



Best's disease family case report

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ABSTRACT

Vitelliform macular dystrophy, or Best disease, is an autosomal dominant retinal dystrophy that is generally bilateral. It is often defined by classic “egg-yolk” lesions seen in the macula.

The diagnostic for Best disease is done by Electrooculogram (EOG) test with abnormal Arden ratio. Other tests used to support the diagnosis include: Optical Coherence Tomography (OCT), Fundus Fluorescence Angiography (FFA) and full-Field Electro-retinograph (ERG).

We present a two-generation family which suffers from Best's disease. Our patients are: father, his daughter and his son. They demonstrate changes in different development phases. The described cases show importance of the whole family members' examination in case of Best's disease. Early diagnosis of this serious disease makes possibility of proper treatment.

Keywords: Best disease, Fundus fluorescence angiography, Optical coherence tomography

INTRODUCTION

Vitelliform macular dystrophy, or Best disease, is an autosomal dominant retinal dystrophy characterized by incomplete penetrance and variable expression. This disease is due to the accumulation of lipofuscin in the macular pigment epithelium which typically is observed in the childhood. [1].

In the following paragraphs, we will present three medical cases of three patients belonging to the same family, then we will discuss it through a literature review related to this particular disease.

Case report:

We report the observations of 3 patients; a brother, a sister and their father with a macular lesion characteristic of BEST disease.

The interest of these observations lies on one hand in the evidence of the autosomal dominant transmission of the disease and on the other hand in the spontaneous evolution in the youngest patients.

Case N° 1:

In this case, we will describe a 14 year-old boy with no medical history presenting Progressive decrease of visual acuity for 6 months without associated signs.

Ophthalmologic examination showed corrected visual acuity 5/10 in the right and 3/10 in the left eye; P4 near in both eyes. The examination of the anterior segment was normal. Intraocular pressures of both eyes were within the standards. In addition, fundus examination in the right eye showed a yellow macular lesion, with a large vertical axis, measuring about 2 papillary diameters with a fibrotic aspect. However, in the left eye, we observed a similar lesion, oval, but with horizontal long axis, measuring about 3/2 papillary diameters with a grayish and irregular aspect in the center (FIGURE 1):

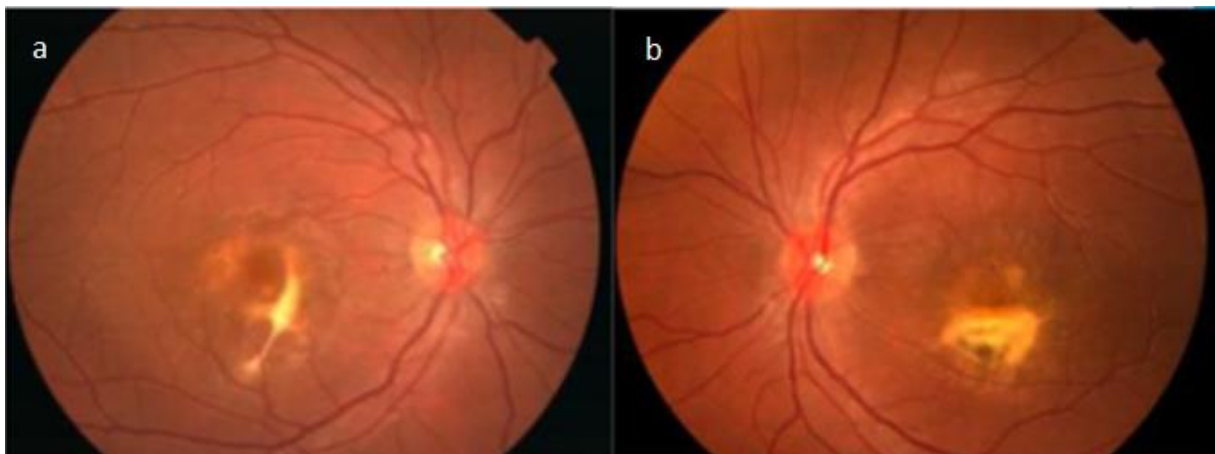


Figure 1: right and left fundus showing yellow macular lesion.

