Published in final edited form as:

Retina. 2007 October ; 27(8): 1101–1106. doi:10.1097/IAE.0b013e3181451617.

Autofluorescence of Basal Laminar Drusen

Catherine B. Meyerle, MD¹, R. Theodore Smith, MD, PhD², Irene Barbazetto, MD², and Lawrence A. Yannuzzi, MD^{1,2}

¹Vitreous-Retina-Macula Consultants of New York and the Macula Foundation, Inc. of LuEsther T. Mertz Retinal Research Center, Manhattan Eye, Ear & Throat Hospital, New York, New York

²Columbia University, Department of Ophthalmology, New York, New York

Abstract

Purpose—We report three cases illustrating autofluorescence (AF) of basal laminar drusen (BLD) in comparison to conventional fundus photography and fluorescein angiography (FA). Since patients with BLD are at risk for development of pseudovitelliform detachment of the macula which may masquerade as choroidal neovascularization (CNV), detection is essential for proper clinical evaluation and management.

Methods—Twenty patients with BLD were studied with AF and conventional imaging. AF imaging employed an excitation filter at 580 nm and a barrier filter at 695 nm with acquisition by a Topcon 50X fundus camera. Three selected patients with different degrees of BLD are presented. Corresponding detail regions in each image modality were enlarged for comparison. The AF detail image was registered by a projective transformation in Matlab (Mathworks 7.0, Natick, MA) with the color photograph/red free photograph (RF) and/or FA image detail for exact superimposition in Photoshop and lesion comparison.

Results—Each visible drusen in the color or red free photograph corresponded when superimposed to a focal hypofluorescent lesion in the AF image. However, similar to the “starry-sky pattern” in FA, the AF lesions significantly outnumbered the clinically evident drusen. Image registration revealed subtle depigmentation in the color image for some of the remaining AF lesions. When BLD lesions were not advanced enough to show the classic “starry sky” fluorescein hyperfluorescence, the BLD were detectable with AF.

Conclusions—AF imaging demonstrates a higher level of sensitivity than conventional fundus photography and is less invasive than FA. When BLD lesions are not advanced enough to show the classic “starry-sky” fluorescein hyperfluorescence, fundus AF appears to demonstrate a higher level of sensitivity. This imaging modality, therefore, is a valuable aid in diagnosing and following BLD, particularly since these patients are at risk for development of pseudovitelliform detachment which may simulate CNV.

Keywords

autofluorescence; basal laminar drusen; Bruch's membrane; drusen; fluorescein angiography; image registration; macula; retinal pigment epithelium

Introduction

In 1977, Gass described basal laminar drusen (BLD) as small subretinal raised yellow lesions that fluoresce and stain during fluorescein angiography (FA) resulting in a “stars-in-the-sky appearance.”¹ Eight years later, light and electron microscopic analysis localized the pathology to the inner portion of Bruch's membrane with basement membrane-like material originating from the retinal pigment epithelium (RPE).² Gass reported in 1985 that BLD were actually focal nodular thickenings of the RPE basement membrane.³ Russell challenged this notion with his immunofluorescence studies, stating that BLD were not RPE basement membrane proliferations but rather were cellular aggregations of carbohydrates, lipid and protein located between the basal lamina of the RPE and the inner collagenous layer of Bruch's membrane.⁴

Clinically, BLD are significant because they can affect vision and be associated with pseudovitelliform macular detachment which may simulate choroidal neovascularization (CNV).³ In the case of pseudovitelliform detachment masquerading as CNV, proper detection is essential to avoid unnecessary and even harmful treatment. Early BLD lesions are difficult to detect with slit-lamp biomicroscopy. FA with RF photography is helpful as it often reveals more extensive BLD than seen on clinical examination. More advanced BLD are best imaged with FA, as associated RPE atrophy and an intact choriocapillaris result in transmitted choroidal hyperfluorescence or so-called “window defects.” FA in such cases results in a pattern of multifocal hyperfluorescence referred to as a “starry sky.” This has been a standard reference for diagnosing BLD, at least lesions of this level of severity.

