Fundus Autofluorescence as a Diagnostic Tool for Retinal Emboli Classification: A Case Series

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Abstract

Fundus autofluorescence (FAF) is a relatively new imaging technique that is becoming more widely used in optometric practices. Images are typically obtained with either an enhanced fundus camera or a scanning laser ophthalmoscope as part of an optical coherence tomography (OCT) device, and can provide additional diagnostic information for a wide variety of retinal pathologies.

This case series highlights the benefit of using FAF to visualize retinal emboli. Specifically, the cases demonstrate how this technology can help identify embolus composition, allow better visualization of an embolus within the optic nerve, and differentiate an embolus from adjacent vascular sheathing. Once the retinal embolus is correctly identified, further, more appropriate, ocular and systemic testing can be ordered.

KEY WORDS:
retinal emboli, autofluorescence, retinal artery occlusion, Hollenhorst plaque

INTRODUCTION

Most retinal emboli are comprised of cholesterol, calcium, or platelet-fibrin.[1,2] The most common type of retinal embolus is a cholesterol embolus, historically referred to as a Hollenhorst plaque.[1-3] These are very small, refractile particles that typically lodge transiently at a retinal arteriole bifurcation without obstructing blood flow; therefore, the patient is usually asymptomatic.[3] Calcific emboli are larger, non-refractile, yellow-white in color and ovoid in shape. Their larger size makes them more likely to obstruct blood flow and cause visual symptoms.[4,5] Platelet-fibrin emboli are longer than the other two subtypes, transient in nature, and more grey-white in color.[6] Due to their long shape, platelet-fibrin emboli may obstruct large portions of arteries but create transient and varying visual symptoms, as they are quite mobile compared to the other two subtypes.[6]

Definitively classifying retinal emboli based on subtype can guide management protocols but can be challenging based solely on a fundus evaluation or fundus photography.[7,8] Of the five major population-based studies that have been conducted on asymptomatic retinal emboli, only the Blue Mountains Eye Study classified all emboli into one of the three compositions mentioned above.[9] The Beaver Dam Eye Study, the Atherosclerosis Risk in Communities and Cardiovascular Health Studies, and the Los Angeles Latino Eye Study did not feel they could adequately classify emboli based on fundus photographs alone, and instead described the emboli by appearance and whether they were bright or dull.[9-11] In the more recent Singapore Epidemiology of Eye Disease Study, emboli were classified by subtype, but 13% of emboli were still ungradable.[2] These large studies confirm that fundus appearance alone is often not sufficient to define composition, and further information is needed.

Fundus autofluorescence (FAF) is a non-invasive retinal imaging modality that is increasingly being used in clinical optometric practice to study a growing number of ocular conditions.[12] It is normally employed using an enhanced fundus camera or scanning laser ophthalmoscope as part of an optical coherence tomography (OCT) device. FAF allows the visualization of fluorophores in the retina which absorb light and then emit fluorescence. The most common retinal application of FAF is mapping of lipofuscin, which contains at least 10 different fluorophores with a broad excitation range of 300 to 600 nm.[13] FAF is commonly used to aid in the diagnosis and prognosis of retinal conditions including macular degeneration, where lipofuscin is known to play a role in the pathogenesis. However, FAF also has clinical applications in diseases without lipofuscin, such as in the visualization of buried disc drusen, which have been shown to not include lipofuscin on histopathological examination.[14]

Within the past decade, several case series have been published which demonstrate how retinal emboli and arteriolar occlusions can be further investigated with the aid of FAF.[7,15-17] By fundoscopy alone, platelet-fibrin emboli look quite distinct due to their long grey-white shape and can easily be diagnosed based on appearance, but calcium and cholesterol retinal emboli can be more difficult to differentiate. It has been postulated that emboli of a calcific composition will hyperautofluoresce while emboli of cholesterol composition will disappear on FAF.[7,15-17] While the exact mechanism by which calcium emboli hyperautoflouresce remains elusive, multiple published case reports along with the cases described below demonstrate this phenomenon.[7,15-17] Correct identification of the composition through the use of FAF can help narrow down the origin of the plaque and focus further testing.

CASE 1:

A 74-year-old Caucasian man presented for a routine eye examination. He was asymptomatic of any sudden or noticeable vision changes and denied any visual field loss or transient loss of vision. Vision was best corrected to 20/25 OD and 20/30 OS with minimal refractive change. Dilated examination revealed early cataracts consistent with his best corrected vision, healthy optic nerves and normal macula in each eye. There was a small, bright, reflective arteriolar embolus at the second bifurcation of his superior temporal retinal artery in the right eye, consistent with a cholesterol plaque.

