

## Case report

### Adult onset Best's macular dystrophy (VMD2) with unilateral presentation

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#### Abstract

**Background:** Vitelliform macular dystrophy is an autosomal-dominant disease and has two clinical variants: Best's (VMD2) and adult onset vitelliform macular dystrophy (AOVMD). We report an atypical presentation of VMD2. **Case:** A 50-year-old male presented with history of blurring of vision in left eye since two year. On fundus examination, left eye revealed a single, circular, yellow-opaque egg yolk-like macular lesion with no other abnormality. Fundus examination of right eye was unremarkable. Fundus fluoresceine angiography showed blocked fluorescence in the area of lesion. EOG-Arden ratios were found to be severely reduced bilaterally. OCT left eye showed sub-retinal hyperreflective echo. **Conclusion:** The age of onset and presentation can be highly variable in VMD2 and the vitelliform phase of VMD2 in elderly can be confused for adult onset vitelliform macular dystrophy(AOVMD). However, Arden ratio  $<1.5$  is diagnostic of VMD2.

**Keywords:** Vitelliform dystrophy, Best's, AOVMD, Arden ratio.

#### Introduction

Vitelliform macular dystrophy (VMD) was first described by Friedrich Best in 1905 with a complete description of the various stages of the disease from eight related individuals. Vitelliform macular dystrophy type 2 (VMD2; also known as Best's disease) is the second most common macular dystrophy and presents with a great range in age of onset as well as a variable pre-symptomatic period which makes it difficult for a clinician to diagnose especially in an elderly individual. The vitelliform phase of VMD2 in elderly individuals can often be confused with adult onset vitelliform macular degeneration (AOVMD).

AOVMD was 1<sup>st</sup> described by Gass (1974) as a vitelliform lesion that was found in older individuals, was smaller and more symmetrical with a normal or sub-normal Electro-oculogram Arden ratio.

We present a case of Best's disease with atypical clinical presentation.

#### Case report

A 55-year-old male from India presented with blurring of vision in his left eye since two years. He had no significant past ocular or systemic history. There was no family history of any ocular disease.

On ocular examination, anterior segments of both eyes were unremarkable. Best corrected visual acuity was 6/6,N6 in right eye and 6/9,N8 in left eye. Fundus examination of his right eye( Fig. 1a) was unremarkable. Left eye fundus revealed a single, well circumscribed, dome shaped, opaque, homogenous egg-yolk

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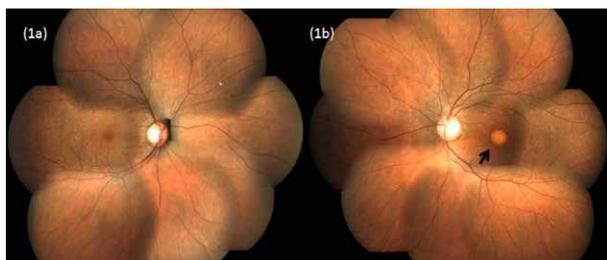
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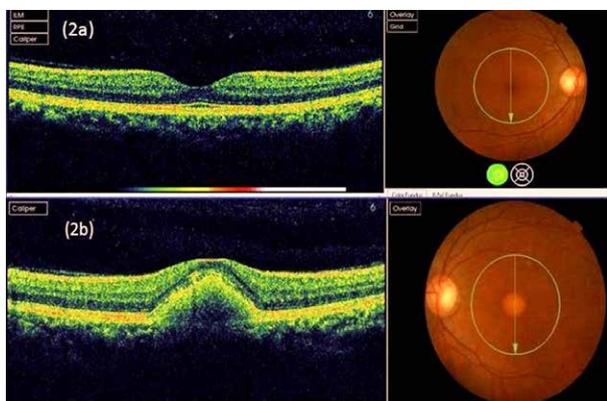
like macular lesion, and approximately half disc diameter in size (Fig 1b).

Optical coherence tomography(OCT) of right eye was within normal limits (Fig 2a) while left eye showed evidence of a hyper-reflective sub-retinal lesion at the macula ( Fig 2b), causing elevation of overlying retina and back shadowing. Central foveal thickness was 413 microns in left eye. Electro-oculogram of both eyes was found to be reduced significantly (Fig 3) with Arden ratios of 1.306 and 1.286 in right and left eyes respectively, suggestive of bilateral disease. Electro-retinogram (ERG) of both eyes was normal.

Patient was diagnosed as a case of VMD and advised yearly follow-up.

