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Choroidal Neovascularization in Genetically Confirmed Best Vitelliform Macular Dystrophy: Sequential Anti-VEGF Treatment with Aflibercept and Faricimab

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ABSTRACT: *Purpose: To describe choroidal neovascularization (CNV) in genetically confirmed Best vitelliform macular dystrophy (BVMD) and to document the course after sequential intravitreal anti-VEGF treatment. Methods: A 43-year-old woman with a pathogenic BEST1 variant and bilateral vitelliform/atrophic macular changes was followed with serial OCT-angiography (OCT-A; SOLIX, Zeiss) for 29 months (October 2023-February 2026). Active CNV was detected in the right eye (OD). Results: The initial treatment consisted of three intravitreal aflibercept injections. Visual acuity was maintained and the quantitative OCT-A parameters showed limited stabilization (CST 247 to 237 µm; FLV 2.23% to 2.15%). After a 20-month interval without treatment, OCT-A demonstrated CNV reactivation (FLV 7.22%; CST 292 µm). Retreatment with faricimab was followed by partial anatomical control and a weaker OCT-A flow signal (final FLV 4.22%; CST 302 µm). BCVA remained 0.3 (20/67) in both eyes during the whole follow-up, and no CNV activity was detected in the fellow eye. Conclusion: In BVMD-related CNV, the most realistic therapeutic endpoint is preservation of the remaining macular structure and function, not visual gain. Aflibercept maintained initial stability, while faricimab provided partial control after recurrence. The possible value of dual VEGF-A/Ang-2 inhibition in dystrophy-related CNV remains insufficiently studied. Genetic counseling is an essential part of care in autosomal dominant BEST1 disease.*

KEYWORDS: *Best vitelliform macular dystrophy, BEST1 gene, choroidal neovascularization, anti-VEGF, aflibercept, faricimab, OCT-angiography*

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I. INTRODUCTION

Best vitelliform macular dystrophy (BVMD), or Best disease, is an autosomal dominant macular dystrophy related to pathogenic variants in BEST1, which encodes bestrophin-1. Bestrophin-1 is mainly located at the basolateral membrane of retinal pigment epithelium (RPE) cells and participates in chloride conductance and RPE function [1,2,9]. When this pathway is disturbed, vitelliform material accumulates, the RPE-photoreceptor interface becomes progressively unstable, and outer retinal degeneration may follow [1,2].

CNV is a relevant complication of BVMD, although in practice it may be missed or diagnosed late. The reason is straightforward: vitelliform deposits, subretinal fluid, fibrosis, and atrophic remodeling can all obscure the distinction between inactive dystrophic change and active neovascular tissue on structural imaging. OCT-A has changed this assessment, because flow-based imaging can reveal CNV in lesions that are ambiguous on color photography or standard OCT [3,4].

Anti-VEGF treatment is the usual therapeutic approach once active CNV is confirmed in non-AMD settings, including inherited macular dystrophies, angioid streaks, myopic CNV, and inflammatory CNV [4-6,8]. Still, the expected result is not the same as in typical neovascular age-related macular degeneration. In BVMD, the macula is already structurally compromised, so treatment is often aimed at preventing further deterioration rather than producing a measurable visual improvement.

Faricimab blocks VEGF-A and angiopoietin-2 (Ang-2) and has proven efficacy in neovascular age-related macular degeneration [7]. There is, however, little direct evidence for its use in BVMD-related CNV. Its rationale in such cases is therefore mechanistic and pragmatic: recurrent vascular activity in an already damaged RPE-Bruch's membrane complex may justify retreatment with an agent that also targets vascular instability.

Here, we present a patient with genetically confirmed BVMD and unilateral active CNV, followed with serial OCT-A and treated first with aflibercept and later with faricimab during a 29-month observation period.

