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Acute Zonal Occult Outer Retinopathy: Structural and Functional Analysis Across the Transition Zone between Healthy and Diseased Retina

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Abstract

Purpose—To assess structure and function across the transition zone (TZ) between relatively healthy and diseased retina in acute zonal occult outer retinopathy (AZOOR).

Methods—Six patients (6 eyes; age 22 to 71 years) with AZOOR were studied. Spectral domain optical coherence tomography (SD-OCT), fundus autofluorescence (FAF), near-infrared reflectance (NIR-R), color fundus photography (CFP), and fundus perimetry (MP-1) were performed and images were registered to each other. The retinal layers of the SD-OCT scans were segmented and the thicknesses of two outer retinal layers i.e. the total receptor and outer segment plus layers, and the retinal nerve fiber layer (RNFL) were measured.

Results—All eyes showed a TZ on multimodal imaging. On SD-OCT the TZ was in the nasal retina at varying distances from the fovea. For all eyes, it was associated with loss of the ellipsoid zone (EZ) band, significant thinning of the two outer retinal layers, and in 3 eyes with thickening of the RNFL. On FAF all eyes had a clearly demarcated peripapillary area of abnormal FAF delimited by a border of high AF; the latter was associated with loss of the EZ band and with a change from relatively normal to markedly decreased or non-recordable visual sensitivity on MP-1.

Conclusion—The results of multimodal imaging clarified the TZ in AZOOR. The TZ was outlined by a distinct high AF border that correlated with loss of the EZ band on SD-OCT. However, in fundus areas that appeared healthy on FAF, thinning of the outer retinal layers, as well as thickening of the RNFL were observed near the TZ. The TZ was also characterized by a decrease in visual sensitivity.

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Keywords

acute zonal occult outer retinopathy; azoor; fundus autofluorescence; microperimetry; optical coherence tomography; retina

Introduction

Acute zonal occult outer retinopathy (AZOOR) is a rare disease first reported by Gass in 1992.¹ He described a previously unrecognized syndrome that affected one or both eyes and that occurred predominantly in young Caucasian females. The 13 patients in his cohort presented with complaints of acute loss of one or more visual field zones or scotomas, photopsia, minimal fundusoscopic changes, and electroretinographic abnormalities. On follow-up, areas of retinal pigment epithelium and photoreceptor atrophy, accompanied by retinitis pigmentosa-like changes such as narrowing of arterioles and pigment clumping, were apparent in some of the patients. Subsequent studies have further characterized AZOOR in larger cohorts of patients.² There seems to be a predilection for young myopic Caucasian women, who often share a history of autoimmune diseases. In most patients, central visual acuity is only minimally affected. The disease typically presents unilaterally but often evolves to become bilateral.³ In the majority of cases visual field loss stabilizes within 6 months and rarely shows signs of progression. Electrophysiological testing in the form of full field electroretinography (ERG) and electrooculography (EOG) has revealed generalized dysfunction at the level of the photoreceptor and RPE complex and also at inner retinal levels.⁴ There is still uncertainty regarding the etiology of AZOOR and currently there is no clear evidence that treatment in the form of corticosteroids can change the visual outcome or alter the natural course of disease.³

Over the years there has been an increasing lack of consistency regarding the definition of this disease. A variety of white spot syndromes, most prominently multiple evanescent white dot syndrome (MEWDS) and multi focal choroiditis, have become associated with AZOOR. These white spot syndromes previously classified by Gass as “AZOOR complex” diseases have led to AZOOR becoming a general diagnostic term for chorioretinal diseases with visual loss of uncertain origin. Recently, a specific definition of AZOOR based on clinical fundus features and multimodal imaging has been proposed by Mrejen et al.⁵ AZOOR is a distinct clinical entity, and can be distinguished from other diseases of the posterior pole including white spot syndromes and other inflammatory neuropathies. According to Mrejen et al. although the appearance of the AZOOR lesions vary depending on their duration, they have characteristic features. These include a demarcating line of progression at the level of the outer retina and a trizonal pattern of sequential involvement of the outer retina, the retinal pigment epithelium and choroid. Advanced cases demonstrate disruption of the inner and outer retina and damage or loss of the RPE and choroid.⁵