The fluorescein angiography test showed in the right eye an hyperfluorescence surrounding an area of hypofluorescence confirming the appearance of fibrosis seen on fundus of the eye. In the left eye, the hyperfluorescence is limited to the lesion and irregular in the center (Figure2):

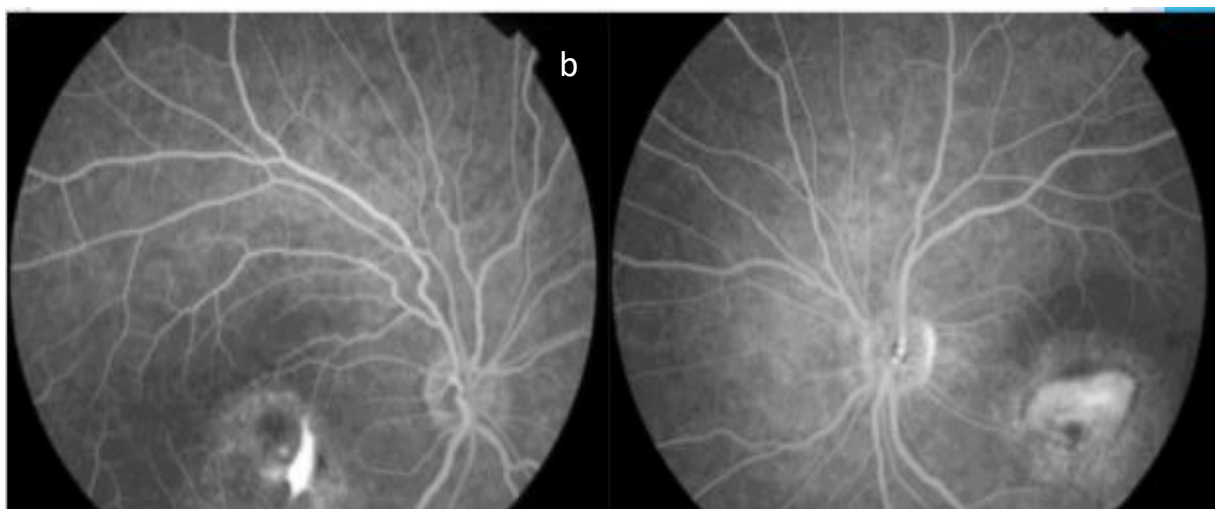


Figure 2: right and left eyes fundus under fluorescein angiography.

The patient investigations had rule out any specific cause of sub-retinal inflammation and all systemic investigations were normal. The Macular imaging by optical coherence tomography (OCT) showed a

deposit of homogenous hyper-reflective lesion beneath a of the retinal pigment epithelium (RPE) at macular area. This scanning explained the RPE disruption and the thickening suggested by the pigment accumulation (Figure 3):

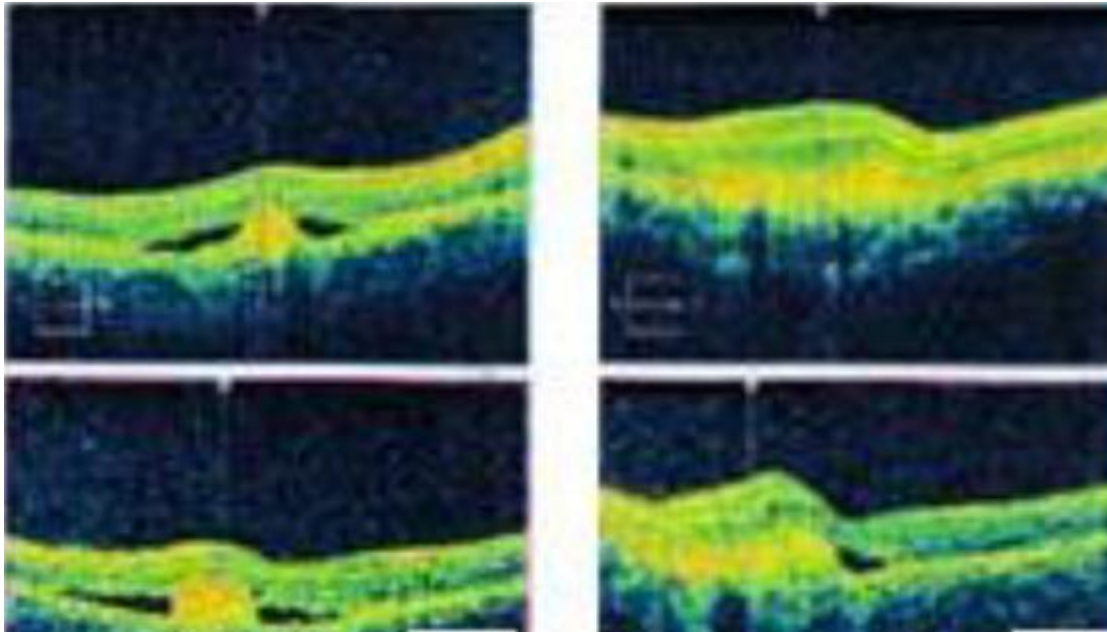


FIGURE 3 : showing a deposit of homogenous hyper-reflective lesion at the macula

Finally, the electrooculogram (EOG) demonstrated through the Arden ratio that: the right eye was 0.7 and 0.69 of the left eye which are significantly below the normal of 1.8.