Another useful imaging technique for the macula is autofluorescence photography (AF). Fundus autofluorescence is a non-invasive test that provides discrete fundoscopic images based on stimulated emission of light from lipofuscin. Lipofuscin is a cellular waste product containing lipid, protein and fluorophores such as A2E. Visualization of the signal depends on the distribution pattern of the fluorophore-containing lipofuscin.

The following three cases were selected from a study group of 20 BLD patients as examples to compare AF to conventional color photography, RF and FA. The fourth case illustrates the contrasting AF findings in age-related macular degeneration (AMD) of the non-exudative type with very small drusen. AF images were obtained with a Topcon 50X fundus camera utilizing an excitation filter at 580 nm and a barrier filter at 695 nm. Corresponding detail regions in each image were enlarged for comparison. The AF detail image was registered by a suitable projective or polynomial transformation in Matlab (Mathworks 7.0, Natick, MA) with the color photograph/RF and/or FA image detail for exact superimposition in Photoshop and lesion comparison. Drusen identification was performed by our previously described algorithm.⁵ Other lesions (hypoautofluorescence, hyperfluorescence, etc.) were identified either by an appropriate version of this algorithm or manually.

Patients and Methods

Twenty consecutive patients were studied with various degrees of BLD. The gender distribution was 50% men and 50% women. All patients were over the age of 40 years with a range of 43 to 85 and a mean of 65 years old. The following three cases were selected to illustrate AF photography, as compared with conventional imaging, in BLD patients. The fourth case demonstrates the contrasting AF findings in non-exudative AMD involving very small drusen.

Case 1

A 47-year-old woman with a family history of BLD presented for evaluation. Her corrected visual acuity was 20/25 OU. Both AF and FA reveal more BLD than conventional color

photography. The hypoautofluorescent lesions on AF corresponded precisely to the hyperfluorescent “stars-in-the-sky” on FA (Figure 1).

Case 2

A 50-year-old man presented for his first diabetic screening and was found to have basal laminar drusen. Corrected visual acuity was 20/25 OU. Matlab projective transformation and lesion co-localization show that both AF and FA provide better detection of BLD than RF. AF demonstrated approximately twice the number of BLD visible on RF. When compared with FA, the number of hypoautofluorescent lesions corresponding to BLD was essentially identical to the hyperfluorescent window defects on FA. (Figure 2)

Case 3

A 75-year-old healthy woman presented with BLD. Her corrected distance and near visual acuity was 20/25 OD and 20/30 OS. Fundoscopic examination and conventional color photography revealed BLD, while FA did not show the classic “starry sky” appearance. As illustrated by image registration and lesion co-localization, AF surpassed both conventional color photography and fluorescein angiography in documenting the extent of RPE involvement. Also, the AF lesions were larger than the BLD visible on color photography (Figure 3).

Case 4

An 80-year old woman presented with non-exudative AMD on fundoscopic examination and color photography. Corrected visual acuity was 20/25 OU. The color and RF show myriad hard drusen, but these lesions do not correspond with any findings on AF or FA. The FA is granular with a few faint hyperfluorescent foci not corresponding to the drusen. The AF has a non-specific mottled appearance that also has no correlation with the drusen. The typical drusen of this AMD patient do not show the hypoautofluorescent pattern seen in BLD.

Discussion

Conventional ophthalmic color photography, RF and FA, in conjunction with fundus biomicroscopy, have historically been the preferred imaging test for BLD. Clinical detection can be difficult since the lesions are not associated with a lipoidal or melanin discoloration, reducing contrast at the level of the RPE. Furthermore, they are not elevated enough to distinguish stereoscopically. Color fundus photography is not effective at identifying BLD, particularly at early stages, because of low lesion contrast and poor photographic resolution. Larger lesions can be detected with RF photography, which enhances contrast with the RPE. The current standard for diagnosing BLD is the FA which results in a “starry sky” pattern or multifocal areas of hyperfluorescence from window defects as the BLD erode through the RPE. However, early BLD lesions have not yet eroded enough through the RPE to result in sufficient surrounding RPE atrophy to produce this classic pattern. Fundus AF, as evident in our cases, appears to be more sensitive in detecting BLD than conventional color and RF photography, and at least equivalent to invasive FA showing the classic “starry sky” (cases 1 and 2). However, when the FA does not have a “starry sky” appearance, more lesions are visible on AF (case 3). This suggests that AF can detect these drusen before they have eroded enough through the RPE to create the classic “starry sky” appearance. Indeed, the larger size of the AF lesions as compared with conventional imaging suggests that the visible drusen are the central foci of more widespread damage. These larger multifocal hypoautofluorescent lesions appear to be specific for BLD because ordinary small, hard drusen seem to have a different AF presentation (case 4).