Structural changes on SD-OCT such as loss and/or disruption of the ellipsoid zone (EZ) band (aka the inner segment/outer segment junction), thinning of the outer nuclear layer, retinal pigment epithelium, choroid, and inner retina, have been reported in cases of AZOOR.^{5–10} These areas of pathology appear to correspond to visual field scotomas

detected on static and dynamic perimetry and to areas of decreased multifocal electroretinogram responses.⁶ Abnormalities in fundus autofluorescence (FAF) have also been reported in patients with AZOOR. It has been suggested that FAF is a useful tool for identifying the diseased retinal areas, and that the trizonal pattern of FAF imaging is a defining feature, particularly the hyperautofluorescent line demarcating the normal retina from the AZOOR lesion.¹⁰ However based on the results of a recent case study, the hyperautofluorescent line may also be seen in forms of multifocal choroiditis with geographic atrophy.¹¹

To help clarify the structure-function relationship of this rare retinal disease and to aid in its diagnosis we compared localized measures of structural and functional changes across the transition zone (TZ), the boundary between relatively healthy-appearing retina and severely affected retina. On SD-OCT we define the TZ as the location associated with loss of the ellipsoid zone (EZ) band and with significant thinning of the outer retinal layers; i.e. thinning of the layers extending from the border between Bruch's membrane and the choroid to the border between the outer plexiform layer and the inner nuclear layer. The TZ offers a potential model of disease progression, if we assume that the sequence and nature of structural changes observed spatially across the TZ at one specific time (that of SD-OCT acquisition) can also occur at other locations in the retina as the disease progresses. Structural changes were evaluated qualitatively and quantitatively with SD-OCT scans of the affected eyes; they were compared to areas of abnormal AF on FAF, and to localized measures of visual function assessed with fundus tracking perimetry (MP-1).

Methods

Subjects

This retrospective study includes 6 affected eyes of 6 patients referred to a retina specialist (SHT); all matched the diagnostic criteria for AZOOR described by Mrejen et al.⁵ None of 6 cases showed evidence of belonging to the AZOOR complex category. Possible differential diagnoses, such as optic neuropathies, hereditary disorders, diffuse unilateral subacute neuroretinitis (DUSN), cancer associated retinopathy, melanoma associated retinopathy and autoimmune retinopathies were excluded. All patients had a full ophthalmic examination that included best-corrected visual acuities, refraction, slit-lamp examination, and a dilated fundus examination. Full-field electroretinograms and electrooculograms (Diagnosys LLC, Lowell, Massachusetts, USA) were obtained according to the International Society for Clinical Electrophysiology of Vision standards.^{12, 13} All procedures adhered to the tenets of the Declaration of Helsinki, and written informed consent was obtained from all subjects after a full explanation of the procedures was provided. The protocol was approved by the Institutional Review Board of Columbia University.

Multimodal Imaging

Pupils were dilated with topical 1% tropicamide and 2.5% phenylephrine. A fundus autofluorescence (FAF, 488 nm excitation) image was acquired with the Spectralis HRA +OCT (Heidelberg Engineering, Heidelberg, Germany) after bleaching of photopigments for 20 seconds in AF mode.¹⁴ In addition, a horizontal 9-mm SD-OCT scan through the fovea

was recorded with the Spectralis and automatically registered to a simultaneously acquired near-infrared reflectance (NIR-R) fundus image. A color fundus photograph (CFP) was acquired with the FF450+IR fundus camera (Carl Zeiss Meditec, Jena, Germany).