Waves a and b of the standard electroretinogram were normal.

Visual fields and color vision test were normal.

Thus, on basis of bilateral circumscribed yellow macular lesions, OCT findings and revealed EOG-ERG dissociation on electro-physiology, a diagnosis of Best's vitelliform dystrophy was made, and a family investigation was initiated.

Case N°2:

In the second medical case, we describe an 13 years old girl, sister of the previous case, which has no medical history, examined as a part of family investigation.

The ophthalmologic examination showed corrected visual acuity 8/10 in the right eye and 7/10 on the left one. The examination of the anterior segment was normal.

The fundus examination revealed maculopathy of vitelliform appearance (egg yolk) in both eyes (FIGURE 4):

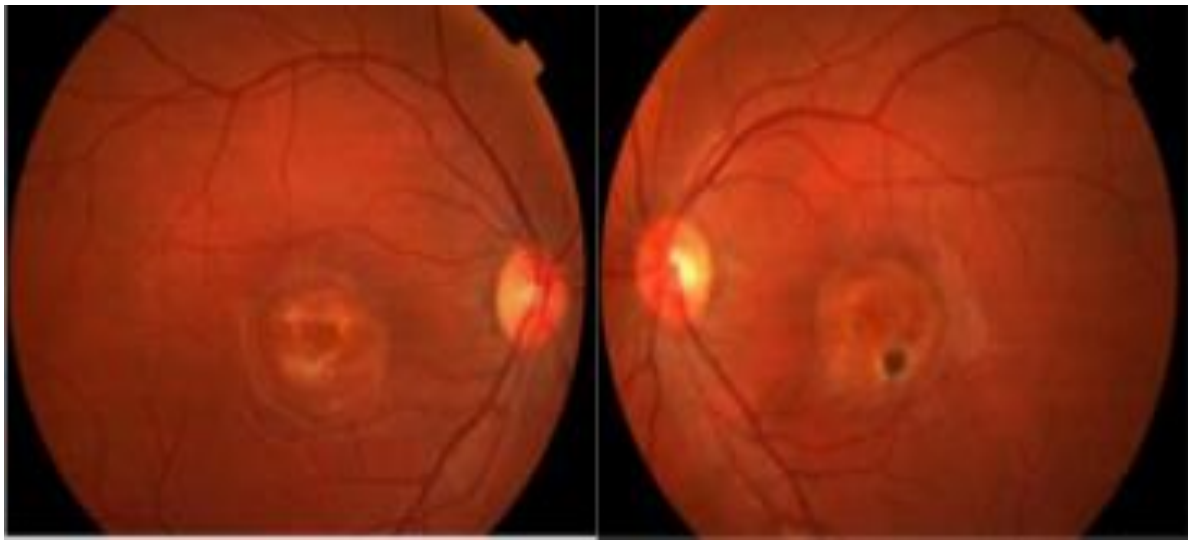


FIGURE 4 : maculopathy of vitelliform appearance (scrambled egg) in both eye

The Optical Coherence Tomography (OCT) revealed Pigmentary Epithelial Detachment (PED) and atrophic scar without neovascularization (Figure 5)

