal spots in normal and diabetic eyes: B-scan and en face spectral domain optical coherence tomography evaluation. *Retina*. 2017;37:1092–1103.

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