Supplementary Online Content


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eFigure 8. Case of a 53-Year-Old Female 25 Years Following Onset of Progressive Vision Loss With Enlarged Blind Spot OU and Central Scotoma OD

eFigure 9. A 23-Year-Old Male Presented With an Enlarging Blind Spot and Photopsia in the Left Eye

eTable. Stages of AZOOR

This supplementary material has been provided by the authors to give readers additional information about their work.
**eFigure 1.** Trizonal Pattern of Differential Degeneration of the Outer Retina, Retinal Pigment Epithelium (RPE), and Choroid in AZOOR With Multimodal Imaging in Both Eyes of a 61-Year-Old Female Complaining of Photopsia and Enlargement of the Blind Spot OU for 5 Years

![Image of eye scans](image)

The FAF images (A, B) show the trizonal pattern at the level of the peripapillary AZOOR lesions OU. The SD-OCT scans (C, D) are at the level of the green arrows OU. In the right eye, there is a peripapillary zonal AZOOR lesion with a trizonal pattern on both FAF (A) and corresponding SD-OCT (C) and another skip lesion superotemporal to the macula with a coarse granular hyperautofluorescent pattern. The corresponding SD-OCT (C) shows a normal zone (1) where the ellipsoid zone is preserved, a second zone of disruption of the ellipsoid zone with subretinal dot-like hyperreflective deposits (2) and a third zone of complete loss of the outer retina, atrophic RPE with subsequent increased light transmission and thinning of the choroid (3). The same trizonal pattern is visualized in the left eye in both the FAF (B) and corresponding SD-OCT (D) images.

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**eFigure 2.** Wide-Field FAF Imaging of 2 Patients With Peripheral Concentric AZOOR Lesions Progressing Toward the Posterior Pole

A, B: AZOOR lesions in both eyes of a 78 year-old female complaining of photopsia OD for 7 years and asymptomatic OS with wide field FAF imaging. The visual acuity was 20/25 OU. In the right eye (A), there are 2 AZOOR lesions, one peripapillary and one peripheral concentric lesion on 360 degrees progressing centripetally (white arrows). In the left eye (B), there are 2 AZOOR lesions, one peripapillary and one along the superior vascular arcade. Note the presence of two small scattered hypoautofluorescent spots inferior to the left optic disc (B).

C, D: AZOOR lesions in both eyes of a 59 year-old female complaining of scotoma photopsia and nyctalopia OU at presentation with wide field FAF imaging. The visual acuity was 20/20 OD and 20/25 OS at presentation and decreased to 20/40 OU after 3 years of follow-up. This patient also has non proliferative diabetic retinopathy OU. There is a peripapillary AZOOR lesion in both eyes (C, D) and an additional skip lesion in the posterior pole OD (C). There is an additional peripheral concentric lesion on 360 degrees progressing centripetally OU (white arrows) in the FAF images (C, D), while the peripapillary lesions progress centrifugally. The most recent areas of progression in the peripheral lesion appear hyperautofluorescent (asterixis) while the older parts of the lesion appear hypoautofluorescent OU (C, D).
eFigure 3. Progression of the AZOOR Lesions Over 1 Year of Follow-up in the Left Eye of a 34-Year-Old Myopic (−3.00 D) Caucasian Female Complaining of Photopsia OU at Presentation

The visual acuity was 20/20 OS at presentation. At 1 year, the visual acuity had remained stable OS. The color photograph (A) and FAF image (B) at presentation show two temporal AZOOR lesions, one in the posterior pole and one in the mid-periphery. There is a demarcating hyperautofluorescent line around the peripheral one (white arrows) that appears brownish in the color photograph (yellow arrow). At 4 month follow-up, this lesion has progressed (C, D) and is still surrounded by a demarcating line that appears brownish in the color photograph (C) and hyperautofluorescent in the FAF image (D). At 6 month follow-up, this lesion has progressed on
both the color photograph (E) and the FAF image (F) and is not bordered anymore by a hyperautofluorescent demarcating line in the FAF image (F). AT 1 year follow-up, the lesion has not progressed any further in the color photograph (G) or the FAF image (H). Note that the other AZOOR lesion without a demarcating line has almost not progressed over the course of 1 year. Note the presence of a smaller peripapillary AZOOR progressing lesion (white arrow).
eFigure 4. Trizonal Pattern of Abnormalities of the Outer Retina, Retinal Pigment Epithelium (RPE), and Choroid Differential Consecutive Degeneration in AZOOR With Multimodal Imaging in the Right Eye of a 70-Year-Old Male Complaining of Vision Loss and Photopsia OD for 2 Weeks

