Archives of
Ophtalmological Research

Case Report

DOI: 10.51271/AOR-0037

Misdiagnosis and mismanagement in stage 4 best vitelliform macular dystrophy: a case report highlighting the role of multimodal imaging

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Cite this article: Beyazyıldız E, Çıtırık M, Bingül E, Yüksel E, Teke MY. Misdiagnosis and mismanagement in stage 4 best vitelliform macular dystrophy: a case report highlighting the role of multimodal imaging. *Arch Ophthalmol Res.* 2025;2(3):55-57.

Received: 14/04/2025 ◆ **Accepted:** 02/07/2025 ◆ **Published:** 28/07/2025

ABSTRACT

Best vitelliform macular dystrophy (BVMD) is a typically autosomal dominant retinal disorder characterized by accumulation of lipofuscin in the macula, leading to progressive visual impairment. We report the case of a 42-year-old male diagnosed with stage 4 BVMD (vitelloruptive stage) who was previously mismanaged with multiple intravitreal anti-VEGF injections under the incorrect assumption of exudative pathology. Fundus photography revealed the characteristic "scrambled egg" appearance, while optical coherence tomography and fundus autofluorescence demonstrated hyperreflective subretinal deposits and hyperautofluorescence without any evidence of fluid accumulation or choroidal neovascularization. Despite the absence of electrooculography data, the diagnosis was supported by multimodal imaging. This case highlights the importance of accurate diagnosis and staging of BVMD, and emphasizes the need to avoid unnecessary therapeutic interventions in the non-exudative stages of the disease.

Keywords: Best vitelliform macular dystrophy, best disease, anti-VEGF therapy, multimodal imaging, optical coherence tomography, fundus autofluorescence, choroidal neovascularization, misdiagnosis

INTRODUCTION

Best vitelliform macular dystrophy (BVMD), commonly known as Best disease, is a hereditary macular dystrophy characterized by lipofuscin accumulation in the subretinal space, resulting in progressive visual decline.[1-3] The condition is typically inherited in an autosomal dominant manner and most often arises from mutations in the BEST1 gene on chromosome 11q13, which encodes bestrophin-1, a calcium-sensitive chloride channel critical for retinal pigment epithelium (RPE) function.[4,5] Less commonly, mutations in other genes such as PRPH2 (formerly RDS) have been implicated.[6]

Clinically, BVMD presents with a distinctive yellowish vitelliform lesion in the macula, often described as having an "egg-yolk" appearance.[7,8] Disease staging is based on ophthalmoscopic and multimodal imaging findings, progressing from a subclinical stage to atrophic or fibrotic phases.[9] Although visual acuity can remain preserved in early stages, misdiagnosis and inappropriate management may occur, particularly in later stages when the lesion breaks down or mimics other exudative maculopathies such as age-related macular degeneration (AMD).[10,11]

Multimodal imaging, such as fundus autofluorescence (FAF), optical coherence tomography (OCT), and fundus photography, play a central role in staging and differentiating BVMD from neovascular pathologies. Importantly, the absence of intraretinal or subretinal fluid in intermediate stages, particularly in the vitelloruptive stage, can help avoid misinterpretation and unnecessary therapeutic interventions such as anti-vascular endothelial growth factor (anti-VEGF) injections.[4]

In this report, we present a case of stage 4 BVMD that was mismanaged with anti-VEGF therapy due to presumed exudative maculopathy. This case emphasizes the importance of accurate staging, appropriate imaging, and clinical judgment in avoiding overtreatment of inherited retinal diseases.

CASE

A 42-year-old male presented to our retina clinic with progressive bilateral visual decline that was more pronounced in the left eye. His medical and systemic history was unremarkable. The best-corrected visual acuity (BCVA)

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was 0.1 in both eyes. Intraocular pressure (IOP) was within normal limits bilaterally, and anterior segment examination revealed no signs of inflammation or anterior pathology.

Fundus examination revealed irregular, yellowish subretinal deposits in the macular region of both eyes, resembling the classic "scrambled egg" appearance characteristic of the vitelloruptive stage (stage 4) of BVMD. Disruption of the retinal architecture was also noted, suggestive of advanced retinal involvement.

Multimodal imaging was then performed. Fundus photography (**Figure a**) revealed fragmented yellow deposits localized within the macula, consistent with the breakdown of the vitelliform material. OCT imaging (**Figure b**) revealed hyperreflective subretinal material without intraretinal or subretinal fluid accumulation. The outer retinal layers were preserved and no disruption of the ellipsoid zone or signs of choroidal neovascularization (CNV) were detected.

FAF imaging of both eyes (**Figure c, d**) revealed marked hyperautofluorescence within the macular region. Collectively, these findings confirmed the diagnosis of stage 4 BVMD without exudative activity or CNV.

Despite these imaging results, the patient had previously undergone ten intravitreal injections of bevacizumab (anti-VEGF) at another institution under the assumption of exudative maculopathy. Additionally, oral acetazolamide therapy was initiated but was later discontinued due to lack of benefit.

Fluorescein angiography and electrooculography (EOG) were not performed. However, based on clinical and imaging findings, a definitive diagnosis of non-exudative stage 4 BVMD was established. The patient was managed conservatively with close observation and no further pharmacological interventions were pursued.