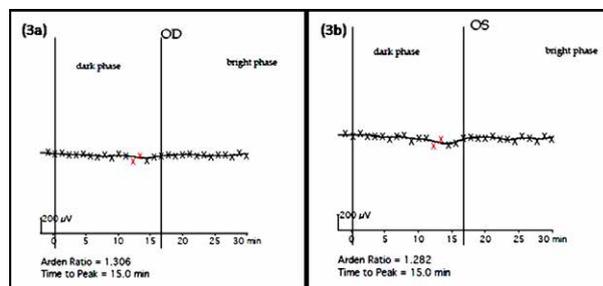


**Figure 1:** Fundus photographs of both eyes. Figure 1(a) is a montage of right eye with no detectable fundus abnormality. Figure 1(b) shows a single, circular, well-circumscribed, yellow-opaque, homogenous egg yolk-like macular lesion (black arrow) with no other abnormality in the fundus montage of the left eye.



**Figure 2:** Shows optical coherence tomography images of both eyes. Right eye OCT as seen in figure 2(a) shows a normal foveal contour.

Left eye shows sub-retinal hyper-reflective echo causing shadowing with central foveal thickness -413 microns as seen in figure 2(b).



**Figure 3:** Shows EOG findings of right (3a) and left eye (3b) respectively with bilaterally diminished light to dark ratio (Arden ratio).

### Discussion

Vitelliform macular dystrophy is an autosomal-dominant disease caused by mutation in the gene coding for bestrophin, a Ca<sup>2+</sup>-sensitive Cl<sup>-</sup> channel protein located on the baso-lateral membrane of retinal pigment epithelial cells. The phenotypic appearance varies with the stage of the disease. It has two clinical variants: Best's (VMD2) and adult onset vitelliform macular dystrophy( AOVMD). Both Best's and AOVMD are characterised by an autosomal dominant inheritance, vitelliform lesion at the macula, autofluorescent deposits within and beneath the retinal pigment epithelium, a variable pre-symptomatic period prior to diagnosis and a slow progression. Visual function generally remains good despite ophthalmoscopically visible lesion until the disease process progresses to cause structural alterations in the outer retinal layers.

AOVMD is much less frequent than Best's (VMD2) but represents its main differential diagnosis. It differs from VMD2 by many characteristics such as a later onset (40-60 years of age), milder symptoms, bilaterally symmetrical lesions, lesions smaller than 1 disc diameter, and a normal or sub-normal electro-oculogram Arden ratio . These criteria are however not absolute. Renner et al (2005) did a detailed morphologic and functional evaluation of Best macular dystrophy (BMD) associated

with mutations in the VMD2 gene found that VMD2 can present any time up to 60 years of age. Besides the clinical picture, EOG (Arden ratio), ERG, OCT, Fundus autofluorescence and FFA help us in not only reaching the diagnosis of VMD but also in staging and differentiating between its two variants. However, gene analysis is necessary for absolute confirmation of the disease and its type. At this stage it is important to note that VMD in elderly patients should be differentiated not only from AOVMd but also from age-related macular degeneration, RPE detachment and chronic serous retinopathy based on the presenting complaints, family history and investigatory modalities mentioned above.

Symmetry of the fundus findings is a typical sign for an inherited disease, especially in cases of AOVMd. Unilateral presentation of vitelliform lesion as noted in our case is an extremely rare occurrence. However, the EOG Arden ratio was found reduced in both eyes comparably suggesting a bilateral pathology. An abnormal diminished light to dark ratio (Arden) of the electrooculogram is the hallmark of the disease and, since then it has been used as a criterion to differentiate between Best's and AOVMd, with EOG Arden ratio being markedly reduced ( $< 1.5$ ) in Best's disease and normal to sub-normal in AOVMd. Full field ERG is found to be normal in both these conditions (Cross HE & Bard L, 1974).

Based on the HD OCT findings, Querques et al hypothesized that early changes in vitelliform macular dystrophy involve the layer between the RPE and the IS/OS interface, first with accumulation of material beneath the sensory retina, and then with disruption and attenuation of IS and OS; late changes seem to affect the RPE, which undergoes hypertrophy, disruption, and attenuation. Spaide and associates illustrated by optical coherence tomography

(OCT) that the yellow vitelliform accumulates in the sub-retinal space and on the outer retinal surface. OCT is also helpful in diagnosis of neo-vascular membrane in the later stages of the disease.

Our patient demonstrated features that were both in favour as well as going against either of these two clinical entities which posed a diagnostic dilemma. A late onset, non-specific family history and a smaller vitelliform lesion were suggestive of AOVMd. On the other hand, an asymmetric presentation with severely reduced arden ratio in both eyes were strongly in favour of Best's macular dystrophy.

Hence we concluded that this is an atypical case of Best's macular dystrophy with a late onset and a strikingly unilateral clinical presentation.

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