A. FAF showing a trizonal appearance. The first zone (1) is isoautofluorescent in the area outside of the delineating AZOOR-line; the second zone (2) is composed of speckled hyperautofluorescence within the AZOOR lesion; and the third zone (3) shows confluent hypoauflorescence corresponding to complete RPE cell loss.

B. Mid-phase indocyanine green angiography angiography (ICGA) showing a trizonal appearance colocalizing exactly with the three zones described in the FAF image. The first zone is normal staining of the extrachoroidal space by the ICG molecule outside of the AZOOR-line. The second zone is inside the AZOOR-line where there is minimal extrachoroidal leakage, and the third zone shows late hypofluorescence since there is RPE cell loss and choriocapillaris atrophy and no leakage of the ICG molecule into the RPE and extrachoroidal space. Note that the demarcating line corresponds to a hypocyanescent line.

C. Spectral-domain optical coherence tomography (SD-OCT) macular horizontal scan showing a trizonal appearance colocalizing exactly with the trizonal appearance in both the FAF and the ICGA images. The normal fundus outside of the AZOOR lesions constitutes the first zone. The second zone is within the AZOOR lesion demarcated by the AZOOR-line. It shows disruption of the ellipsoid and interdigitation zones and multiple mound-like hyperreflective deposits in the subretinal space. These two zones are separated on SD-OCT by a mound-like deposit corresponding to the demarcating line (dotted lines). The third zone corresponds to complete loss of the outer retina and RPE and choroidal thinning with increased light penetration and enhanced choroidal signal. Note the posterior shadowing associated with the subretinal deposits.
**eFigure 5.** Multimodal Imaging of the Subretinal Deposits Visualized in Figure 9 in the Right Eye of a 70-Year-Old Male Complaining of Vision Loss and Photopsia OD for 2 Weeks

The color photograph (A), FAF (B) and ICGA (C) images are at the scale with the SD-OCT scans (D, E, F). The SD-OCT scan (same scan showed in D, E, F) is at the level of the white arrows (A, B, C). Note the demarcating line is yellow-grey in the color photograph(A), hyperautofluorescent in the FAF image (B) and hypocyanescent in the ICGA image (C) and corresponds precisely (white lines) to a mound-like hyperreflective deposit on corresponding SD-OCT (D, E, F).

