njretina®
An affiliate of PRISM Vision Group
July // 2023 // njretina.com

Physicians

Nneka O. Brooks, MD
Nicholas D. Chinskey, MD
Rishabh C. Date, MD
Lekha K. Desai, MD
Leonard Feiner, MD, PhD
Howard F. Fine, MD, MHSc
Eric S. Friedman, MD
Luis A. Gonzalez, MD, MPH
Jonathan P. Greenberg, MD
Paul Hahn, MD, PhD
Vincent Y. Ho, MD
Bruce J. Keyser, MD
David Y. Kim, MD
Anton Kolomeyer, MD, PhD
Jennifer M. Krawitz, MD
Marisa K. Lau, MD
Tamara Lee Lenis, MD, PhD
Steven A. Madreperla, MD, PhD
Akosua Nti, MD
Alexander D. Port, MD
Jonathan L. Prenner, MD
Daniel B. Roth, MD
Christopher M. Seery, MD
Sumit P. Shah, MD
Harris C. Sultan, MD, MS
Elizabeth O. Tegins, MD
Vinod B. Voleti, MD
Marlene Wang, MD
H. Matthew Wheatley, MD

Locations

North Jersey

Belleville
973-450-5100

Clifton
973-472-4114

Elizabeth
908-409-4900

Morristown
973-630-7700

Ridgewood
201-445-6622

Teaneck
201-837-7300

Union City
201-867-2999

Vauxhall
908-349-8155

Wayne
973-633-9898

Central Jersey

Bridgewater
908-218-4303

Eatontown
732-389-2333

Edison
732-906-1887

Lakewood
732-363-2396

Lawrenceville
609-896-3655

Monroe
609-655-8301

New Brunswick
732-220-1600

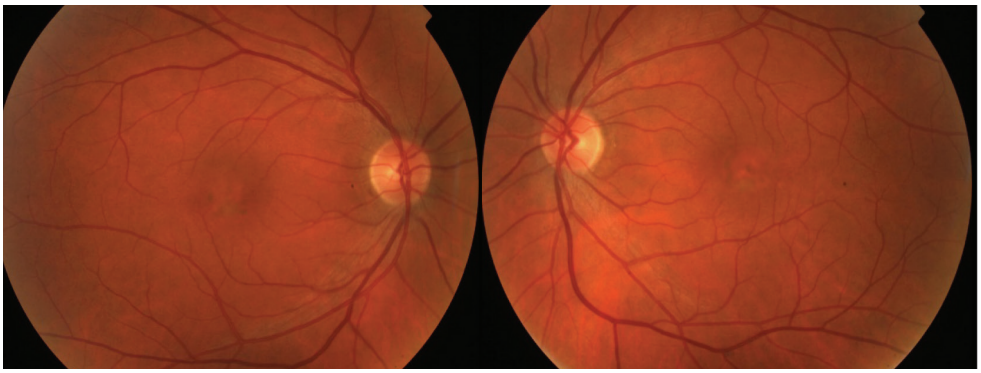
Toms River
732-797-3883

Best's Disease

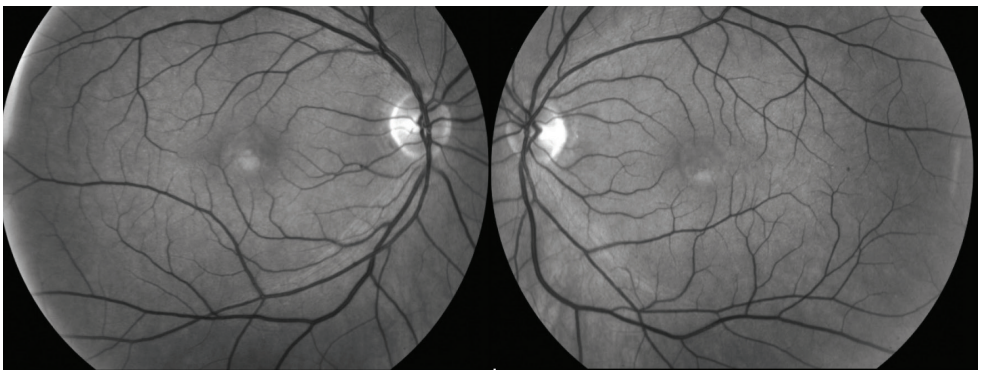
A 52-year-old female presented for a second opinion after receiving anti-VEGF injections every 8 weeks in her left eye for neovascular age-related macular degeneration (AMD) for 2 years without an improvement in her vision. Fundus photos (Figure 1), redfree images (Figure 2), and optical coherence tomography (OCT, Figure 3) of the right and left eyes (a & b, respectively) are shown here. There was notable absence of typical findings of age-related macular degeneration. Could this be something else? Perhaps an inherited condition?