Figures 1 and 2 were taken with a Heidelberg Spectralis Optical Coherence Tomography (OCT) device. Figure 1 was obtained by infrared confocal scanning laser ophthalmoscopy (IR cSLO); the retinal plaque is visible at the second bifurcation of the superior temporal retinal artery in the right eye. Figure 2 shows that the plaque is no longer visible by FAF, which confirms the diagnosis of a cholesterol embolus.

Figure 1: *IR cSLO image*

Figure 2: *OCT FAF image*

This patient had a significant medical history including atrial fibrillation and a right carotid endarterectomy 20 years previously. He had never smoked. He had not attended his recommended follow-up appointments and 3 years had passed since his last carotid ultrasound. Therefore, the optometrist ordered an updated carotid ultrasound and referred the patient again to the vascular clinic. The carotid ultrasound showed 50-69% occlusion of both internal carotid arteries, and no further surgical or medical intervention was recommended by the vascular clinic. Results were communicated to the primary care doctor, and subsequent eye examinations at 3 months, 6 months, and then annually revealed a stable plaque with no corresponding artery occlusion or field loss.

CASE 2

A 74-year-old African-American man presented with an acute loss of vision inferiorly in his left eye beginning 10 days prior to the exam. He had no other associated systemic or visual symptoms. His best corrected vision was

20/20 OD and OS, while visual field testing showed an inferior altitudinal defect in the left eye. Dilated fundus exam revealed a superior branch retinal artery occlusion of the left eye, with a large refractile plaque at the optic disc.

Figure 3 is a color fundus photograph of the left eye that was taken with a Zeiss Visucam. It shows the initial fundus presentation of retinal whitening from the branch retinal artery occlusion and visible retinal arteriolar embolus.

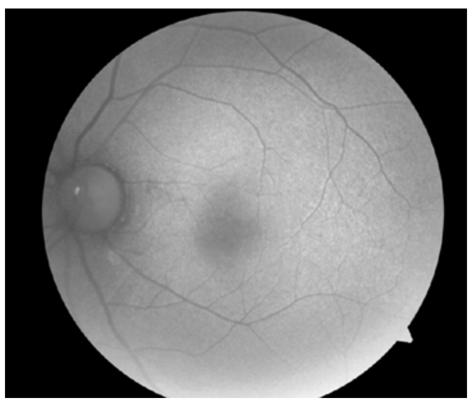
Figure 3: *Initial RAO presentation*

The patient was transferred to the Emergency Department where a full stroke work-up was performed. Head computed tomography (CT), magnetic resonance imaging (MRI) of the brain, computed tomography angiography (CTA) of the head and neck, and echocardiogram of his heart were all unremarkable. He had previously been taking daily aspirin but was switched to clopidogrel by neurology due to the new retinal findings. He had also previously been on atorvastatin and the dosage was increased from 40 mg to 80 mg daily.

Figures 4 and 5 are color and FAF photographs, respectively, taken with a Zeiss Visucam about 7 months after his initial presentation. Figure 4 shows the arteriolar sheathing and retinal atrophy beginning to appear. Figure 5 shows that the embolus remains visible on FAF, suggesting that it is calcific and demonstrating how fundus autofluorescence can help visualize emboli that may otherwise be obscured by vascular sheathing or the optic nerve.

Figure 4: *Follow up RAO presentation*

Figure 5: *Follow up RAO presentation with FAF*



CASE 3

A 68-year-old Caucasian man presented to the Emergency Department with acute, partial vision loss in his left eye beginning one day previously. His best corrected vision was 20/20 OD and 20/25 OS. On dilated examination, a large, refractile, calcific plaque was visible in the second bifurcation of the left superior retinal artery with adjacent retinal whitening consistent with a branch retinal artery occlusion. His work up was extensive and included comprehensive blood work, CT head, MRI brain, CTA head and neck, carotid duplex, electrocardiogram, and echocardiography. Due to elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), he also underwent a temporal artery biopsy which was negative for giant cell arteritis. After all testing was complete, he was diagnosed with paroxysmal atrial fibrillation, coronary artery disease, severe mitral regurgitation and mitral valve prolapse. He was placed on clopidogrel and apixaban and is now followed closely by cardiology.