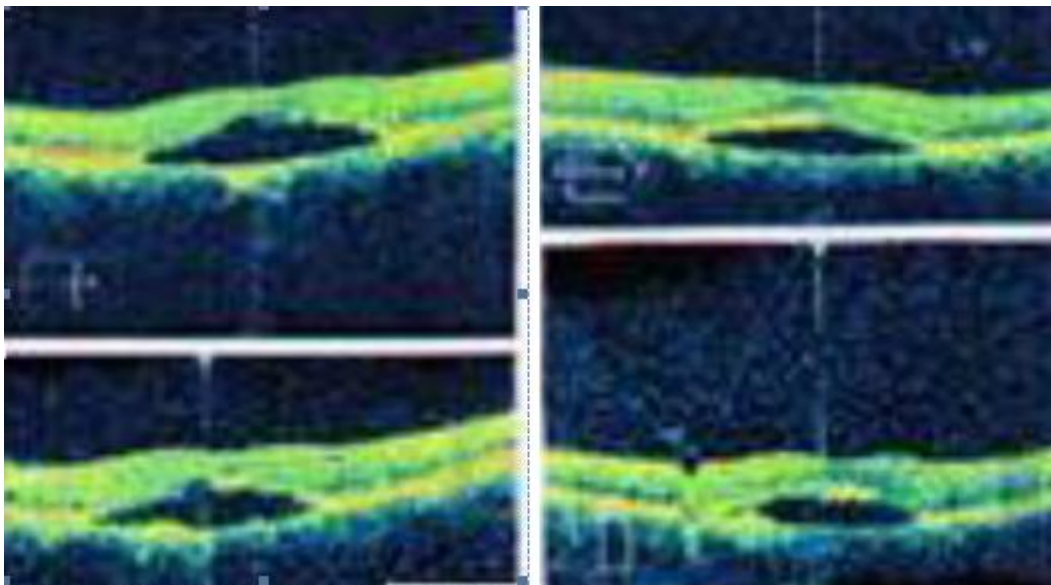


Figure 5: OCT of both eye show pigmentary epithelial detachment (PED).

Visual field: normal. EOG: decrease of the Arden ratio. ERG: normal.

Case N° 3:

We report here the last case of this family, which is describing the findings of a 46 old aged father with no historical antecedents, examined in the context of family investigation.

- The visual acuity: OD = 9/10, OG= 6/10.
- The examination of the anterior segment was normal

The fundus examination on both eyes showed : vitelliform maculopathy with "egg yolk" appearance.

Anerithic image: pseudohypopion aspect.

OCT: Pigmentary Epithelial Detachment (PED) in both eyes appearance of RPE/Bruch complex duplication without neovascularization. (FIGURE 6).

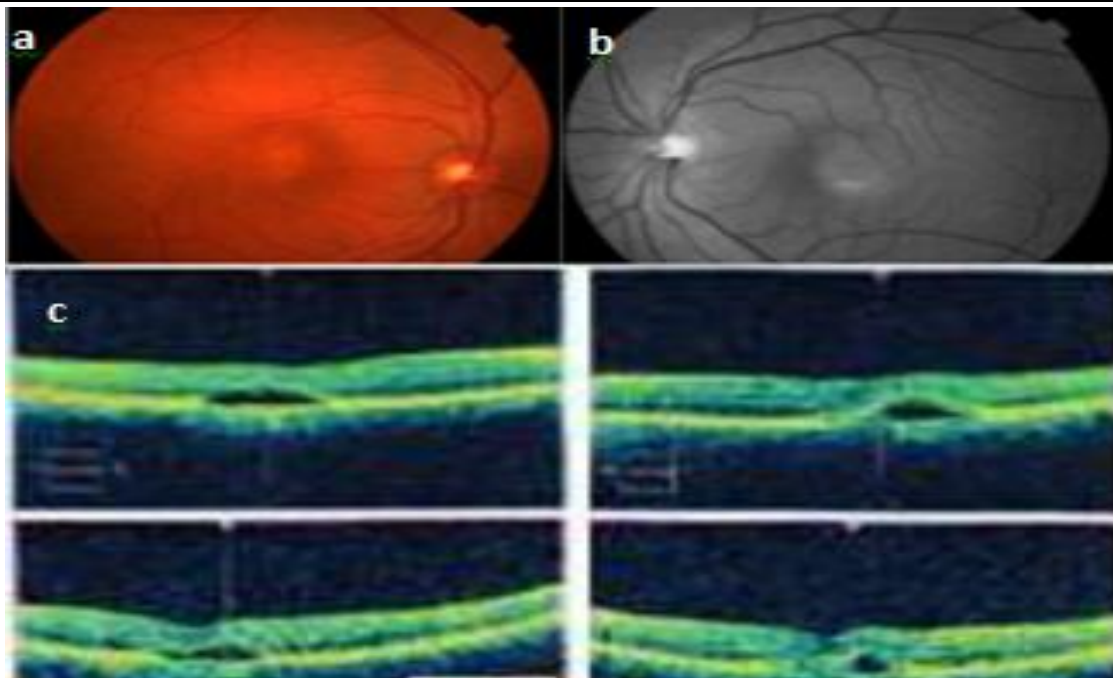


FIGURE 6 a: vitelliform maculopathy of "egg yolk" appearance. b: pseudohypopyon aspect on the left eye. c: appearance of pigmentary epithelial detachment (PED) in both eye.