Fundus perimetry was performed with the Nidek MP-1 (NAVIS software version 1.7.3; Nidek Technologies, Padua, Italy). A 10-2 pattern, similar to the 10-2 pattern of the Humphrey visual field, and custom patterns were used to assess visual sensitivities following pupil dilation and a 15-minute adaptation period to the mesopic 1.27 cd/m² background. The non-tested eye was occluded. White test lights (stimulus size Goldmann III, 200 ms in duration) were presented on the 1.27-cd/m² white background using a 4-2 threshold strategy. The subjects were asked to maintain fixation on a 2° red cross. The MP-1 results in dB were manually registered to the imported FAF images in the Nidek MP-1 using dedicated software (NAVIS; Nidek Technologies).

All images of the same field were aligned to the NIR-R image of the SD-OCT scan using i2kRetina software (DualAlign LLC, Clifton Park, NY). This process allowed us to subsequently correlate AF with superimposed MP-1 results, NIR-R, CFP and SD-OCT.

SD-OCT Segmentation

Horizontal SD-OCT line scans through the fovea of the affected eyes were segmented in Matlab (MathWorks, Natick, MA, USA) by one of the authors (FJ), using a manually corrected automated program. The segmentation technique has been described previously.¹⁵ The following borders were segmented: (1) the border between the vitreous and inner limiting membrane (ILM); (2) the border between the retinal nerve fiber layer (RNFL) and the retinal ganglion cell (RGC) layer; (3) the border between the inner nuclear layer (INL) and the outer plexiform layer (OPL); (4) the proximal border of the band corresponding to the ellipsoid zone (EZ); (5) the proximal border of the retinal pigment epithelium (pRPE); and (6) the border between Bruch's membrane (BM) and the choroid. The thicknesses of two outer retinal layers, the OS plus layer (OS+, from the BM/choroid border to the proximal border of the EZ band), and the total receptor layer (TRec+, from the BM/choroid border to the OPL/INL border), and the thickness of an inner retinal layer, the RNFL were determined (Figure 1). Although our primary interest was to assess the thickness of the outer retinal layers we measured the thickness of the RNFL as well because of reports of inner retinal thickening in the nasal retina in patients with RP that has been attributed to a thickening of the RNFL.¹⁵

Results

Demographically, the cohort consisted of five females (4 Caucasian, 1 Asian) and 1 male (Caucasian). The patients ranged in age from 17–71 years (mean/median = 44 years). Each patient presented with unilateral disease exhibiting characteristics consistent with AZOOR. Chief complaints at initial presentation included acute onset of photopsias, blurred vision and scotomata. Best-corrected visual acuity ranged from 20/20 to 20/30 in the affected eye. Four patients were myopic. On fundus examination, RPE mottling and pigment migration and/or atrophy was observed in the peripapillary regions of the affected eye in three patients (P1, P2 and P4) while a comparatively larger and more advanced area of peripapillary

atrophy extending toward the nasal region (relative to the optic disc) of retina were exhibited by P3, P5 and P6. Two of the patients (P1 and P4) were seen at the early or acute phase, the other patients were referred when clinical findings were at a more advanced or chronic phase.

Full-field ERG and EOG results showed inter-ocular differences for measured parameters reflecting rod and cone system function and the retinal pigment epithelium. For example, for all 6 patients, the EOG light rise was reduced in the affected eye compared to values for the unaffected eye. With the exception of P2, the full-field ERG 30Hz cone flicker response, i.e. the cone system response, showed decreased amplitudes in the affected eye and for P6, this was accompanied by increased implicit time. For 4 patients (P1, P3, P4, P5) the rod system response in the affected eye was also decreased in amplitude compared to the unaffected eye.

Multimodal Imaging of the Transition Zone

The affected eyes of all patients showed a localized area of pathology surrounding the optic nerve. Each presented with a depigmented area of RPE atrophy, which was quite faint on color fundus photography (Figs. 2–7D), but more prominent on infrared imaging (NIR-R) as an area of hyperreflectance due to increased choroidal reflectance (Figs 2–7C).