Figures 6 and 7 were obtained with a Zeiss Visucam several years after the first presentation. Figure 6 is a color photograph of the left eye showing that the calcific embolus is still present and lodged at the second bifurcation of the superior temporal artery.

Figure 7 shows that the calcific embolus appears hyperautofluorescent on FAF. As the initial occlusion has now resolved, the retina surrounding the embolus is of normal autofluorescence; an active artery occlusion with retinal ischemia would show hypoautoflourescence since the edematous inner retinal layers will block the normal autofluorescence of the retinal pigment epithelium.[16]

Figure 6: *Calcific plaque*

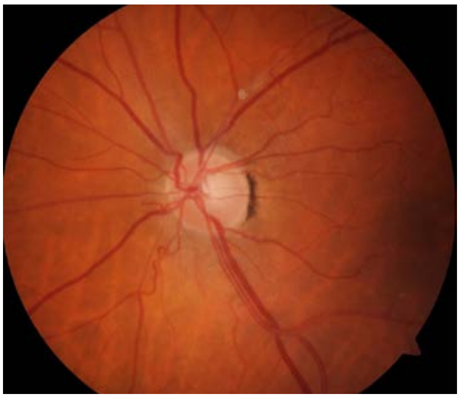


Figure 7: *Calcific plaque on FAF*

DISCUSSION

Patients who present with acute symptoms and retinal findings consistent with branch or central retinal artery occlusion should be sent directly to the nearest stroke center or emergency department (ED) due to a heightened risk of giant cell arteritis or other life-threatening conditions.[18] Many larger central or hemi-central artery occlusions are caused by an embolus lodging at or near the optic nerve head, and the embolus itself can be difficult to visualize. The use of fundus autofluorescence to help visualize an embolus and confirm if an artery occlusion is of an embolic nature can help focus the work-up at the ED.

The guidelines surrounding the optimal management of asymptomatic retinal emboli are much less clear. In the case of an asymptomatic embolus, the use of fundus autofluorescence to help more conclusively classify the embolus by composition can guide the clinician in deciding what testing should be ordered, and inform best medical management of the patient, specifically related to the need for an echocardiogram. Many generalized recommendations can be taken from the current literature and the five large population-based studies to date that include asymptomatic retinal emboli. The population-based studies all note that asymptomatic emboli are closely correlated with current or past smoking, and smoking cessation should be encouraged if applicable.[1,2,9-11,19] Primary care providers should be notified of the retinal findings and a basic investigation into vascular status is warranted given other significant associations with vascular disease.[11,19-21] The Beaver Dam Study, in particular, looked at not only the prevalence of asymptomatic retinal emboli at baseline, but also the incidence over a 10-year period and the relationship to stroke and ischemic heart disease. After accounting for other systemic conditions, the study found that participants with retinal emboli were 2.4 times more likely to die with stroke listed as the cause.[10] Carotid ultrasound should be ordered for all new asymptomatic retinal emboli given the association between asymptomatic retinal emboli and the presence of carotid artery plaque, despite the poor predictive value between an asymptomatic embolus and the degree of carotid stenosis.[9,19] Carotid ultrasound is a very safe, non-invasive procedure that may reveal a life threatening, modifiable condition.[22-24]

The current literature suggests that echocardiography is the only useful diagnostic test for retinal emboli of a calcific nature. One study in which echocardiography was performed for all patients regardless of embolus composition found no instances in which a cardiac source of the embolus was suspected.[20] However, when echocardiography was performed on all patients specifically with calcific emboli, symptomatic or not, 83% were found to have significant echocardiographic findings of either calcific aortic disease or calcific mitral valve disease, or both.[25] Additionally, a retrospective study of diabetic retinal photographs in 2008 found that, among patients with asymptomatic retinal emboli, a possible source was detected in 13 of 60 (21.7%) referred for echocardiography.[21] Therefore, if fundus autofluorescence can help confirm whether a retinal embolus is calcific, it is likely that an echocardiogram should be ordered in addition to the previously mentioned recommendations for cholesterol retinal emboli.[19]

As fundus autofluorescence becomes more widespread in optometry and ophthalmology offices as part of fundus cameras or optical coherence tomography (OCT) devices, this technology can be used to help refine the diagnosis and optimize further testing ordered for many patients. Eye care providers should be aware of the role of fundus autofluorescence to help identify areas of retinal ischemia, visualize plaques that may otherwise be difficult to distinguish, and differentiate between a cholesterol or calcific embolus and guide further investigation and management. ●

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