BEST DISEASE

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Abstract:
Best Disease also known as Vitelliform Macular Dystrophy (VMD), classically presents with defective central vision. Macula which is responsible for the central vision and colour perception is affected. Individuals affected by Best disease, initially have normal vision followed by decrease in central visual acuity as well as metamorphopsia. The case presented is of 45-years-old female with complaints of gradual progressive defective Vision of over 2 years . A well-circumscribed single greyish lesion of size 1.5 DD was noted in the macula, which was confirmed to be Best disease.

Keywords:- choroidal neovascular membrane, defective centrsl vision , vitelliform macular dystrophy

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Introduction

Best disease, also termed vitelliform macular dystrophy, is typically an autosomal dominant disorder, which classically presents in childhood with the striking appearance of a yellow or orange yolk-like lesion in the macula. It is a rare entity and occurs in about 1 in 10,000 individuals. Dr. Franz Best, a German ophthalmologist, described the first pedigree in 1905 [1]. A hallmark of the disease is a markedly abnormal electro-oculogram in all stages of progression and in phenotypically normal carriers [2].

Lesions in Best disease are restricted to the eye. The mutations responsible for Best disease are found in a gene called VMD2. It encodes a transmembrane protein named bestrophin-1 (hBest1) [3]. The protein is located in the basolateral plasma membrane of RPE cells. A dysfunction of the protein bestrophin results in abnormal fluid and ion transport by the RPE [4]. Lipofuscin (periodic acid-Schiff [PAS] positive) accumulates within the RPE cells and in the sub-RPE space, particularly in the foveal area. The RPE appears to have degenerative changes in some cases, and secondary loss of photoreceptor cells has been noted [5]. Breakdown of RPE/Bruch's membrane can allow CNV to develop as a late complication.

Visual acuity is good in the previtelliform stage. Even with the egg-yolk appearance, visual acuity is maintained in the range of 20/20 to 20/50 for many years. It is the final stages of geographic RPE atrophy with possible development of choroidal neovascular membrane that is associated with further deterioration in acuity . Usual onset of Best disease is from 3 to 15 years. The condition often is not detected until much later in the disease because visual acuity may remain good for many years. The atrophic stage usually occurs after age 40 years. Some individuals will never have progression beyond the earliest stages of the disease and will maintain better than 20/40 vision in both eyes. In general, most people will maintain reading vision in at least one eye throughout life .

Case Report

A 45-years-old female presented with complaints of progressive and painless defective vision of both eye over a period of 2 years. There was no history of trauma or any other associated symptoms. On examination, eyes were orthophoric. Both eyes had clear cornea, normal anterior chamber depth, normal iris pattern and clear lens. Visual acuity :OD 6/24 and OS 6/18 p. Colour Vision was normal. Fundus examination revealed normal disc and retinal vessels in both the eyes. A well-circumscribed single greyish lesion of size 1.5DD was noted in the macula both eyes [Fig-1a,b]. The rest of retina and peripheral retina was normal.

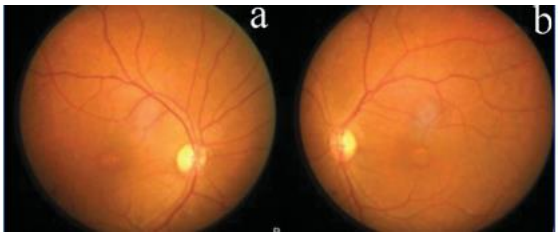

Figure 1 a, b

Routine blood investigations and systemic investigations were normal. Optical Coherence Tomography (OCT) was done which showed discontinuity of Retinal Pigment Epithelial (RPE) membrane and ellipsoid layer with Sub RPE deposits as shown in (Fig-2).

