

Is Fundus Autofluorescence Clinically Useful in Primary Vitreoretinal Lymphoma?

Correlations seen between patterns on FAF images and those on OCT and FA.

BY LISA J. FAIA, MD

Primary vitreoretinal lymphoma (PVRL) is a subset of primary central nervous system lymphoma that was recently renamed from primary intraocular lymphoma.¹ It is usually an aggressive, diffuse, large B-cell lymphoma.

Of patients who initially present with PVRL alone, more than half will go on to develop cerebral lesions. Symptoms include decreased vision and floaters, probably as a result of chronic vitritis and subretinal lesions. Chemotherapy and radiation are used in treatment, but there is a high relapse rate.

Diagnosing PVRL can be challenging: The mean period for diagnosis is 12 to 24 months, and a mean of 4.3 procedures are needed before diagnosis is made. The diagnostic gold standard is histologic confirmation, and typical findings are large, atypical lymphoid cells that display a high nuclear-to-cytoplasmic ratio, prominent nucleoli, and basophilic cytoplasm. In addition to cytology, flow cytometry, immunohistochemistry, cytokine analysis, and identification of gene rearrangements can be used as diagnostic adjuncts.

Because diagnosis may require multiple invasive procedures, it is important to identify patients at higher risk. Noninvasive imaging techniques that have been used to help identify patients at risk for PVRL include fluorescein angiography (FA), spectral-domain optical coherence tomography (SD-OCT), and indocyanine green angiography (ICGA).²⁻⁴

FAF FOR PVRL

Fundus autofluorescence (FAF) is a noninvasive imaging modality that is used to record naturally occurring fluorescence in the eye, as opposed to fluorescence from injected dyes, as in FA and ICGA. FAF is increasingly being used as an imaging tool in the diagnosis and monitoring of a number of ocular diseases, including choroidal melanoma, macular degeneration, and posterior uveitis.

FAF can be used to assess the health of the retinal pigment epithelium (RPE) by determining the presence or absence of the retinal pigment lipofuscin. Lipofuscin, a yellow-brown pigment that fluoresces on FAF, is a byproduct of oxidative stress that is known to accumulate in the RPE. Increased autofluorescence on FAF is consistent with RPE dysfunction, and decreased autofluorescence is indicative of loss of RPE.

Colleagues at the National Eye Institute (NEI) and I performed a study to evaluate FAF patterns in patients with PVRL.⁵ The records of all patients with suspected PVRL who underwent FAF at the NEI from 1994 to 2010 were reviewed. To be included, patients must have undergone 2 of 3 imaging procedures (FAF, FA, or OCT) yielding adequate quality images. Inclusion also required confirmation of disease on histopathology from vitreous biopsy, core retinal biopsy, lumbar puncture, or brain biopsy.

Images were assessed with attention to areas of abnormal autofluorescence on FAF; granularity, RPE mottling,

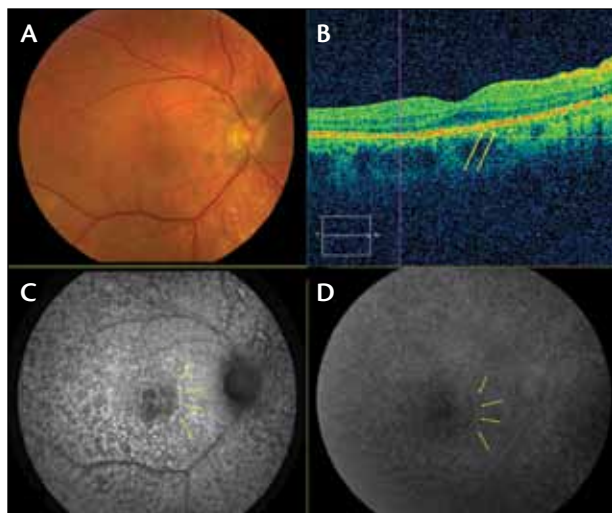


Figure 1. A 50-year-old patient known to have active PVRL: color fundus photography (A); nodular hyperreflective spots (yellow arrows) on OCT (B); hyperautofluorescent spots (yellow arrows) on FAF (C) corresponding to hypofluorescent spots (yellow arrows) on FA (D).

and window defects on FA; and nodular hyperreflective spots on OCT. FAF patterns were assessed in relation to clinical disease status and the findings of FA and OCT imaging studies.

RESULTS

Eighteen eyes of 10 patients met the inclusion criteria; of these, 16 eyes had active disease, and 2 eyes were in remission. Abnormal autofluorescence, in the form of granular hyperautofluorescence and hypoautofluorescence, was noted on FAF in 11 eyes (61% of all eyes and 69% of active eyes). All eyes that had this granular pattern on FAF had active PVRL at the time of imaging, but 5 eyes with active disease had unremarkable FAF imaging. Two eyes that were in remission also had unremarkable FAF.

FAF patterns were compared with those on FA and OCT. The most common pattern seen on FA was the appearance of “leopard spot” hypofluorescent round spots; these were seen in 43% of eyes with FA images. These hypofluorescent areas on FA corresponded to hyperautofluorescent areas on FAF in 36% of all eyes with FA and 42% of eyes with active disease with FA.

Nodular hyperreflective spots at the level of the RPE were seen on SD-OCT in 43% of eyes with OCT images. These hyperreflective areas corresponded to areas of granularity on FAF in 43% of all eyes with OCT and 50% of active eyes with OCT.

Examples of corresponding patterns on FAF, FA, and OCT images can be seen in Figures 1 and 2.

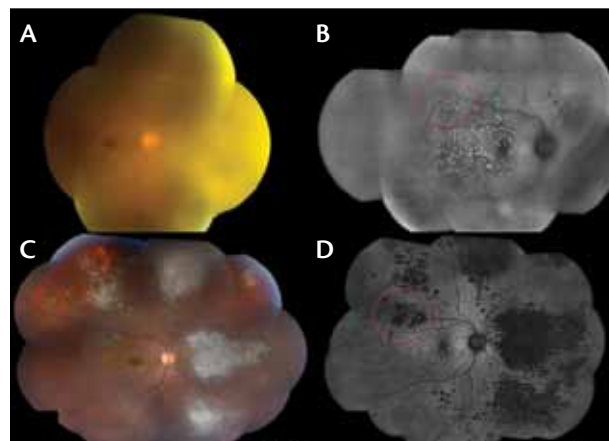


Figure 2. A 62-year-old patient referred for recurrent idiopathic panuveitis, later diagnosed with active PVRL via vitreous cytopathology: color fundus photo montage (A); hyperautofluorescence on FAF (B); after treatment with systemic intravenous methotrexate in high doses, fundus photo montage demonstrates the resulting lesions (C); areas that were previously hyperautofluorescent on FAF (B) now appear hypoautofluorescent (D).

CONCLUSION

The majority of patients in this study diagnosed with active PVRL had distinctive and unique patterns on FAF. The pattern that was most often observed was that of a granular appearance, meaning hyperautofluorescence mixed with hypoautofluorescence; this granularity was associated with active lymphoma in a majority of cases. FAF changes were more likely to occur in patients with active malignancy, although there were areas of atrophy that revealed hypoautofluorescence.

Because patients with PVRL may have to undergo multiple diagnostic procedures, it is important to have tools that can help identify those at higher risk. FAF may serve as such an adjunctive tool, helpful not only to elevate suspicion, but also to follow patients for recurrences. ■

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