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Kinetics of Punctate Subretinal Deposits in Mitogen-Activated Protein/Extracellular Signal-Regulated Kinase Inhibitor–Associated Retinopathy Using En Face Optical Coherence Tomography

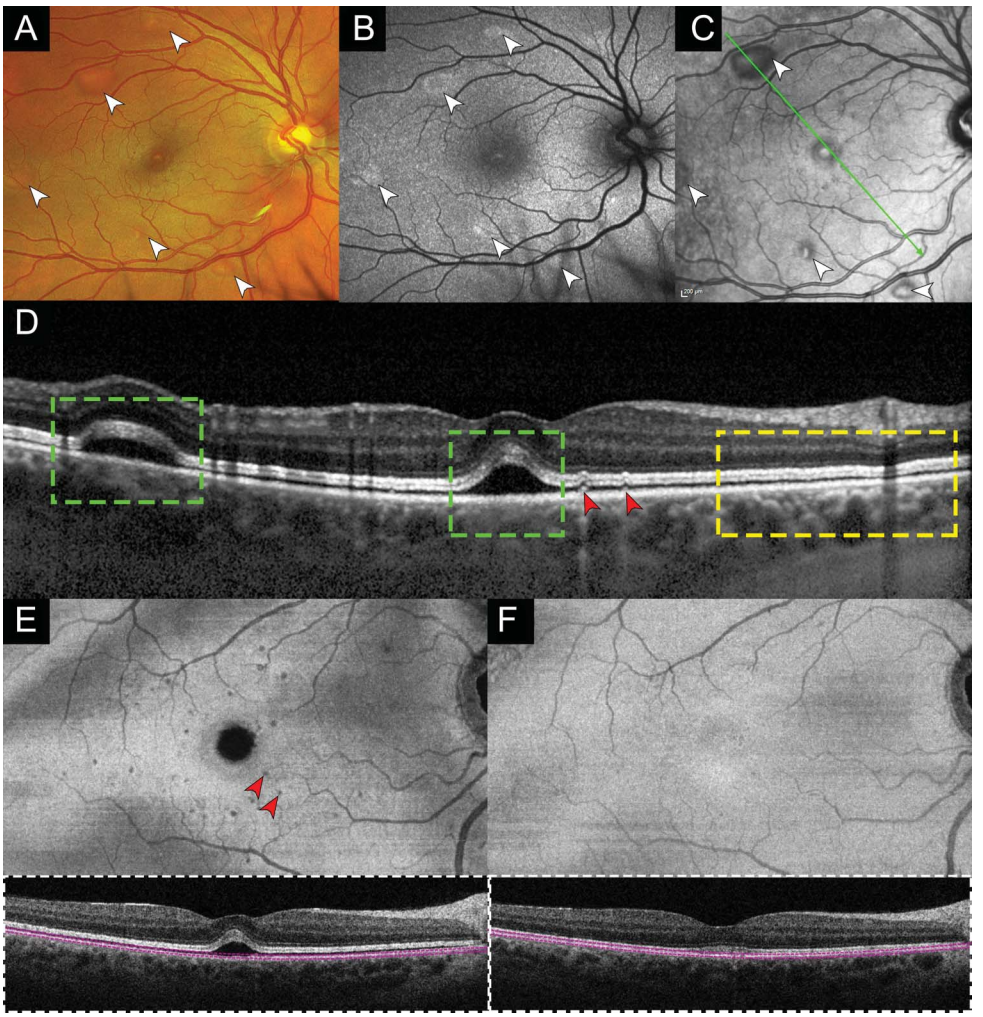

Fig. 1. Multimodal imaging features of Punctate Subretinal Deposits (PSD) in MEK inhibitor–associated retinopathy. **A.** Ultrawide-field color fundus image shows yellow–orange elevated areas subfoveally and along the arcades (white arrowheads). **B.** Fundus autofluorescence image shows hyperautofluorescent lesions (white arrowheads). **C.** Near-infrared reflectance image shows hyporeflective lesions (white arrowheads) corresponding to the yellow–orange spots on color fundus photography. Note the small punctate hyporeflective lesions in the macular area. The green line indicates the position of the OCT B-scan in (**D**). **D.** OCT B-scan demonstrates dome-shaped fluid accumulations subfoveally and along the temporal vascular arcade ("*dome*" pattern, *green dashed boxes*) and a broad low-lying fluid accumulation between the RPE and the IZ ("*splitting*" pattern, *yellow dashed box*). Note the multiple, hyporeflective, PSDs (red arrowheads) with a distinctive tail of posterior hypertransmission. **E.** Baseline en face OCT image segmented at the level of the RPE illustrates numerous, hyporeflective, dot-like deposits (red arrowheads). The inset (white dashed box) is the horizontal OCT B-scan showing the segmentation lines of the corresponding en face OCT image. **F.** After 6 hours, follow-up en face OCT image segmented at the level of the RPE demonstrates regression of the PSD without newly apparent deposits, and cross-sectional OCT shows rapid resolution of the subretinal fluid. Note the persistent attenuation of the ellipsoid/IZs subfoveally. The inset (white dashed box) is the horizontal OCT B-scan showing the segmentation lines of the corresponding en face OCT image.