Family history revealed that her father had slightly reduced vision in both eyes due to "yellow spots in his retinas." This was highly suspicious for Best's disease, a condition in a group of diseases called "bestrophinopathies." Genetic testing was positive for a mutation in the *BEST1* or *VMD2* gene that encodes for the bestrophin protein.

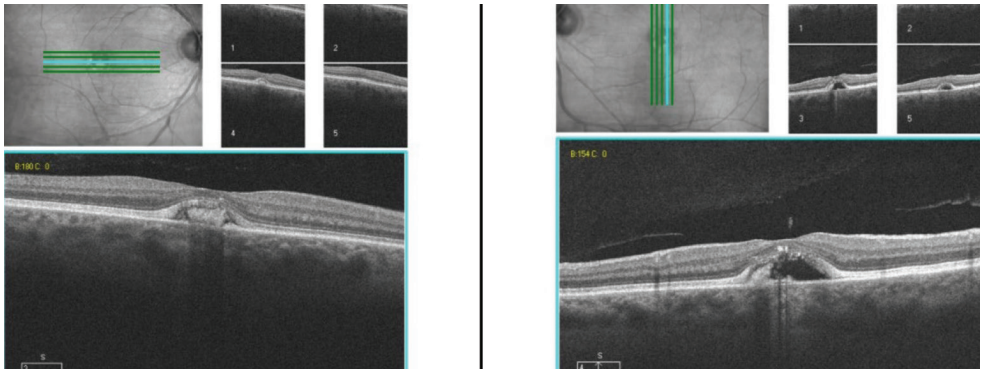
Bestrophinopathies encompass a group of diseases caused by various mutations in the *BEST1* gene. Classically, it is thought that this gene encodes for the bestrophin protein, which serves as a chloride channel on retinal pigment epithelial (RPE) cells.



Figures 1a & b Fundus photos showing foveal abnormalities of the right and left eyes.



Figures 2a & b Redfree photos highlighting foveal abnormalities of the right and left eyes.



Figures 3a & b OCT images of the right and left eyes.

This genotype can have many different phenotypes, the most common of which is Best's Disease. Other conditions include autosomal recessive bestrophinopathy (ARB) and autosomal dominant vitreoretinochoroidopathy (ADVIRC). Of note, another common related condition, adult-onset foveomacular vitelliform dystrophy (AOFVD), can have a very similar appearance, but is more commonly caused by gene mutations that make up the family of pattern dystrophies; only a minority are caused by mutations in *BEST1*.[1]

Best's disease, also known as vitelliform macular dystrophy, is inherited in an autosomal dominant pattern. With subsequent dysfunction of bestrophin, there is abnormal accumulation of lipofuscin in the subretinal space. Lipofuscin appears yellow (yolk-like) or "vitelliform" clinically. These abnormalities are most commonly in the subfoveal region, but can also be present extrafoveally. Vitelliform lesions are usually bilateral and begin to appear between 3-15 years of age, but can develop later in life as well.[1]

There are several stages of Best's disease, as listed in Table 1. Despite the abnormal macular appearance, visual acuity is relatively preserved for the first few stages and becomes compromised when atrophic or neovascular complications develop. This can range from choroidal neovascularization to sub-RPE fibrosis, geographic atrophy, and macular holes. Of note, choroidal neovascularization only occurs in about 20% of patients.

