Photoreceptor Structure in the Spectrum of Best Vitelliform Macular Dystrophy

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Introduction
Best Vitelliform Macular Dystrophy (BVMD) is an autosomal dominant form of macular degeneration with variable penetrance. BVMD is caused by mutations in the BEST1 gene. Best vitelliform macular dystrophy (BVMD) is an autosomal dominant form of macular degeneration with variable penetrance. BVMD is caused by mutations in the BEST1 gene. An integral membrane protein of the basolateral membrane of the retinal pigment epithelium (RPE) that exhibits properties of Ca++ and Cl- ion channels. Clinically, a characteristic yellow “egg yolk” vitelliform lesion develops in the macula, although appearance of BVMD varies by disease stage. The extent of photoreceptor involvement in BVMD is not well understood. Here we used high-resolution retinal imaging tools to describe photoreceptor structure alterations due to BVMD in a family with members at various stages of disease.

Methods
Four members of a family with BVMD, found to harbor a previously described heterozygous mutation in the BEST1 gene (p.Arg218Cys), underwent an ophthalmic examination, fundus photography, and high-resolution retinal imaging. The integrity of the outer retina was assessed using SD-OCT volumetric images acquired using the Bioptigen SD-OCT and line scans through the fovea acquired using the Cirrus HD-OCT. Images of the photoreceptor mosaic were obtained using a previously described adaptive optics scanning laser ophthalmoscope (AOSLO). Images were processed and registered using custom software. Color fundus photos, SD-OCT images and AOSLO images were aligned using Photoshop for further analysis.

Patient Findings
Early Vitelliform (IV-3, OS)
16-year-old male with 1 year history of decreased vision. Vision was 20/20 OU. Fundus exam showed a focal area of granularity just temporal to the fovea. SD-OCT scans revealed normal retinal lamina. Increased hyperreflectivity in both outer retinal bands (outer segment layer and RPE) in area of granularity on exam was seen. AOSLO images showed photoreceptor mosaic disruption corresponding to the area of hyperreflectivity on OCT. Surrounding photoreceptor mosaic appears normal. Arrows on SD-OCT indicate area subtended by AO montage in lower right, scale bar = 100 μm.

Vitelliform with Beginning Pseudohypopigment Changes (IV-2, OS)
18-year-old female with fundus changes since age 5. Vision was 20/20 OU. Exam showed a single, well defined, heterogeneous vitelliform lesion. SD-OCT scans localized fluid and hyperreflective material to the subretinal space. Retinal lamina underlying lesion showed patchy disruption of the photoreceptor IS ellipsoid layer. AOSLO images over the lesion showed coarse, variable photoreceptor structure. Areas surrounding vitelliform lesion show normal rod and cone photoreceptor mosaic. Arrows on SD-OCT indicate area subtended by large AO montage.

Vitellinruptive (III-5, OD)
55-year-old female with stable scotoma. Vision 20/30 OD. Exam showed a central area of hyperpigmentation with yellow nodules of varying sizes and focal hypopigmentation. SD-OCT scans revealed multiple reflective deposits, some separated by fluid in the subretinal space. Significant disruption of the outer retinal structure is present. Thickening of photoreceptor outer segment layer is present next to lesion. AOSLO images revealed photoreceptor disruption overlying nodules but a relatively preserved photoreceptor mosaic between nodules. Arrows on SD-OCT indicate area subtended by AO montage in lower right, scale bar = 100 μm.

VIrtexis (IV-3, OS)
55-year-old female with BVMD since age 8. Vision 20/30 OS. Exam revealed an epiretinal membrane (ERM) with lamellar hole and lamellar bands. SD-OCT revealed hyperpigmentation with focal intraretinal fluid. Outer retinal structures are disrupted centrally at and temporal to the hole. AOSLO images revealed diffuse areas of photoreceptor disruption with patches of intact photoreceptors. Arrows on SD-OCT indicate area subtended by AO montage in lower right, scale bar = 150 μm.

Conclusions
• Photoreceptor mosaic disruption was visible by AOSLO at all imaged stages of BVMD, including very early in the disease. The degree of disruption varied by stage of the disease and was often patchy within the lesion, with areas of intact mosaic surrounded by areas of significantly disrupted mosaic.
• Although bestrophin has been found throughout the retina, its effects on BVMD may be more widespread, the photoreceptor mosaic immediately surrounding lesions was continuous and unaffected.
• When comparing SD-OCT and AOSLO images from the same location, AOSLO images offered greater photoreceptor disruption overlying nodules but a relatively preserved photoreceptor mosaic between nodules.

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