

Vitelliform Macular Dystrophy

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A twenty-one-year-old generally healthy gentleman presented to the ophthalmology clinic with progressive reduction of vision over 3 years and family history of Best's Disease. Best's disease is a rare autosomal dominant congenital vitelliform macular dystrophy. Patients usually present with deterioration of central vision in the second decade of life and gradually worsening over the years. The disease is untreatable and low visual aids are used. Genetic and clinical counseling is accessible to affected individuals along with their asymptomatic relatives.

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Best's disease is a rare autosomal dominant congenital vitelliform macular dystrophy¹. This disease is caused by dysfunction of Bestrophin protein resulting in abnormal fluid and ion exchange in the retinal pigment epithelium (RPE) especially at the macula²⁻⁴. Hence, it leads to RPE swelling and subretinal accumulation of lipofuscin⁵.

It is a progressive macular disease which is usually detected in the second or third decade of life when central vision is affected (reduction of visual acuity, colour vision impairment, and metamorphopsia) but night vision is unaffected. In the fifth or sixth decade, the vision is severely impaired⁶. There is no specific treatment for the disease; the main aim is to enhance visual rehabilitation with low visual aids. In certain stages, such as secondary choroidal neovascularization or hemorrhage, it can be managed with direct laser treatment, intravitreal injection of bevacizumab and photodynamic therapy to prevent unnecessary complications⁶⁻¹⁰. This disease is avoidable by genetic counseling.

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The aim of this report is to present this rare disease which was not reported before in the Kingdom of Bahrain.

THE CASE

A twenty-one-year-old gentleman with no known medical illnesses presented to the ophthalmology clinic with progressive reduction of vision for 3 years. He had a family history of Best's disease in three members of first degree relatives.

On clinical examination, visual acuity was 6/12 with normal intraocular pressure (14 mmHg) bilaterally. The rest of anterior segment examination was unremarkable.

On dilated fundus examination, the macula showed a typical scrambled-egg appearance in the right eye and egg-yolk appearance in the left eye, see figure 1. Optical coherence topography (OCT) showed enlargement of the retinal pigment epithelium (RPE) cells and accumulation of fluid between the RPE layer and Bruch's membrane more in the left than the right, see figure 2. Fluorescein fundus angiography (FFA) showed variable degree of fluorescence and marked hypo-fluorescence due to fluorescence blockage by the cystic fluid in the right and left eye respectively, see figure 3.



Figure 1: Right and Left Fundus Photo

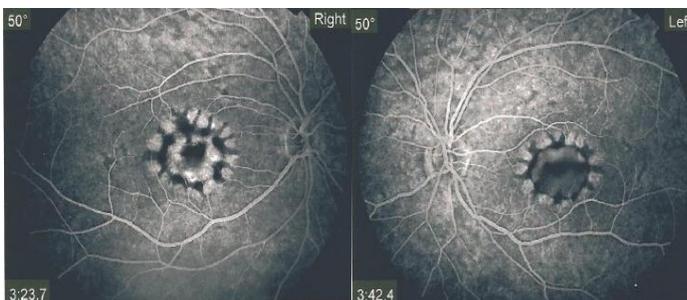


Figure 2: Right and Left Fluorescein Fundus Angiography (FFA)

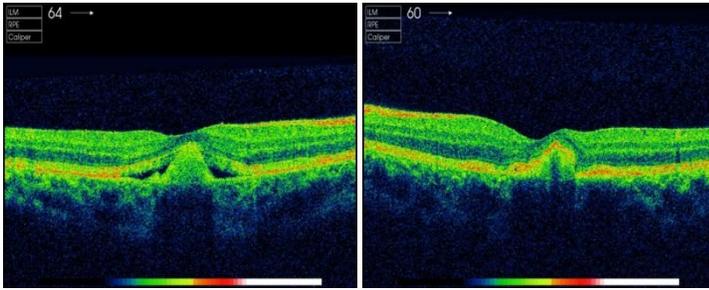


Figure 3: Right and Left Posterior Segment Optical Coherence Topography (OCT)

The electrooculogram (EOG) was not done as it is unavailable in our unit. The patient was informed about Best's disease. Also, he was given the option of managing the reduction of vision at this stage with visual aids.