Why is early recognition and continued surveillance of BLD with AF important? The presence of BLD alone does not represent a high risk of severe vision loss compared to patients with large drusen who are subject to progressive atrophy and neovascular disease. This consideration by itself suggests a better visual prognosis for such patients. However, recognition of BLD in elderly patients is essential since they commonly develop concomitant soft drusen and even CNV. In contrast to typical AMD patients, patients with BLD are at risk for developing a pseudovitelliform macular detachment. The subretinal fluid seen in these cases may simulate CNV and actually result in unnecessary and even harmful interventional therapy if not diagnosed properly. Finally, beyond its potential level of sensitivity and specificity for detecting and identifying BLD, AF offers a simple, inexpensive imaging technique that is non-invasive compared to FA for detecting and monitoring these changes.

AF imaging, therefore, is a valuable technique for the assessment and management of patients with BLD. Documentation of BLD with AF is simple, inexpensive and reliable. Precise identification of BLD is essential in making appropriate management decisions, particularly when complicating exudative manifestations evolve.

References

1. GassJStereoscopic atlas of macular disease: diagnosis and treatment (2nd ed.). St LouisMosby1977
2. KenyonKMaumeneeARyanSDiffuse drusen and associated complications. Am J Ophthalmol1985100 (1):119-128 [PubMed: 2409799]
3. GassJJallowSDavisBAAdult vitelliform macular detachment occurring in patients with basal laminar drusen. Am J Ophthalmol198599(4):445-459 [PubMed: 3985082]
4. RussellSMullinsRSchneiderBLocation, substructure and composition of basal laminar drusen compared with drusen associated with aging and age-related macular degeneration. Am J Ophthalmol2000129(2): 205-214 [PubMed: 10682974]
5. SmithRTChanJKNagasakiTAutomated Detection of Macular Drusen using Geometric Background Leveling and Threshold Selection. Arch Ophthalmol2005123200-206 [PubMed: 15710816]

Fig 1.

A, B, C. Color photograph, FA and AF image of basal laminar cuticular drusen. Note that the FA has the characteristic “starry sky” appearance, and the AF image has myriad uniform focal hypoautofluorescent lesions.

D, E, F. The area of detail in each image enlarged for comparison. The color photograph detail is **D**. The AF detail image, **F**, has been registered by a polynomial transformation with the FA detail, **E**, for superimposition as layers in Photoshop. The effect of morphing the AF image can be seen along the upper border.

G, H, I. Image analysis. **G.** The color photograph from **D** has been highly contrast-enhanced to emphasize in golden tones subtle areas of decreased pigmentation that correspond both to

the AF and the FA lesion clusters. A few drusen are barely visible. **I.** Clusters of hypoautofluorescent lesions from **F** have been marked with green dots. **H.** These AF lesion clusters were then superimposed in Photoshop on the FA image **E**. Where the AF lesion clusters aligned exactly with hyperfluorescent clusters of “stars” in the FA image, they were marked in green also. The correspondence of these clusters, even lesion by lesion, was almost exact. (An AF lesion cluster that was shifted slightly with respect to an FA star cluster during registration is marked in red.) In this eye AF imaging and FA demonstrate essentially identical sensitivity and specificity for BLD.

Fig 2.

A, B, C. Registered images of BLD. 2500 micron diameter central macular region. **A.** Original RF photograph, **B,** FA (27 second frame) and **C,** AF image. The FA and AF images have been registered to the RF photograph. The FA has also been digitally push-processed to enhance central hyperfluorescence.