The boundaries of the peripapillary lesion in the affected eyes spatially corresponded to a well-demarcated hyperAF border on AF imaging (see white arrowheads in Figs. 2–6B). For P6, who had comparatively more advanced disease, the border had a beaded appearance and was formed by a speckled band of hyperAF dots (Fig. 7B). The size and extent of the peripapillary lesion varied. Affected areas within the smaller lesions (~3–5mm radius from center of optic disc) (see P1, P2 and P4, Figs 2, 3, 5) exhibited minimal changes on AF. Areas within larger lesions (P3,5 and 6 Figs. 4,6,7) were visibly atrophic with hyper- and hypoAF mottling, and Increased visibility/reflectivity of the underlying choroidal vasculature within the demarcated lesion was evident in NIR-R imaging (Figs 2–7, C). Severe choroidal thinning and atrophy was observed in P6. Horizontal foveal SD-OCT scans in all affected eyes across the TZ (indicated in Figs 2A–7A by the dashed vertical line(s)), revealed varying changes in the photoreceptor-attributable bands in the nasal retina. The hyperAF border corresponded to the location of EZ loss, this is indicated by the dashed vertical lines in the multimodal fundus images. The EZ band loss was associated with apparent thinning of the ONL, the RPE and loss of the interdigitation zone (IZ) (see Figs. 2A, 5A, 6A) that occurred closer to the fovea, nearer the relatively “healthy” retina than the location of EZ loss (Figs. 2–7). Qualitatively, the inner retinal layers appeared to be unaffected.

Visual sensitivity as measured with the MP-1 was markedly decreased across the TZ. Figures 2–7B shows the results of overlaying the MP-1 visual sensitivity maps onto the FAF images. For P1-5, the location of EZ band loss (vertical dashed line) and the border of abnormal FAF i.e. the TZs, were associated with decreased visual sensitivity that became non-recordable (<0dB) with increasing eccentricity from the fovea in the nasal retina. For P6, the most advanced of our cases, the retinal region with a residual thickened hyper-reflective EZ band was associated with decreased visual sensitivities, and absence of the EZ

band was associated with non-recordable visual sensitivities. Figure 8 summarizes the change in visual function that occurred for the 6 eyes when mean visual sensitivity values obtained at locations in relatively “healthy” retina (−1 mm) were compared to those obtained in the affected diseased retina (+1 mm). With the exception of P5, sensitivity even in relatively “healthy” retina is decreased compared to values for normal controls (range from 17 to 20 dB) in similar locations.

SD-OCT Quantitative Analysis

Qualitatively, all 6 eyes of the patients share similar features on SD-OCT, loss of the EZ band in the nasal retina, nasal to the fovea involving the peripapillary region, and thinning of the outer retinal layers. Quantitative analysis confirmed that the thicknesses of the outer retinal layers were significantly decreased. Figures 9A and B show the thickness values for TRec+ and OS+ layers for the 6 eyes as a function of distance from the foveal center together with the mean (black bold trace) and 95% confidence intervals (CI) (black dotted traces) of the controls. These layers were significantly thinned for all 6 eyes in the nasal retina compared to controls; the values fell below the 95% CI represented by the lower black dotted line in Figs 9A and B, and decreased with increasing eccentricity from the fovea. In the temporal retina OS+ thickness values were within normal limits for 3 eyes (P3-P5) and TRec+ values were also within normal limits for 3 eyes (P1, P3 and P5). P6, the most advanced case, showed the greatest decrease in OS+ and TRec+ thickness. For all eyes in the nasal retina, significant thinning of the OS+ and/or TRec+ occurred at retinal locations that were in relatively “healthy” retina within ± 0.5 mm (approx. 1.7 deg.) of the central fovea i.e. prior to the location of the EZ band loss,

We also measured the thickness of the RNFL because of reports of inner retinal thickening in the nasal retina in patients with RP that has been attributed to a thickening of the RNFL.¹⁵ Figure 9C shows the thickness values for the RNFL for the 6 eyes; they are significantly increased in the nasal retina for P3, P5 and P6.