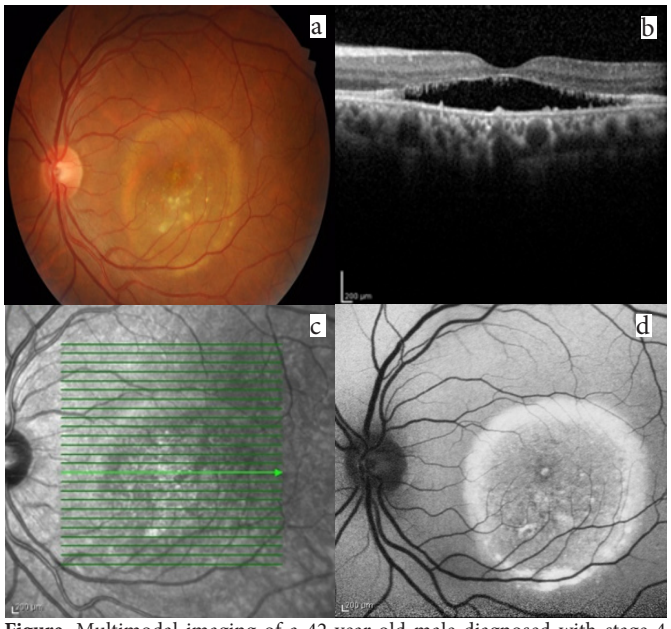


Figure. Multimodal imaging of a 42-year-old male diagnosed with stage 4 best vitelliform macular dystrophy. (a) Color fundus photograph of the right eye showing irregular, yellowish subretinal deposits in the macula resembling a "scrambled egg" pattern, (b) Optical coherence tomography scan revealing hyperreflective subretinal material without intraretinal or subretinal fluid, (c) Fundus autofluorescence image of the right eye showing intense hyperautofluorescence in the macular region, (d) Fundus autofluorescence image of the left eye showing a similar autofluorescence pattern with well-demarcated macular involvement

DISCUSSION

BVMD is an inherited macular dystrophy characterized by abnormal accumulation of lipofuscin beneath the subretinal space, primarily due to mutations in the BEST1 gene.[1-3] Although full-field electroretinogram (ERG) findings are typically normal, EOG remains a hallmark diagnostic test, often revealing a significantly reduced Arden ratio as a result of RPE dysfunction.[4-6] In our case, EOG was not performed; however, multimodal imaging provided sufficient diagnostic clarity.

Many patients with BVMD are asymptomatic in the early stages of the disease, with only subtle funduscopic changes. As the disease progresses, metamorphopsia and progressive visual loss, typically bilateral and symmetrical, become more apparent. The condition progresses through six recognized stages, although not all patients follow a strict sequential pattern.

In stage 1 (previtelliform), the retina may appear normal or show minor pigment changes, although the EOG is typically abnormal. Stage 2 (vitelliform) features a central, yolk-like yellow lesion with preserved surrounding retina. Stage 3 (pseudohypopyon) involves the accumulation of subretinal material with fluid-level separation. In stage 4 (vitelloruptive), the lesion disintegrates into a "scrambled egg" pattern with pigment clumping and early atrophy. Stage 5 (atrophic/fibrotic) is marked by the resorption of vitelliform material and RPE atrophy, making differentiation from other macular diseases more difficult. Stage 6 (cicatricial) may involve CNV and subretinal fibrosis, leading to more pronounced visual impairment. A summary of the estimated visual acuity range according to the disease stage is presented in **Table**.

Table. Estimated range of visual acuity at different stages of best vitelliform macular dystrophy

Stage	Visual acuity
Stage 1 (previtelliform)	100%
Stage 2 (vitelliform)	40-100%
Stage 3 (pseudohypopyon)	40-100%
Stage 4 (vitelloruptive)	20-100%
Stage 5 (atrophic/fibrotic)	<10-100%

Multimodal imaging is critical for BVMD diagnosis and staging. OCT, FAF, and fundus photography can delineate the disease stage, presence or absence of subretinal fluid, and potential complications such as CNV.[7,10,11] In our patient, the presence of hyperreflective subretinal material on OCT and intense hyperautofluorescence on FAF, in the absence of exudation or neovascularization, were characteristic of the vitelloruptive stage (stage 4).[5] Notably, this stage can be easily misinterpreted as exudative maculopathy due to lesion breakdown, leading to misdiagnosis and unnecessary treatment.

A major clinical error in this case was the administration of ten intravitreal anti-VEGF injections (bevacizumab) under the false presumption of CNV or exudative AMD. Although anti-VEGF therapy is a standard intervention for neovascular diseases, it has no proven benefit in BVMD stages lacking fluid or neovascular components.[8,9] Moreover, unnecessary pharmacological interventions pose avoidable risks, burden the patient financially, and delay appropriate management strategies.

This case highlights the importance of integrating clinical evaluation with targeted imaging modalities. While electrophysiological studies can aid diagnosis, careful analysis of OCT and FAF findings may provide sufficient evidence to differentiate BVMD from other mimicking conditions.[8]

CONCLUSION

Accurate staging and interpretation of multimodal imaging are essential for the management of vitelliform macular dystrophy. In the absence of fluid accumulation or neovascularization, unnecessary therapeutic interventions such as anti-VEGF injections should be avoided. This case underscores the potential consequences of misdiagnosis and reinforces the critical role of imaging-guided decision making in inherited retinal diseases.

ETHICAL DECLARATIONS

Informed Consent

The patient signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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