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Clinical Findings and Management of Dark without Pressure

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Abstract:

Dark without pressure presents as an island or a patch of darker but otherwise normal retina in fundus examination with a condensing lens and a light source. On optical coherence tomography, these lesions show an abrupt attenuation of reflectivity in the ellipsoid zone and the outer segment layer. There have been few case reports since 1975 discussing these findings. To date, little is known about the structural and functional significance of this retinal presentation. Interestingly, these dark without pressure retina have been found in eyes with Oguchi's disease. The relationship of dark without pressure to Oguchi's disease remains unknown.

Keywords:
Dark without Pressure, Retina, Geographic Areas of Retinal Darkening, Oguchi's Disease, Ellipsoid Zone Hyporeflectance, Outer Segment, Optical Coherence Tomography

Introduction

During clinical evaluations, abnormalities and uncommon variations of normal often initiate additional workup and/or a second opinion. In an otherwise normal retina with appearance of darker colored patches, the lesions have been described in the literature as “dark without pressure.” These lesions appear to have a hyporeflective ellipsoid zone and outer segment layer on optical coherence tomography (OCT). The significance of this retinal presentation remains unknown. Therefore, careful documentation and imaging if available will help in future studies into the structure and functions of this retinal presentation.

Case Report

A 26-year-old, Hispanic, male, new patient presented to clinic on March 23, 2016 for a routine eye exam and a contact lens prescription update. His last eye exam was on August 27, 2010 at the medical treatment facility at Miramar Marine Corps Air Station in San Diego, CA. That exam was remarkable for bilateral compound myopic astigmatism and inferior midperipheral scattered white areas on the retina, flat with scleral depression. The patient did not have any other significant visual or ocular complaints besides blurry vision without correction.

The patient denied personal and familial eye history of blindness, glaucoma, and macular degeneration. The patient also denied any history of diabetes, hypertension, high cholesterol, heart disease, thyroid disease, or cancer. A review of systems was unremarkable. The patient was not taking any prescription or over the counter medications.

The patient presented wearing unknown toric contact lenses, corrected to 20/25 in both eyes. The patient reported replacing his contact lenses every 30 days, and the age of the current pair was 3-weeks-old. He admited to occasionally sleeping in the contact lenses 1-2 nights a week, and averaging 12-hours of wear each day. The patient was using a Renu brand multi-purpose contact lens solution for his cleaning system.

The entrance examination was unremarkable, OU. The patient did not manifest any phorias on cover tests. Extraocular motilities were full, extensive, smooth, and accurate, without complaints of pain or diplopia. Pupillary testing was equal, round, reactive to light, without any afferent pupillary defect in either eye. The patient was corrected to 20/20 in each eye, with the refractive error of OD: -5.00-3.00x170 and OS: -5.50-2.25x015, without scissoring reflex during retinoscopy. Intraocular pressures measured 12mmHg OD and 13mmHg OS at 08:45AM with a non-contact tonometer (NCT)

The patient was refitted into CooperVision Biofinity Toric lenses in 8.7mm base curve and 14.5mm diameter for each eye. The patient saw 20/20 in each eye with a -4.75-2.25x170 lens in the right eye and a -5.25-1.75x010 lens in the left eye. The right lens rotated 10 degrees to the left, while the left lens rotated 10 degrees to the right. Both lenses showed good centration, coverage, and movement under the slit lamp. Since vision and comfort were not compromised, the rotation of the axes were not adjusted for the final prescription.

The patient initially declined dilation at the visit, but the undilated fundus examination revealed multiple patches of retinal darkening just beyond the superior arcade and the nasal retina of both eyes. The patient was then convinced to be dilated for a proper evaluation. The patient was dilated at 09:58 AM with one drop of 0.5% Proparacaine hydrochloride ophthalmic solution, followed by one drop of 1% Tropicamide ophthalmic solution, and one drop of 2.5% Phenylephrine hydrochloride in each eye.