II. CASE REPORT

Patient History and Clinical Presentation

A 43-year-old woman with a known diagnosis of BVMD presented to the Clinic of Ophthalmology, University Hospital "Alexandrovska", Sofia, in October 2023, reporting bilateral reduced vision since early childhood. Childhood ophthalmic assessment had shown bilateral visual impairment and macular degenerative changes. Genetic testing subsequently confirmed a pathogenic BEST1 variant. The family history was consistent with autosomal dominant inheritance: the patient's grandfather and father were also affected, but their visual impairment had previously been attributed to antibiotic toxicity rather than to an inherited macular dystrophy. This delayed recognition prevented appropriate genetic counseling and family surveillance.

At presentation, BCVA was 0.3 in both eyes without correction. Intraocular pressure was 13 mmHg OD and 12 mmHg OS. Anterior segment examination was unremarkable bilaterally. Fundoscopy revealed bilateral vitelliform and atrophic macular changes. An elevated subretinal lesion in the right eye raised suspicion for active CNV.

Table 1: Clinical Status at Presentation

Parameter	Right Eye (OD)	Left Eye (OS)
BCVA (initial, 10/2023)	0.3	0.3
BCVA (final, 02/2026)	0.3	0.3
Intraocular pressure	13 mmHg	12 mmHg
Anterior segment	Unremarkable	Unremarkable
Macula	Vitelliform/atrophic + CNV	Vitelliform/atrophic changes

OCT-Angiography Findings

Serial OCT-angiography was performed during follow-up. At baseline, OCT-A of the right eye demonstrated a lobular CNV network with flow signal in the outer retina and choriocapillaris slabs. The corresponding B-scan showed a hyperreflective subretinal deposit with vitelliform material overlying the neovascular complex (Fig. 1).

During the aflibercept treatment phase, OCT-A demonstrated persistence but no expansion of the CNV flow signal. Quantitative parameters showed modest stabilization/improvement: CST decreased from 247 to 237 μm and FLV from 2.23% to 2.15%. BCVA remained stable at 0.3 (Fig. 2).

After a 20-month treatment-free interval, CNV reactivation was documented in November 2025, with FLV increasing to 7.22%, CST increasing to 292 μm, and worsening GCC-related parameters. This recurrence is best interpreted as interval-related reactivation in a chronically disrupted RPE-Bruch's membrane complex, rather than as immediate failure of the previous aflibercept course. Following the switch to faricimab, OCT-A showed partial reduction of outer retinal flow signal and partial improvement in quantitative OCT-A parameters (Fig. 3).

The left eye (OS) consistently showed no flow signal in the outer retina on any serial OCT-A examination. The subfoveal hyperreflective lesion corresponded to accumulated vitelliform material in varying stages of resorption — a characteristic finding of BVMD without complicating CNV. OCT-A with outer retina slab segmentation was the critical tool discriminating this from active CNV (Fig. 4).

Table 2: Serial Quantitative OCT-A Parameters (Right Eye)

Date	Avg GCC (μm)	FLV (%)	GLV (%)	CST (μm)	CNV Status
08/2023 (baseline)	108	2.23	2.32	247	Active
10/2023 (post-inj. 1)	110	2.15	2.18	237	Stable
11/2025 (reactivation)	114	7.22	7.30	292	Worsened
12/2025 (post-inj. 4)	114	4.18	4.22	308	Reduced
02/2026 (post-inj. 5)	112	4.22	4.28	302	Reduced

Treatment Course

Following OCT-A confirmation of active CNV in OD, the patient received intravitreal aflibercept (2 mg/0.05 mL): three injections were administered between October 2023 and March 2024. During this phase, BCVA remained stable at 0.3, while OCT-A parameters showed modest anatomical stabilization. Because there was no visual deterioration or clear expansion of the CNV, observation with close monitoring was chosen after the initial treatment phase.

In November 2025 — 20 months after the last aflibercept injection — OCT-A documented CNV reactivation, with FLV rising to 7.22% and deterioration of GCC-related parameters. Anti-VEGF treatment was

therefore restarted. Faricimab (6 mg/0.05 mL) was chosen for retreatment because of its VEGF-A/Ang-2 mechanism and because an every-8-week approach was clinically practical in a chronic condition with limited potential for visual recovery. After two faricimab injections (December 2025 and February 2026), OCT-A showed partial reduction of CNV flow signal and FLV decreased to 4.22%. BCVA remained 0.3 OD throughout. No injection-related adverse events were recorded.