- Visual field: normal.
- EOG: decrease of the Arden ratio.
- ERG: normal



Discussion

Vitelliform macular dystrophy, or Best's disease, is an autosomal dominant disorder with variable penetration and highly variable phenotypic expression also [2]. Typically affecting young patients in whom a macular lesion gradually evolves through several stages, the age of onset of Best's disease is often between 7-12 years of age, its discovery is often incidental or in the context of a family investigation. It is caused by the mutation of a gene located on chromosome 11q13. [3].

This gene codes for a protein named bestrophin, located at the basolateral plasma membrane of the retinal pigment epithelium RPE. This disorder causes lipofuscin to accumulate as a sub-retinal yellow deposit, which is a characteristic of the disease [4].

In addition, the OCT provides clarification in the staging and pathogenesis of Best's disease. The exact location of the vitelliform material, above, below or within the RPE, has not been clearly elucidated by the various clinical or histological studies. Indeed, histopathological examination shows a diffuse deposit of lipofuscin both in the RPE, in the retina and even in the choroid. [5]

- In the early stages of Best's disease, when visual acuity is maintained
 - the changes essentially affect the layer between the RPE and the photoreceptors' cells PRC in the junction of the inner and outer segments of the photoreceptors, or IS/ OS junction.
 - The accumulation of material occurs between the retina and the RPE.

- In the latest stages, when there is a significant decrease in VA, there are:
 - Destruction of IS and OS of PRC ;
 - Hypertrophy and rupture of RPE.

Mohler and Fine classified the evolution of Best disease in different stages: [6]

- Stage 0: Normal macula with abnormal EOG.
- Stage I: Disturbance of the RPE of the macula.
- Stage II: Typical vitelliform or egg yolk lesion.
- Stage IIa: Break up of the vitelliform cyst or scrambled egg phase.
- Stage III: Pseudo-hypopyon phase where yellow material forms a fluid level in the vitelliform cyst.
- Stage IVa: Atrophy of pigment epithelium and possibly retina produces an orange-red lesion in the macula.
- Stage IVb: White hypertrophic scar of fibrous tissue in the macula.
- Stage IVc: Neovascularization of the fibrous scar.

Even if the OCT provides stadification of the disease, it doesn't provide a diagnosis, that is why it is recommended to use electro-oculogram to establish the diagnosis, where abnormalities could be observed even within asymptomatic patients.

Other tests, such as fluorescein angiography, RPE autofluorescence, optical coherence tomography, full-field and multifocal electroretinogram (ERG), could provide additional information for an accurate diagnosis. [7][8].

Initially, many individuals with Best disease do not feel any symptoms, but fundus lesions are noted on examination. Other visual symptoms can include decreased acuity (blurring) and metamorphopsia. These symptoms may become worse if the disease progresses to the atrophic stage [7][8].

Best disease should be differentiated from the other dystrophies of the central part of the retina and choroid [9].

We could mention:

- Stargardt macular dystrophy
- Central areolar pigment epithelium dystrophy
- Cone dystrophy
- Fundus flavimaculatus
- Foveal changes in angioid streaks
- Age-related macular degeneration
- Central chorioretinitis
- Serous retinal pigment epithelium detachment

There is no causal treatment of this disorder. The management includes support concerning school or activities of patients. Additionally, for treatment of choroidal neovascularization (CNV), anti-VEGF (vascular endothelial growth factor) agents such as bevacizumab are used increasingly. [10]. However, long-term follow-up of these patients is unknown and there are currently no clinical trials to demonstrate the effectiveness of anti-VEGF agents. Andrade et al. used verteporfin in photodynamic therapy (PDT) for subfoveal choroidal neovascularization in one person with Best vitelliform macular dystrophy [11]. However, the authors suggested that PDT might be an option for treatment of CNV in Best vitelliform macular dystrophy.

CONCLUSION

Best vitelliform macular dystrophy is a rare autosomal dominant disorder. The Visual function is good in the early stage but gradually decreases in the latest stage. There is no effective treatment available to slow the progression of Best disease. Long term follow up is recommended to see the development of choroidal neo-vascularisation that may have to be treated using intra- vitreal anti-vascular endothelial growth factors or photodynamic therapy.

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