Note the exact colocalization (white lines) between the subretinal mound-like hyperreflective deposits on SD-OCT and the brownish deposits in the color photograph (A), hyperautofluorescent deposits in the FAF image (B) and hypocyanescent deposits in the ICGA image (C). Note the multiplicity of these deposits within zone 2 (white arrow) visualized as brown deposits in the color photographs (A), hyperautofluorescent in the FAF image (B) and hypocyanescent in the ICGA image (C).
Visual acuity is 20/20 in each eye. Dilated fundus examination of the right eye (A) reveals a zone of RPE atrophy extending from the peripapillary region inferiorly. FAF (B) shows hypoautofluorescence in this region with a border of continuous hyperautofluorescence. SD-OCT (C) through this lesion shows trizonal pattern with loss of ellipsoid layer and thinning of the choroid, loss of ellipsoid layer with preserved choroid and relatively normal retina and choroid. Dilated fundus examination of the left eye (D) shows a similar zone of RPE atrophy extending from the peripapillary region to the inferotemporal periphery. FAF (E) and SD-OCT (F) show a trizonal pattern.
eFigure 7. Progression of the AZOOR Lesions Over 13 Years of Follow-up in Both Eyes of a 59-Year-Old Myopic (−1.00 D) Caucasian Female Complaining of Scotoma and Photopsia OD at Presentation and Asymptomatic OS
The visual acuity was 20/40 OD and 20/20 OS and decreased to 20/100 OU after 13 years of progression. At presentation, there is a peripapillary AZOOR lesion OU in both the color (A, B) and red-free photographs (C, D). There is another AZOOR skip lesion nasal to the disc in the left eye (B, D). Note the foveal sparing in the right eye (A, C). Two years later, there is progression of the peripapillary AZOOR lesions OU in the red-free photographs (E, F), still sparing the fovea OD. Four years later, the peripapillary AZOOR lesions have progressed further OU in the FAF images (G, H) and note the presence of new AZOOR lesions in the far periphery inferior OS (H). Thirteen years later, the AZOOR lesions have progressed into a diffuse atrophy of the entire fundus OU with sparing of a zonal area temporal to the macula (white arrows) OU best visualized in the FAF images (I, J), but also in the color photographs (K, L).
**eFigure 8.** Case of a 53-Year-Old Female 25 Years Following Onset of Progressive Vision Loss With Enlarged Blind Spot OU and Central Scotoma OD

Fundus photograph of the right eye (A) shows zonal atrophy extending from the peripapillary area to the inferonasal periphery. There is central atrophy present as well. Fundus photograph of the left eye (B) demonstrates areas of zonal atrophy along the peripapillary zone and temporal macula. FAF of the right eye (C) shows hypofluorescent lesions with a smooth hyperautofluorescent border. There are other scattered hypoautofluorescent lesions within the macula. FAF of the temporal macula of the left eye (D) shows central hypoautofluorescence within the lesion with a border of hyperautofluorescence. SD-OCT of the right fovea (E) demonstrates loss of ellipsoid line and attenuation of the outer nuclear layer. SD-OCT of the left fovea shows preservation of the outer retina at the fovea. The area of hyperautofluorescence temporally corresponds to loss of ellipsoid line with attenuation of the outer nuclear layer.
Visual acuity was 20/20 OU. There was vitreous inflammation in the left eye. Dilated fundus examination of the right eye was unremarkable and in the left eye showed zonal peripapillary pigmentary atrophy and bone spicules nasal to the optic disc. Over the next 9 years, visual acuity was stable. There was progression of the enlarged blind spot and increased intraretinal pigment migration. On subsequent examination, FAF showed peripapillary hypoautofluorescent zone with a smooth hyperautofluorescent border (B). SD-OCT through the superior macula shows loss of the ellipsoid line and attenuation of the outer nuclear layer. There was also cystoid macular edema present.
eTable. Stages of AZOOR

<table>
<thead>
<tr>
<th></th>
<th>EARLY (Weeks to months)</th>
<th>INTERMEDIATE PROGRESSIVE (Months)</th>
<th>LATE (Usually stabilized)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilated Fundus Appearance</td>
<td>Often normal</td>
<td>Yellow/orange line</td>
<td>Zonal, multizonal, peripapillary</td>
</tr>
<tr>
<td>White or gray line (acute annular outer retinopathy)</td>
<td>Atrophy of retina, RPE, and choroid (often atrophy peripapillary)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fundus Autofluorescence</td>
<td>Diffuse/Patchy hyperautofluorescence</td>
<td>1. Normal periphery degeneration</td>
<td>Trizonal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Speckled hyperautofluorescence</td>
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<tr>
<td></td>
<td></td>
<td>3. Central confluent hypoautofluorescence</td>
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</tr>
<tr>
<td>Spectral-Domain Optical Coherence Operative Coherence Tomography</td>
<td>Disruption of the ellipsoid and interdigitation lines Fovea often spared</td>
<td>Trizonal degeneration with loss of photoreceptors, RPE and choriocapillaris possible degeneration of inner retinal layers</td>
<td>Trizonal</td>
</tr>
</tbody>
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