In summary the quantitative analysis provides confirmation of the observation that in this cohort of AZOOR patients ONL thinning and IZ loss occurs spatially before EZ band loss, and despite the Inner retinal layers appearing to be unaffected, RNFL thickness values were significantly increased in the nasal retina over areas of atrophy.

Discussion

All cases of AZOOR in our study presented with a well-defined area of pathology in the peripapillary region. Five that shared similar findings on SD-OCT and FAF represent the earlier stages of the disease. One patient, P6, was more advanced and illustrates the later stages of the disease. The patients not only had clinical features in common with those described by Gass and others^{1-3, 5} but also exhibited electrophysiological findings similar to those previously reported.^{4, 16} The AZOOR patients presented in this study all exhibited the diagnostic criteria defined as characteristic by Mrejen et al., including a demarcating line of the progression at the level of the outer retina and a trizonal pattern of sequential involvement of the outer retina, retinal pigment epithelium, and choroid.⁵ The abnormal electrophysiologic findings not only provide evidence that the visual sensitivity losses seen

on fundus perimetry are retinal in origin but they also point to a generalized dysfunction of the cone and rod system and retinal pigment epithelium/photoreceptor complex.

Our main purpose was to clarify the structure-function relationship of this rare retinal disease and obtain a better understanding of the TZ between relatively healthy appearing retina and affected retina. The structural and functional changes across the TZ observed on SD-OCT should provide a potential model of disease progression, if we assume that the sequence and nature of structural changes observed spatially across the TZ at one specific time (that of SD-OCT acquisition) can also occur at other locations in the retina with disease progression. On SD-OCT, in the less advanced cases, ONL thinning and IZ loss were observed to occur before EZ band loss, supporting previous suggestions that the photoreceptor outer segments are damaged first in AZOOR.⁶ As already reported in retinitis pigmentosa (RP), a group of hereditary retinal diseases known to primarily affect the photoreceptors, there seems to be an orderly progression of structural changes in the TZ between healthy and diseased retina.¹⁷ RPE atrophy, choroidal atrophy and inner retinal attenuation must be secondary processes since they are not present in the early stages of disease. The significant thinning of the OS+ and TRec+ in the nasal retina found on quantitative analysis of the SD-OCT data confirmed the qualitative observation of markedly decreased receptor layers. The increased thickness of the RNFL observed in 3 of the cases resembled previous findings in patients with RP.¹⁴ Disruption of the inner retina has been reported in advanced cases of AZOOR.⁵ The exact mechanism underlying this RNFL thickening is not clear but it may be due to an inflammatory process, or there may be a proliferation of glial cells in the RNFL that contributes to the thickening. The misconfiguration of inner retinal layers, particularly the thickening of RNFL prior to vitrectomy,¹⁸ have been associated with the presence of epiretinal membranes though none of the analyzed patients in this study were found to have such complications. Another possible explanation for the finding is that some of the thickening might be due to a purely mechanical factor; whereby the RNFL “stretches” slightly, possibly antero-posteriorly, to partially fill space emptied by the degeneration of the receptors; this was suggested as an explanation for RNFL thickening in RP patients in Hood et al. (2009).¹⁵

On FAF all the patients showed a marked zone of abnormal AF in the area of pathology analogous to the area between the outer and inner border of the hyperAF ring in RP¹⁹; with the exception of P6, the border of abnormal AF in AZOOR, was hyperAF. In the current study we used short wavelength AF imaging. The hyperAF reflects increased formation of bisretinoid lipofuscin.²⁰ Loss of the RPE results in hypoautofluorescence towards the optic nerve, from where the disease originated. The hyperAF border observed in 5 patients correlated with EZ band loss and a marked decrease in visual sensitivity. Sensitivities decreased with increasing eccentricity from the fovea in the nasal retina and became non-recordable. Although the importance of the integrity of the EZ band for visual function has been demonstrated in various other retinal disease,²¹ little if anything is known about the association between EZ band loss, the border of increased AF and loss of visual function in AZOOR.