Stage	Name	Description	Vision
I	Pre Vitelliform (Figure 4)	RPE changes	Normal to mildly decreased
II	Vitelliform (Figure 5)	"Egg-yolk"- accumulation of lipofuscin in potential	Normal to mildly decreased
III	"Pseudohypopyon" (Figure 6)	Layering of lipofuscin in the inferior portion of lesion	Normal to mildly decreased
IV	Vitelliruptive	"Scrambled eggs"- lipofuscin begins to be broken down	Normal to mildly decreased
V	Atrophic (Figure 7)	RPE/retinal atrophy	20/30-20/200
VI	Choroidal neovascularization (CNV)	Sub and intraretinal fluid and/or hemorrhage	>20/200

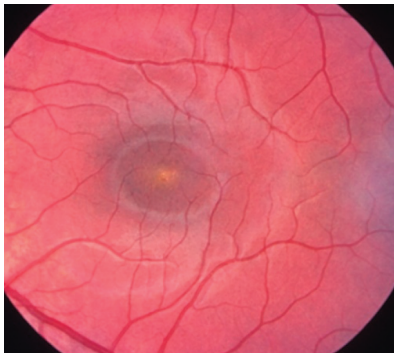


Figure 4 Pre-vitelliform stage showing RPE changes.[2]

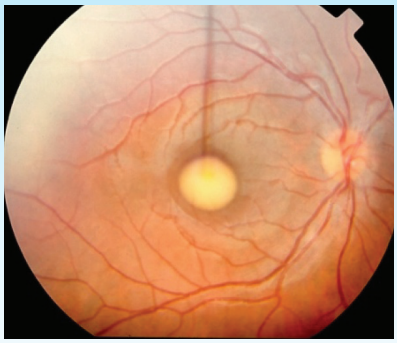


Figure 5 Vitelliform lesion in fovea.[2]

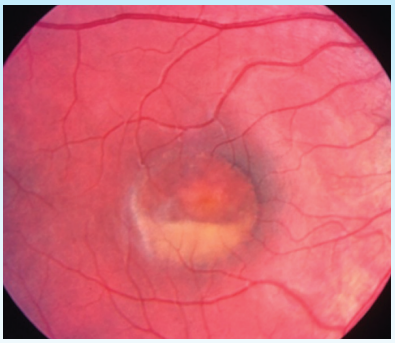


Figure 6 Pseudohypopyon stage showing vitelliform material in the inferior portion of the subretinal cavity.[2]

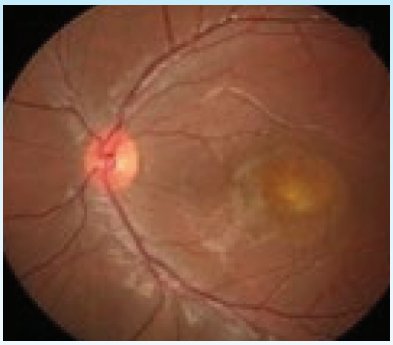


Figure 7 Atrophic stage [2]

Ancillary testing can be useful in diagnosing Best's disease. The classic OCT appearance is of bilateral hyper reflective material in the subfoveal space corresponding to the vitelliform lesions seen clinically. Fluorescein angiography varies based on stage; the vitelliform lesion shows hypofluorescence, which transitions to hyperfluorescence as the atrophic stage ensues. Fundus autofluorescence progresses from hyperautofluorescence in the vitelliform stage to mixed fluorescence and then to hypoautofluroescence when the vitelliform lesion becomes atrophic. More extensive testing can assess the electrical activity of retinal photoreceptors. Although the electroretinogram (ERG) is normal, the Arden ratio (ratio of light peak to dark trough on electrical testing of the retinal photoreceptors) of an electro-oculogram (EOG) is abnormally low. This is actually the most specific test for Best's Disease, and is a feature that unites all bestrophinopathies.[1] However, access to EOG testing is extremely limited. But free genetic testing is more widely available and offered in our offices. The testing involves a simple cheek swab that can screen for hundreds of mutations that can be associated with ocular diseases including Best's disease.