Mitogen-activated protein/extracellular signal-regulated kinase inhibitor–associated retinopathy (MEKAR) designates the spectrum of retinal adverse events induced by MEK inhibitors therapy and is characterized by transient subretinal fluid accumulation between the retinal pigment epithelium (RPE) and the interdigitation zone (IZ) on optical coherence tomography (OCT).[1] We report serial multimodal imaging analysis of an undescribed OCT finding termed "punctate subretinal deposits" (PSDs) during

v-raf murine sarcoma viral oncogene homolog B1 and MEK inhibitors treatment. This report followed the tenets of the Declaration of Helsinki.

A 42-year-old man with metastatic cutaneous melanoma and v-raf murine sarcoma viral oncogene homolog B1 V600E mutation received a combination therapy with encorafenib (second generation of v-raf murine sarcoma viral oncogene homolog B1 inhibitor) and binimetinib (MEK inhibitor). Ultrawide-field color fundus image showed yellow–orange elevated areas subfoveally and along the arcades (Figure 1A) that appeared hyperautofluorescent on fundus autofluorescence and hyporeflective on near-infrared reflectance (NIR) imaging, respectively (Figure 1, B and C). Optical coherence tomography demonstrated dome-shaped fluid accumulations ("*dome*" pattern) and a broad low-lying fluid accumulation between the RPE and the IZ ("*splitting*" pattern) (Figure 1D). En face OCT image (Figure 1E) segmented at the level of the RPE illustrated numerous, hyporeflective, dot-like deposits that displaced anteriorly the ellipsoid zone and IZ on cross-sectional OCT (Figure 1D) and corresponded to punctate hyporeflective lesions on NIR (Figure 1C). After 6 hours, eye-tracked OCT scan demonstrated subretinal fluid resolution, and en face OCT image showed regression of PSDs (Figure 1F).

To the best of our knowledge, "PSDs" have not been described in MEK inhibitor–associated retinopathy.[1,2] Their presumed colocalization within the RPE and their synchronous fluctuations with the subretinal fluid suggest a common pathophysiologic mechanism of RPE toxicity.[3] Tyagi and Santiago[4] have described granular deposits in the subretinal space, but their multimodal imaging characteristics and long-term persistence were distinct from PSD. Although rapid fluctuation of subretinal fluid on encorafenib and binimetinib has been documented by Li et al,[5] our report may expand the multimodal imaging characteristics of MEK inhibitor–associated retinopathy.

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The patient consented to publication of the case orally.

All authors attest that they meet the current ICMJE criteria for Authorship.

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Key words: BRAF inhibitor, MEKAR, MEK inhibitor, multimodal imaging, ocular toxicity, optical coherence tomography, subretinal deposits, subretinal fluid.

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References

1. Francis JH, Habib LA, Abramson DH, et al. Clinical and morphologic characteristics of MEK inhibitor–associated retinopathy. Ophthalmology 2017;124:1788–1798.
2. Weber ML, Liang MC, Flaherty KT, Heier JS. Subretinal fluid associated with MEK inhibitor use in the treatment of systemic cancer. JAMA Ophthalmol 2016;134:855.
3. Méndez-Martínez S, Calvo P, Ruiz-Moreno O, et al. Ocular adverse events associated with MEK inhibitors. Retina 2019; 39:1435–1450.
4. Tyagi P, Santiago C. New features in MEK retinopathy. BMC Ophthalmol 2018;18(Suppl 1):221.
5. Li AS, Leng T, Nagpal S, Liao YJ. Rapid fluctuation of subretinal fluid on encorafenib and binimetinib. RETINA 2020;40: e66–e67.

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