The origin of the hyperAF border in AZOOR is not clear. We found that, similar to retinitis pigmentosa,²² there was loss of the EZ band at the outer border of the hyperAF AZOOR

line. Thus, the hyperAF border may reflect an accelerated production of bisretinoids within degenerating photoreceptors.²³ Another possible explanation is that the hyperAF signal may result from a “window defect”, i.e. the loss of the outer retina might result in less absorption of the AF signal originating from the RPE.⁵

A limitation of this study is that we used an orderly progression of changes in retinal structure and function across the TZ as a proxy for changes over time, as opposed to longitudinal data. In addition, given the finding of decreased rod mediated ERG responses in 4 of the affected eyes, a comparison of rod versus cone system sensitivity would have provided information regarding the extent and degree of impairment of the rod and cone system in these patients with AZOOR.

In conclusion the structure and function of the TZ, between relatively healthy to disease-affected retina in AZOOR was analyzed. The edge of the lesion visible on funduscopy corresponded to a hyperAF border in AF imaging that delineated a region of increased choroidal visibility on NIR-R and EZ loss on SD-OCT. The multimodal imaging approach revealed a progression of structural and functional changes across the TZ such as atrophy and AF granularity and a marked decrease in visual sensitivity.

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Summary Statement

Multimodal imaging was used to clarify structure and function of the transition zone (TZ) between relatively healthy and diseased retina in AZOOR. The TZ was associated with loss of the ellipsoid zone band outlined by a hyperautofluorescent border, thinning of the outer retinal layers and markedly decreased visual sensitivity.

Figure 1. Retinal layer segmentation of SD-OCT scans

Image of horizontal SD-OCT scan from a healthy control subject. Segmented boundaries are indicated as colored lines: *red*, the border between vitreous and inner limiting membrane (ILM); *white*, the border between inner nuclear layer (INL) and outer plexiform layer (OPL); *green*, proximal border of the ellipsoid zone (EZ); *pink*, the proximal border of the retinal pigment epithelium (RPE); and *blue*, the border between Bruch's membrane (BM) and choroid. Two layers were derived from these boundaries: OS+, distance between EZ and BM/choroid; TRec+, distance between INL/OPL and BM/choroid.

Figure 2. Patient 1

A. Horizontal SD-OCT scan through the fovea. The retinal layers corresponding to retinal pigment epithelium (RPE)/Bruch's membrane, interdigitation zone (IZ), ellipsoid zone (EZ), external limiting membrane (ELM) and outer nuclear layer (ONL) are indicated. The position of EZ loss is marked by a dashed vertical line. **This is defined as the transition zone (TZ).** The fundus position of the SD-OCT scan and the position of EZ loss are indicated in the multimodal fundus images (B–D), which were aligned to each other. Corresponding fundus positions are indicated by arrowheads. **B.** Fundus autofluorescence image with overlay of MP-1 10-2 visual sensitivity map. **Sensitivity values are in dB; values in red represent low sensitivity and green high sensitivity.** **C.** Near-infrared reflectance image. **D.** Color fundus photograph.

Figure 3. Patient 2

A. Horizontal SD-OCT scan through the fovea. Between the dashed vertical lines, the retinal layer corresponding to the EZ band is lost. The outer nuclear layer (ONL) is also decreased in thickness. The fundus position of the SD-OCT scan and the outer limits of the area of EZ loss are indicated in the multimodal fundus images (B–D), which were aligned to each other. Corresponding fundus positions are indicated by arrowheads. **B.** Fundus autofluorescence image with overlay of MP-1 custom visual sensitivity map. **C.** Near-infrared reflectance image. **D.** Color fundus photograph.