Dilated fundus evaluation revealed multiple, flat patches of varying sizes from 1 disc diameter (DD) to 4DD of darker retina (Figure 1) with well demarcated borders scattered throughout the midperiphery of both retinae, superiorly, nasally, temporally, and inferiorly. The right eye also revealed an area of white without pressure spanning 5-8 o'clock inferiorly. The left eye revealed a small patch of white without pressure at 8 o'clock and another at 4:30 o'clock in the peripheral retina.

Differential diagnoses considered at this point include:

Oguchi's Disease
X-Linked Congenital Retinoschisis
Acquired Retinoschisis
Asymptomatic Retinal Breaks
Sub-Retinal Pigment Epithelium (RPE) Hemorrhages
Choroidal Nevi
Dark without Pressure

- Oguchi's Disease is a rare congenital stationary night blindness caused by an autosomal recessive gene mutation. The retina has a golden or greyish-white tapetal-like reflex that disappears after prolonged dark adaptation, known as the Mizuo-Nakamura phenomenon. In many of these patients, there are dark regions with clear demarcation of varying size and shape where the tapedal-like reflex is absent. These dark areas are usually located along the equator.[1,2]
- X-Linked Congenital Retinoschisis is a recessive trait that causes a split in the nerve fiber layer in both eyes. The macula typically appears spoke-like due to microcystic edema, resulting in poor visual acuity, nystagmus, and/or strabismus.[3,4] Furthermore, large, inner layer breaks occur more frequently in the area of the schisis.[4]
- Aquired Retinoschisis is an intraretinal degeneration that leads to a split in the outer plexiform layer and occasionally the inner nuclear layer of the retina.[4,5] There are two histologic variants of retinoschisis. The flat form, also known as reticular cystoid degeneration, is thought to be a milder variant affecting a slightly deeper retinal layer.[5] The bullous or reticular form involves a slightly more superficial layer of the retina. Outer retinal holes may develop under the schisis and appear as patches of deeper colored retina.[1,4,5] Visual field defects usually show sharp borders corresponding to the area of the schisis.[4]
- Retinal Breaks are full-thickness separation of the sensory retina. They can be atrophic holes without signs of traction, or they can be tears with an operculum or an anterior flap. The area of the break often appears a darker shade due the exposed underlying RPE. Retinal breaks are an important precursor to rhegmatogenous retinal detachment. However, studies into the risk

factors for retinal detachment found that only 2% of atrophic holes associated with lattice degeneration resulted in clinical or progressive subclinical detachments.[4,5]

- Sub-RPE hemorrhages are pools of blood between retinal pigment epithelium and Bruch's membrane. Because of the tight junctions between RPE cells, the hemorrhages exhibit a well-defined border. They appear dark and obscure underlying choroidal vasculature. These hemorrhages can be caused by choroidal neovascular membranes, tumors, or trauma.[6]
- Choroidal Nevi are relatively flat, pigmented benign lesions consisting of atypical uveal melanocytes.[1] They appear brown or slate-grey with feathery margins. Overlying drusen and amelanoic lesions are possible variations.[7]
- Dark without Pressure is a geographic area of darker appearing retina in central to midperipheral fundus. The lesion has been described as a "flat, discrete patch of darker retina with well-defined edges." The patients are asymptomatic, and the optical coherence tomography over the lesion shows a characteristic abrupt transition to a hyporeflective ellipsoid zone.[8]

