Re: Francis et al.: Clinical and morphologic characteristics of MEK inhibitor-associated retinopathy: differences from central serous chorioretinopathy (Ophthalmology. 2017;124:1788-1798)

TO THE EDITOR: We read with interest the work by Francis et al., describing the clinical characteristics and OCT findings of a novel pathologic condition named mitogen-activated protein kinase (MEK) inhibitor-associated retinopathy (MEKAR). They explained that the toxicity profile of a novel class of chemotherapeutics that specifically blocks the mitogen-activated protein kinase pathway includes the acute accumulation (within approximately 2 weeks from the first intake) of focal or multifocal, self-limited (approximately 32 days), nongravitational, subretinal fluid (SRF) pockets, distributed through the entire macula in one or both eyes. The fluid may be located subfoveally and may cause mild visual symptoms with no permanent damage. Morphologically, the accumulation of SRF can be divided into 4 distinct classes (dome, caterpillar, wavy, and splitting) depending on their individual appearance on OCT.1 In addition, the authors detailed the reasons why they believe MEKAR differs from other macular pathologies like central serous chorioretinopathy (CSC), as well as exploring the existence of concomitant pachychoroid.

We agree with the authors that MEKAR constitutes an individual pathological process and it is not part or related to other macular pathologies. However, we would like to suggest certain key clinical observations that could help to speed and improve the differential diagnosis of MEKAR. First, we believe that, even though there was a bilateral presentation, the number of SRF foci and the nonexistence of inferior tracking of fluid (gutter) are hallmarks of the clinical spectrum of MEKAR and could help to distinguish it from CSC; the clinician should consider these clinical presentations along with the patient’s medical history as a whole, and not as individual differential characteristics. Indeed, CSC is a pathology with a clinical presentation that may vary widely. It certainly can include patients of all ages and fundus abnormalities can include bilateral multifocal serous detachments in almost one-half of them.2 Furthermore, the existence of inferior tracking in CSC is a reflection of chronicity and is not part of the acute presentation of the disease.3 Given the chance of exploring the fundus of a patient with CSC that lasted only 2 weeks, the chances of finding inferior tracking are much lower. As the authors correctly point out, MEKAR is of relatively short duration and usually resolves without sequels. Although a patient with chronic CSC that ends up developing an inferior tracking of SRF has a greater probability of developing retinal pigment epithelium changes, foveal scarring, visual sequels, or even had a history of previous treatments.3,4

In addition, patients with advanced cancer receiving chemotherapy that includes a MEK inhibitor have limited mobility during treatment and may receive concomitant steroids. The first limits the effect of gravity over the SRF, making it less likely to develop an inferior tracking of fluid. The second is an obvious confounder that the authors also correctly pointed out during their discussion.5 Because most of the evidence that we currently have regarding CSC pathophysiology points toward a possible vascular abnormality, we believe that the differential diagnosis should be centered on the association of the patient’s medical history (MEK inhibitors intake) with the absence of such abnormalities by fluorescein/indocyanine green angiography, along with all the clinical characteristics and OCT findings listed by the authors in their original manuscript.1–3,6

Second, in their Discussion, the authors tried to explain the origin of the SRF accumulation by citing the tight junctions’ abnormalities and the delocalization of aquaporin 1. The short onset time suggest indeed a rapid biological response.4 In addition, an inhibition of the MEK/ERK pathway could also affect the function and localization of ion channels (chloride channels) at the retinal pigment epithelium, leading to a change in the ion gradient and subsequent fluid accumulation. The MEK/ERK pathway also has a role in the clathrin-independent endocytosis and the phagocytosis of opsonized particles. Its targeted inhibition could explain some of the abnormalities described by the authors at the interdigitation zone—retinal pigment epithelium junction as well as some areas of outer segment elongation.3 However, all this information is mere speculation and should be taken with caution, because there is no definitive proof supporting these observations.

In summary, we greatly enjoyed reading this excellent work by Francis et al. Their remarkable description of the clinical manifestations and OCT findings of MEKAR will definitely help clinicians to make a quick differential diagnosis with other macular pathologies.

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References