Figure 4. Patient 3

A. Horizontal SD-OCT scan through the fovea. The retinal layers corresponding to retinal pigment epithelium (RPE)/Bruch's membrane, interdigitation zone (IZ), ellipsoid zone (EZ), external limiting membrane (ELM) and outer nuclear layer (ONL) are indicated. The position of EZ loss is marked by a dashed vertical line. The fundus position of the SD-OCT scan and the position of EZ loss are indicated in the multimodal fundus images (B–D), which were aligned to each other. Corresponding fundus positions are indicated by arrowheads. **B.** Fundus autofluorescence image with overlay of MP-1 custom map. **C.** Near-infrared reflectance image. **D.** Color fundus photograph.

Figure 5. Patient 4

A. Horizontal SD-OCT scan through the fovea. The retinal layers corresponding to retinal pigment epithelium (RPE)/Bruch's membrane, interdigitation zone (IZ), ellipsoid zone (EZ), external limiting membrane (ELM) and outer nuclear layer (ONL) are indicated. The position of EZ loss is marked by a dashed vertical line. The fundus position of the SD-OCT scan and the position of EZ loss are indicated in the multimodal fundus images (B–D), which were aligned to each other. Corresponding fundus positions are indicated by arrowheads. **B.** Fundus autofluorescence image with overlay of MP-1 custom map. **C.** Near-infrared reflectance image. **D.** Color fundus photograph.

Figure 6. Patient 5

A. Horizontal SD-OCT scan through the fovea. The retinal layers corresponding to retinal pigment epithelium (RPE)/Bruch's membrane, interdigitation zone (IZ), ellipsoid zone (EZ), external limiting membrane (ELM) and outer nuclear layer (ONL) are indicated. The position of EZ loss is marked by a dashed vertical line. The fundus position of the SD-OCT scan and the position of EZ loss are indicated in the multimodal fundus images (B–D), which were aligned to each other. Corresponding fundus positions are indicated by arrowheads. **B.** Fundus autofluorescence image with overlay of MP-1 10-2 visual sensitivity map. **C.** Near-infrared reflectance image. **D.** Color fundus photograph.

Figure 7. Patient 6

A. Horizontal SD-OCT scan through the fovea. The retinal layers corresponding to retinal pigment epithelium (RPE)/Bruch's membrane, interdigitation zone (IZ), ellipsoid zone (EZ), external limiting membrane (ELM) and outer nuclear layer (ONL) are indicated. The position of EZ loss is marked by a dashed vertical line. The fundus position of the SD-OCT scan and the position of EZ loss are indicated in the multimodal fundus images (B–D), which were aligned to each other. Corresponding fundus positions are indicated by arrowheads. **B.** Fundus autofluorescence image with overlay of MP-1 10-2 visual sensitivity map. **C.** Near-infrared reflectance image (NIR-R). In the NIR-R image, the area of hyperreflectivity is marked by dotted line, which is also indicated in B.

Visual Function over Transition Zone

Figure 8.

A. Difference in visual sensitivity inside and outside the EZ band for each affected eye (dashed lines). B. Image of SD-OCT horizontal line scan of the TZ for P2 and corresponding FAF image with overlay of MP-1 sensitivity values. The dashed vertical lines represent the locations 1 mm inside and outside the location of loss of the EZ band, and the corresponding hyper-reflective band. The superimposed numbers represent the sensitivity values above and below the mid-line.

Figure 9.

Foveal line scan thicknesses of the OS+ (A), TRec+ (B), and RNFL (C) layers, as a function of retinal eccentricity for normal control subjects (black lines) and for each affected eye with AZOOR (colored lines). The black dotted lines indicate the 95% confidence interval around the mean normal control values (for n=35 normal controls).