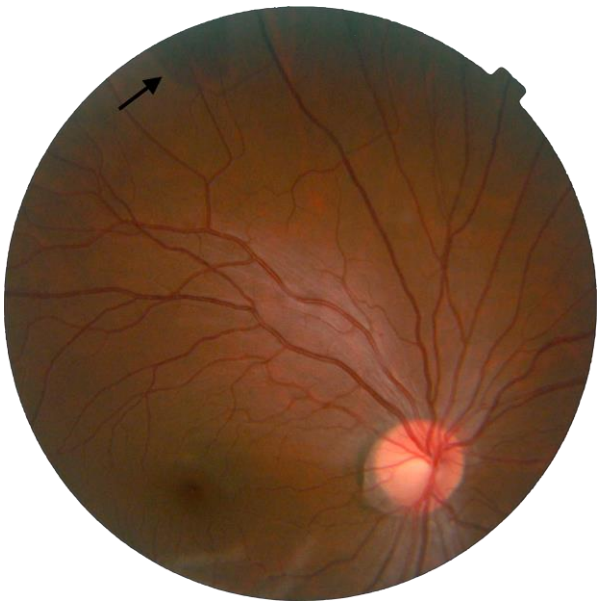
Choroidal nevi were ruled out based on the appearance of these lesions. The borders of the geographic areas of darkening were sharp not feathery, while the coloration was a slightly darker shade of the retina rather than the typical grey-green hue of a nevus. Sub-RPE hemorrhages were ruled out by appearance of the underlying choroid being similarly visible across the retina in this case. Retinal breaks typically are not multi-disc diameter wide without evidence of tuft or cuff of edema. Additionally, the static nature of these lesions without evidence of fluid shift, surface folds or opacification ruled out any retinal detachments. X-linked congenital retinoschisis was ruled out based on absence of cystic macular changes. Acquired retinoschisis are typically unilateral and involving the ora. Oguchi's disease was ruled out by the absence of tapedal-like sheen on fundus examination and the patient's denial of nyctalopia.

Based on the benign, stable appearance of these retinal patches, islands of dark without pressure was suspected. Fundus photography of the lesion was attempted, but did not fully capture the extent of all the lesions (**Figure 1**). OCT scan over the lesion further confirmed the suspicion by revealing a characteristic abrupt change in reflectivity of the ellipsoid zone over the lesion (**Figure2**). The patient was diagnosed with compound myopic astigmatism for each eye, and the findings of dark without pressure retinae were discussed with the patient. The patient was advised to return to the clinic in 12 months for another complete eye exam, but to return sooner if vision changes.

Discussion

Dark without pressure fundus findings have not been well documented nor studied. Most retinal textbooks do not mention this variation of retinal appearance. These dark without pressure lesions were first described by Nagpal et al in 1975 as "homogeneous, geographical, flat, brown areas in the fundi of black patients." Nagpal et al reported on 7 cases, 3 males and 4 females, ranging from 12 to 56 years of age, all African-American. Four of the seven patients had sickle cell anemia (Hb SS), two had sickle cell hemoglobin C disease (Hb SC), and one had normal adult hemoglobin (Hb AA). Some cases showed bilateral presentation while others were unilateral. Nagpal et al found that the lesions varied in size from 1 DD to several disc diameters. The borders of these lesions varied from round, straight margins to irregular, serrated margins.

Figure 1 — Color fundus photograph of the right eye showing the inferior edge of a dark without pressure lesion in the superior midperiphery.