The differential diagnosis of Best's disease includes age related macular degeneration, central serous chorioretinopathy, adult-onset foveomacular vitelliform dystrophy, solar retinopathy, and other causes of central macular atrophy such as myopic degeneration.[1] There are several features that can help distinguish between Best's disease and these similar-appearing conditions, including symmetry, vision, demographics, and family history. In neovascular AMD, one would usually see drusen and other RPE alterations in both eyes. Subretinal hyperreflective material may be present, but usually correlates to areas of hemorrhage. Patients also are older and have worse vision. Central serous chorioretinopathy can manifest as subfoveal pockets of hyporeflectivity on OCT representing fluid, but patients are often much more symptomatic from an acute change in vision and have typical risk factors. Other features seen clinically are pigment epithelial detachments (PEDs) and RPE changes from prior episodes that follow a gravitational "drip" pattern, especially on fundus autofluorescence. Adult-onset foveomacular vitelliform dystrophy clinically can have similar-appearing vitelliform lesions as Best's disease, but develops later in life. The vitelliform lesion often has a pigmented spot in the center, and does not progress through the stages as Best's disease does. Ultimately, ancillary testing and genetic analysis can provide a definitive diagnosis of Best's disease.

There are no FDA approved treatments for Best's disease. But secondary choroidal neovascularization can be treated with anti-vascular endothelial growth factor (VEGF) such as bevacizumab. As occurred with our patient, when hyporeflectivity representing an empty space such as in the pseudohypopyon phase is attempted to be treated with anti-VEGF injections, no response to treatment occurs.

References:

1. Moss H, Epley KD, Tripathy K, et al. Best disease and bestrophinopathies. EyeWiki. eyewiki.aao.org. Accessed 9 June 2023.
2. Best Disease or Viteliform Macular Dystrophy. Re□na Image Bank. American Society of Re□na Specialists. Accessed 13 June 2023.

At the forefront of clinical research

NJRetina continuously conducts clinical trials at key locations. Our clinical research coordinators will be happy to discuss the inclusion/ exclusion criteria or any other aspect of these studies with you or your patients. If you have any questions, please feel free to contact:

Lauryn Onkendi - Teaneck: 201-837-7300, lonkendi@njretina.com
Kerowyn Smith - Teaneck: 201-837-7300, ksmith@njretina.com
Aline Diaz - Toms River: 732-797-3984 and Edison: 732-906-1887, adiaz@njre□na.com
Andy Merino - Toms River: 732-797-3984 and Edison: 732-906-1887, amerino@njretina.com
Joseph Portelli - Teaneck: 201-837-7300, jportelli@njretina.com
Nelly Velasco, MS - Teaneck: 201-837-7300 ext. 2022, nvelasco@njretina.com

Enrolling Studies:

Wet AMD
Edison
Opthea Coast: A Phase 3, Multicenter, Double-masked, Randomized Study to Evaluate the Efficacy and Safety of Intravitreal OPT-302 in Combination with Aflibercept, Compared with Aflibercept Alone, in Participants with Neovascular Age-related Macular Degeneration (nAMD)

Toms River
Opthea ShORe: A Phase 3, Multicenter, Double-masked, Randomized Study to Evaluate the Efficacy and Safety of Intravitreal OPT-302 in Combination with Ranibizumab, Compared with Ranibizumab Alone, in Participants with Neovascular Age-related Macular Degeneration (nAMD)

Teaneck
Luna: A Multi-Center, Randomized, Double-Masked Phase 2 Study to Assess Safety and Efficacy of ADVM-022 (AAV.7m8-aflibercept) in Anti-VEGF Treatment Experienced Patients with Neovascular (Wet) Age related Macular Degeneration

Diabetic Retinopathy
Teaneck
Ocuterra: A Phase 2 Randomized, Double-Masked, Vehicle Controlled, Multicenter Study to Evaluate the Safety and Efficacy of OTT166 Ophthalmic Solution in the Treatment of Diabetic Retinopathy (DR)

Upcoming Studies:

RVO
Teaneck, Toms River, Edison
Bayer Study: A Randomized, Double-Masked, Active-Controlled, Phase 3 Study of the Efficacy and Safety of Aflibercept 8 mg With Macula Edema due to Retinal Vein Occlusion

To read past issues of our newsletter, visit njretina.com.