The patient and interested family members were offered genetic counseling, clinical and genetic screening for unscreened members.

DISCUSSION

The macula is the area responsible for central vision including high spatial acuity and colour vision. This is due to the fine arrangement and high concentration of the light sensitive photoreceptor cones and the delicate neural connection between the retinal layers.

Best's disease is named after the German ophthalmologist Dr. Friedrich Best who described the first pedigree with this disorder in 1905¹. The disorder is a rare congenital autosomal-dominant disease, described as bilateral vitelliform macular dystrophy. It is expressed as subretinal accumulation of yellowish heterogenous fluid Lipofuscin in the macula due to a mutation in the gene BEST'S1 on chromosome 11 (formerly called VMD2)^{2,3}. BEST'S1 encodes the transmembrane protein Bestrophin^{3,4}. The latter act as a chloride ion channel and a modulator of the voltage-gated calcium channels which are located basolaterally in the retinal pigment epithelium cells¹¹. Hence, lipofuscin is accumulated in and underneath the RPE.

It is gradually progressive in nature; develops early in life and not detected until second or third decade when central visual acuity is subjectively decreased by the atrophic changes in the outer retinal layers⁵. The central vision usually decreases very slowly; a vision of 6/30-6/60 or worse usually presents at the fifth or sixth decade⁶.

There is a variable gene penetrance and clinical expression of Best's disease between individuals¹². The diagnosis of Best's disease is based on clinical retinal appearance, EOG and family history.

Best's disease is classified into stages based on clinical appearance⁵. Normal fundus but abnormal EOG, phenotypically normal; pre-vitelliform stage, first representation of the disease on fundus examination resembling yellowish subfoveal pigment; vitelliform stage, circular egg-

yolk cyst appearance on the fundus; pseudo-hypopyon stage, the liquefaction and reabsorption of the cyst with fluid level; vitelliruptive stage, the lesion begins to regress and appears as a scrambled-egg-like lesion; atrophic stage, complete reabsorption of cyst with marked RPE atrophy; cicatricial stage, at this stage, there is a disruption of the RPE with choroidal neovascularization and formation of whitish subretinal fibrous scar.

The next supplementary diagnostic tool to be discussed is EOG, which shows flattening of RPE electrical potential. Along with a decrease in light peak and dark trough ratio 'Arden ratio' which is between 1.0 - 1.3 (normal ratio is greater than 1.8). The EOG could be the diagnostic tool for patients in stage one of Best's disease or atypical cases. The Arden ratio remains plateau throughout disease progression¹³. Genetic and clinical counseling for relatives could aid the diagnosis.

Other tests such as Electroretinography (ERG), FFA, posterior segment OCT facilitate the diagnosis of this condition. ERG is usually normal for full field unless focal macular or multifocal ERG is usually reduced in the affected area¹⁴. The FFA provides information regarding the vasculature and perfusion of the choroid. In posterior segment OCT, high yield provides information of the outer and inner layers of the retina including the choroids, it can be obtained for staging and follow-up.

Best's disease is an untreatable disorder. Patients affected are educated about the disease and offered clinical and genetic counseling. They are also advised to quit smoking as a general rule because it decreases choroidal neovascularisation¹⁵.

Supportive measures such as occupational therapy and low visual aids can be offered to patients with visual acuity impairment.

In the advanced stages of the disease, case studies of monotherapy treatment in choroidal neovascularization and hemorrhage have shown promising result in downgrading the disease progression and improving the vision. The treatments used were direct laser photocoagulation for extra foveal CNV (1 case), photodynamic therapy with verteporfin (1 case) and intravitreal injection the anti-VEGF Bevacizumab (4 cases). However, as formerly stated, this treatment was given for limited number of cases⁷⁻¹⁰.

CONCLUSION

Best's disease is a rare autosomal dominant congenital vitelliform macular dystrophy. It is caused by subretinal lipofuscin accumulation due to mutation in protein-encoded gene BEST'S1. Unfortunately, the disorder is untreatable but avoidable and supportive measures can be offered. More studies with larger samples, for the therapeutic management are recommended.

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