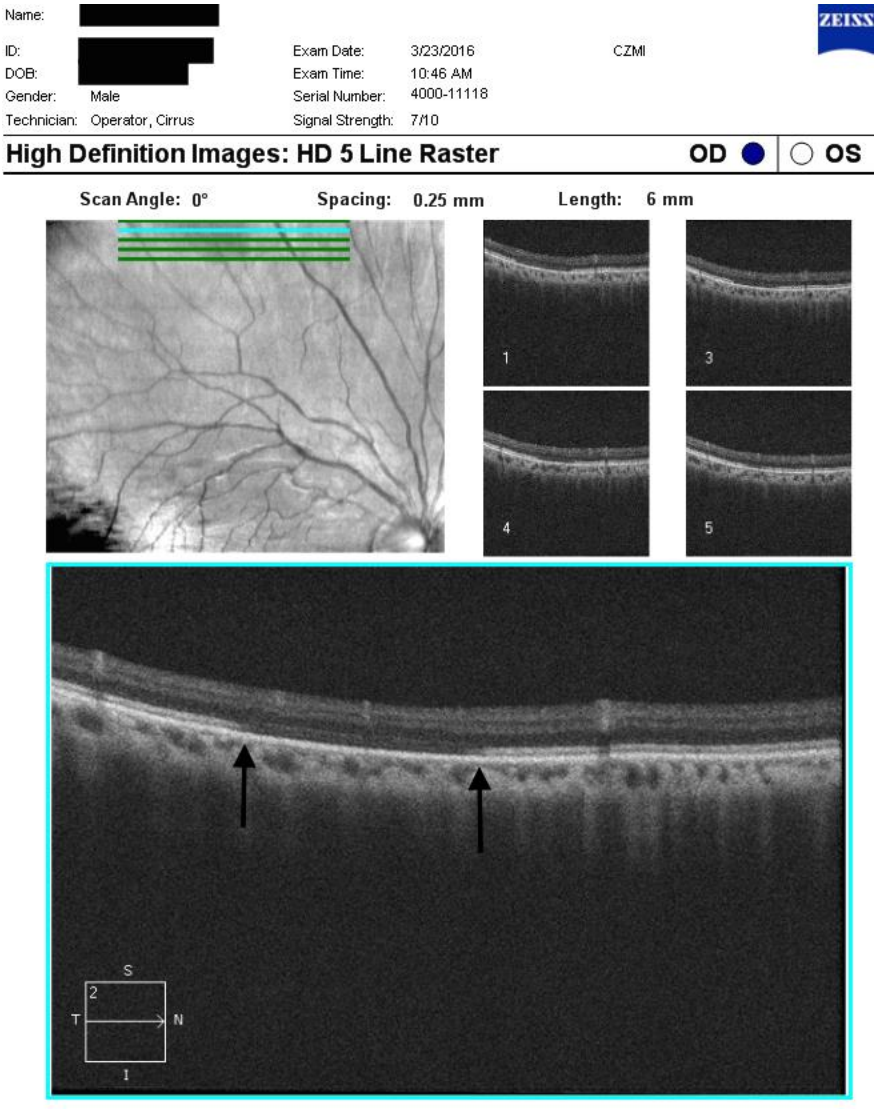


Figure 2 — 5-Line Raster OCT scan over the dark without pressure lesion showing the characteristic hyporeflectance of the ellipsoid and outer segement layers. A faint external limiting membrange (ELM) is visible over the lesion.

The lesions were found near the posterior pole and in the midperiphery. The lesions seem to be transient, changing shape and disappearing over weeks to months. They found the lesions to be unrelated to a residue of salmon patches, schisis cavities, iridescent spots, or sunburst lesions, but rather to be analogous to white without pressure lesions in patterns and behavior.[9]

In 2014, Fawzi et al studied 10 cases of white or dark without pressure retinae using optical coherence tomography, fundus autofluorescence imaging, as well as color and near-infrared fundus photography. This study incorporated cases of 4 African-Americans, 1 Hispanic, 3 Caucasians, and 1 Asian, showing the dark without pressure lesions are not specific to Blacks, but may be more prevalent in darker fundi. Fawzi et al found an abrupt change in the reflectance pattern of photoreceptors seen in the ellipsoid, outer segment, and interdigitation zones associated with the areas of the lesions. In optical coherence tomography, the dark without pressure areas exhibited a distinct hyporeflectance while the white without pressure areas exhibited hyperreflectance in the outer retina. In fundus autofluorescence, both white and dark without pressure lesions appeared to hypofluoresce. This study performed Goldmann perimetry and full field electroretinogram on one of the patients, and found no visual field defects or retinal function abnormalities. Based on this single case, the author suggested that dark without pressure may not have any functional changes associated with the observed structural change in the photoreceptors. The authors speculated that the photoreceptors in these areas of hyper and hyporeflectivity may have different densities or spectral range, but does not offer other insights into possible etiology and consequence.[8]

Another case of unilateral, multiple geographic areas of retinal darkening (GARDEN) was reported in 2015 by Moysidis et al. In this case, the patient was a 35-year-old, Asian male with well-controlled HIV and Crohn's disease. The OCT scans over the areas of darkening revealed similar hyporeflectance of the ellipsoid zone in the lesion, but no change in topography across the retina on en face imaging. The authors could not confirm if the lesions are just reflectivity variations of normal-functioning photoreceptors, a localized dystrophy of the photoreceptors, a decrease in number of photoreceptors, or an absence of photoreceptors. Moysidis et al suggested the OCT presentation of the retinal darkening may be due to an intrinsic hyporeflectivity of the photoreceptors and did not result in clinical symptoms.[10]