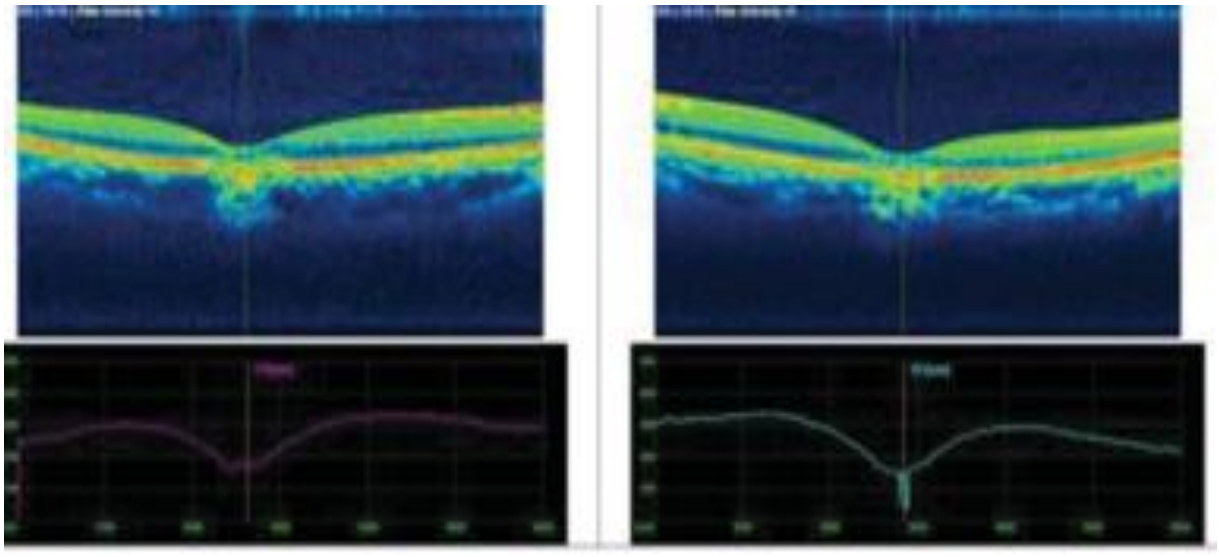

Figure 2

Fundus Fluorescence Angiography (FFA) of both the eye showed normal disc and an area of hyper-fluroscent centre surrounded by hypofluroscent borders . The rest of retina appeared normal . [Fig-3a,b].

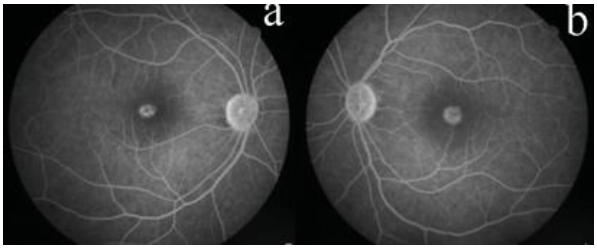

figure 3 a ,b

The patient was subjected to Electro- oculogram (EOG). EOG showed decrease in Arden Ratio of 1.3. Based on these findings, diagnosis of Adult-onset Best disease was made. The patient is on follow-up to identify any development of Choroidal Neovascular Membrane (CNVM) and there is no cure for this disease.
EOG was performed and had revealed a classical decrease in Arden ratio of 1.3.
Waves a and b of standard retinogram were normal.

Discussion:
Best Vitelliform macular dystrophy is an autosomal dominant disease with variable penetrance [1]. Defect in the long arm of chromosome 11 (11q12-q13) has been linked to the disease [2]. Petrukhin K et al., first identified the retina-specific gene and designated it as VMD2 [3]. Protein which is encoded by this gene was proposed as bestrophin. The disease starts at the age of 3-15 years but usually is detected later, since there is no significant vision loss. The macula has abnormal deposits of lipofuscin pigment which was described by Weingeist TA et al., [4]. In the initial stages of the disease, a bright yellow cyst forms in the RPE beneath the macula which shows sunny-side-up egg appearance on fundus examination. Visual acuity may be normal or near normal. Peripheral vision remains unaffected throughout the progression of the disease.
If the cyst ruptures, fluid and yellow deposits from the cyst spreads throughout the macula, giving the appearance of scrambled egg. Further, there is atrophy of the macula and underlying RPE which leads to further deterioration of central vision.

The clinical stages have been described as follows:
- Stage 0: Normal macula but Abnormal Electro-oculography (EOG)
- Stage 1: RPE disruption in the macular region and FFA showing window defects.
- Stage 2: A well-circumscribed, circular, yellow-opaque, homogeneous yolk-like macular lesion. FFA reveals marked hypofluorescence in the zone covered by the lesion.
- Stage 2a: The contents become less homogeneous and develop a "scrambled-egg" appearance. FFA shows partial blockage of the fluorescence with non-homogeneous hyper fluorescence.
- Stage 3: The lesion develops a fluid level of a yellow-coloured vitelline substance. FFA shows inferior hypofluorescence from the blockage by the vitelline material, along with superior hyperfluorescent defects.
- Stage 4a: The lesion has typical orange-red colour with atrophic RPE and visibility of the choroid. FFA shows hyper fluorescence without any leakage.
- Stage 4b: Fibrous scarring of macula. FFA shows hyperfluorescence without any leakage.
- Stage 4c: Choroidal neovascularisation or appearance of subretinal haemorrhage. FFA shows hyperfluorescence as a result of neovascularisation and leakage.

Electro-oculogram is the diagnostic test for Best disease which shows decrease in Arden ratio, the normal value being 1.5. This can differentiate Best disease from Adult-onset Vitelliform Macular Dystrophy in which the Arden ratio will remain normal. The disease has variable prognosis. Some carriers never express their phenotype, while few others maintain better than 20/40 vision in both eyes. In one study, 88% of the patients retained 20/40 or better visual acuity and only 4% of the patients had 20/200 or worse visual acuity in the better eye.
There is no known treatment for the disease [5]. The patient has to be observed for development of any CNVM which can cause dramatically decreased vision. It is important to establish the correct diagnosis and monitor this condition. Comprehensive ocular examination of the patient's family members to rule out any early signs of this rare eye condition is recommended.

CONCLUSION
Hence, the case was presented for its rarity, since Best disease occurs at early stages of life whereas this patient presented as adult, time of onset of best disease. One should also be aware of the importance of EOG as it can confirm various retinal disorder.

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