D, E, F. Segmentations. **D.** Drusen (green), **E,** non-vascular hyperfluorescence (violet), and **F,** focal hypoautofluorescent AF lesions (yellow). The drusen and non-vascular hyperfluorescence were detected by the automated drusen algorithm⁵. The hyperfluorescence of retinal vessels was masked out manually. The areas of hyperfluorescence were significantly more (total 31% of the region) than those of the drusen (total 15%). The AF lesions were each

roughly circular and ranged from 50 to 100 microns in diameter. The 335 total lesions were marked manually.

G, H, I. Co-localizations. **G.** Hyperfluorescence, **E**, overlaid only on the drusen, **D**, as a “stain”, showing almost all drusen have at least a hyperfluorescent core (window defect). However, by area, only 61% of the total drusen area is hyperfluorescent, demonstrating substantial non-fluorescent drusen rims. **H.** Hypoautofluorescent lesions, **F**, overlaid on hyperfluorescence, **E**, showing that almost all (302/ 335) of the AF lesions co-localize with areas of hyperfluorescence. Hence in this eye AF imaging and FA demonstrate essentially identical sensitivity and specificity for BLD. **I.** AF lesions overlaid on drusen, **D**, showing that approximately half (162/335) of the AF lesions co-localize with visible drusen. Thus, similar to hyperfluorescence on FA, the other half of the AF lesions demonstrates pathology that is not seen on the RF as drusen.

Fig 3.

A, B, C. Color photograph, FA and AF image of basal laminar drusen. Note that the FA does not have the characteristic “starry sky” appearance, whereas the AF image has myriad uniform focal hypoautofluorescent lesions.

D, E, F. Regions of detail enlarged for comparison. The AF and FA detail images have also been registered by a projective transformation in Matlab with the color photo detail for exact superimposition.

G, H, I. The corresponding lesions in each detail image have been segmented (green for drusen, yellow for hypoautofluorescence, pink for hyperfluorescence). **G**, the drusen and, **H**, the non-vascular hyperfluorescence were detected automatically⁵. A few foci of hypofluorescence have

also been marked manually on the FA in purple. **I.** The same algorithm⁵ was used to detect the hypoautofluorescence by applying it to the gray-scale inverted AF image.

J, K, L. Lesion co-localizations. **J.** The hypoautofluorescent lesions in **I** have been superimposed in Photoshop on the fundus photograph with overlying drusen from **G**.

Essentially all of the drusen are precisely co-localized with the larger AF lesions, suggesting that the sensitivity of AF imaging is nearly 100% for visible BLD in this eye. The larger size of the AF lesions also suggests that the visible drusen are the central foci of more widespread damage. The greater number of AF lesions than visible drusen could indicate the presence of BLD that are not visible photographically (or angiographically, see **K**). **K.** The drusen in **G** have been superimposed on the angiographic lesions in **H**. Only a few are hyperfluorescent (pink), and a few more show hypofluorescence or blocking defects (purple). Hence, FA has poor specificity and sensitivity for BLD in this eye, whereas the AF image detected all drusen (see **J**). This suggests that AF can detect these drusen before they have eroded enough through the RPE to create the classic "starry sky" appearance. **L.** The reason for the disparity between the angiographic and autofluorescence findings with respect to the drusen is made clearer by superimposing the FA lesions, **H**, on the AF image in **I**. The FA lesions almost completely avoid the AF lesions. Reference to the AF image, **I**, shows that in fact many of the FA lesions are *hyper*autofluorescent instead and correspond to patchy areas of hypopigmentation on the photograph.

Fig 4.

A, B, C, D. The color, RF, FA and AF images of a macula with multiple ordinary small drusen in AMD. The color image has been contrast enhanced for better demonstration of the drusen. **E, F, G, H.** The respective detail images that were boxed in white above. **E, F.** The color and RF show myriad small drusen. **G.** The FA is granular. The few faint foci of hyperfluorescence have no correlation with the drusen. **H.** The AF has a non-specific mottled appearance and a few dark artifacts that also have no correlation with the drusen.