Many of these reported cases were referred by another primary eye care provider for concerns of retinal abnormality. The literature review of these geographic areas of darkening to date seemed to agree that the retinal function was not compromised by the structural variations. Therefore, although the etiology of the retinal appearance is unknown, additional workup for outer retinal dystrophy or degeneration is not necessary.[8,9,10] Similarly, in this case report, the presence of bilateral retinal patches of dark without pressure also did not appear to cause any symptoms for the patient. The lesions also seemed to have evolved over the past 6 years since they were absent during his prior eye exam in 2010, which corroborates with the other case reports of expansion and contraction of these dark regions.

However, these seemingly benign dark without pressure lesions appear strikingly similar to the dark regions that are absent of tapetal-like reflex in cases of Oguchi's disease. Kato et al examined 21 eyes of 11 patients diagnosed with Oguchi's disease and found that 11 eyes of 7 patients had clearly demarcated dark regions in the midperiphery that did not have the tapetal-

like reflex. These dark regions in Oguchi's disease also appeared to have evolved in size and shape over the years. Interestingly, these dark regions showed similar hyporeflectance pattern on OCT as the reported cases of dark without pressure. The OCTs in this study were all taken during the light-adapted stage. However, on fundus photography during light adaptation and after 3-hours of dark adaptation, the demarcated darker regions did not appeared to change, only the regions with the tapetal-like reflex showed the Mizuo-Nakamura effect of reflex disappearance.[2]

In a report by Takada et al of a 61-year-old male with Oguchi's disease, OCT scan of the light-adapted retina revealed intense hyperreflectivity in the IS/OS (Ellipsoid Zone), the outer segment, and the RPE layers of the retina that had the tapetal-like reflex. After dark adaptation, the reflex disappeared from observation, and the OCT of the dark-adapted retina showed a much more attenuated reflectance interspersed with segments of hyporeflectivity in the outer segment layer.[11] The authors suggested that there may be high-intensity deposits in the outer segment of the photoreceptors contributing to the tapetal-like reflex of the retina, which is corroborated by findings by Usui et al. Usui et al used a scanning laser ophthalmoscope (SLO) on a dark and light adapted fundus with Oguchi's disease that found diffuse, fine, white particles in the outer retina.[12]

Based on these findings, an interesting question emerges as to whether the cases studied by Kato et al happened to present with areas of dark without pressure, or whether these dark without pressure areas are also part of the pathophysiology in Oguchi's disease. In either scenario, these dark without pressure lesions have not been well studied in Oguchi's disease; instead, research has primarily been focused on the Mizuo-Nakamura phenomenon. It is also possible that the true histology of the rod outer segments in the cases of dark without pressure is completely different from the histology of the darker areas in the cases of Oguchi's disease, and somehow show similar reflectance properties on optical coherence tomography. Currently, OCT studies of white and dark without pressure lesions after dark adaptation have not been done. Such investigations could reveal other structural changes to the outer segment under different lighting conditions, and could reveal behavioral differences of the different rod outer segment presentations.

Conclusion

Structure and function are closely intertwined in anatomy and physiology. Variations in structure often have profound impact on the performance of a system. In eye exams, the health providers are trained to look for structural abnormalities that indicate a diseased process. Sometimes, abnormalities are difficult to distinguish from variations of normal. In this case, the areas of darker retina have been reported as structurally different from the normal retinal reflectance patterns on the OCT, but functional deficits have not been reported. Additionally, with the findings of dark without pressure areas in Oguchi's disease, questions arise regarding the relationship between dark without pressure and Oguchi's disease. Therefore, more research is needed to truly understand the etiology, the function, and the clinical significance of these lesions. Although cases of dark without pressure in asymptomatic patients without Oguchi's disease may not require additional work-up, careful documentation and recording of these findings using available imaging technology will help create useful data points for future studies into these structural variations.

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