Table 3: Anti-VEGF Treatment Timeline (Right Eye)

Date	Inj. No.	Drug	BCVA OD
27.10.2023	1	Aflibercept (Eylea® 2 mg)	0.3
05.01.2024	2	Aflibercept (Eylea® 2 mg)	0.3
08.03.2024	3	Aflibercept (Eylea® 2 mg)	0.3
03.12.2025	4	Faricimab (Vabysmo® 6 mg)	0.3
05.02.2026	5	Faricimab (Vabysmo® 6 mg)	0.3

Fig. 1. *OCT-A (SOLIX, Zeiss), outer retina and choriocapillaris slab (OD) — baseline, before anti-VEGF therapy. Lobular CNV network with active flow signal. B-scan: hyperreflective subretinal deposit with vitelliform component overlying the choroidal neovascularization.*

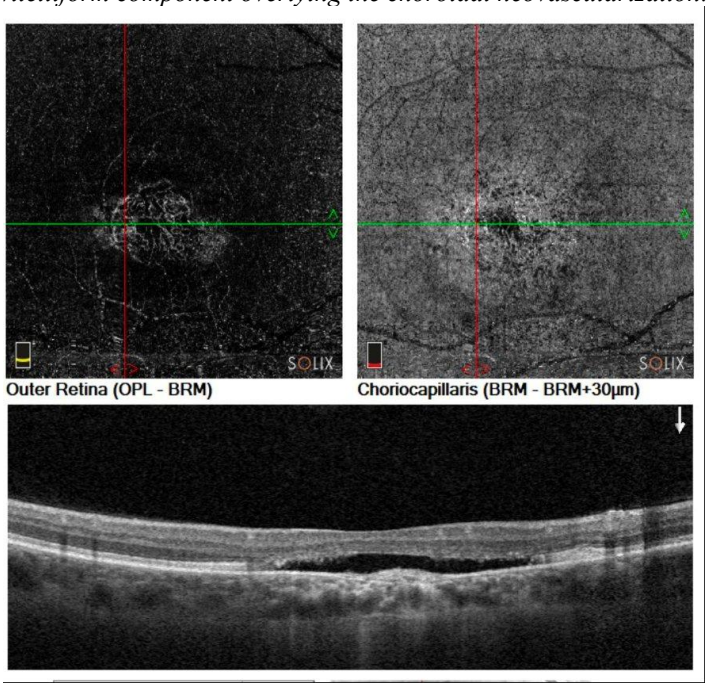


Fig. 2. *OCT-A (SOLIX, Zeiss), OD — during aflibercept loading phase. Flow signal persists but remains stable; no expansion of CNV network. B-scan: subretinal deposit with preserved structural architecture.*

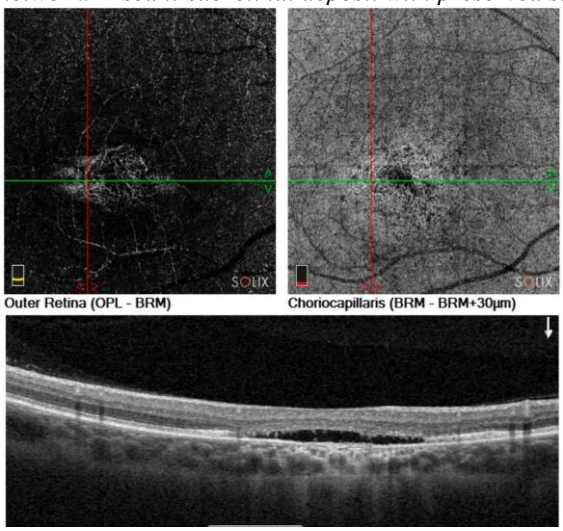


Fig. 3. *OCT-A (SOLIX, Zeiss), OD — after switch to faricimab (Vabysmo®). Partial reduction of flow signal in the outer retina slab. B-scan: partial reduction of the subretinal deposit.*

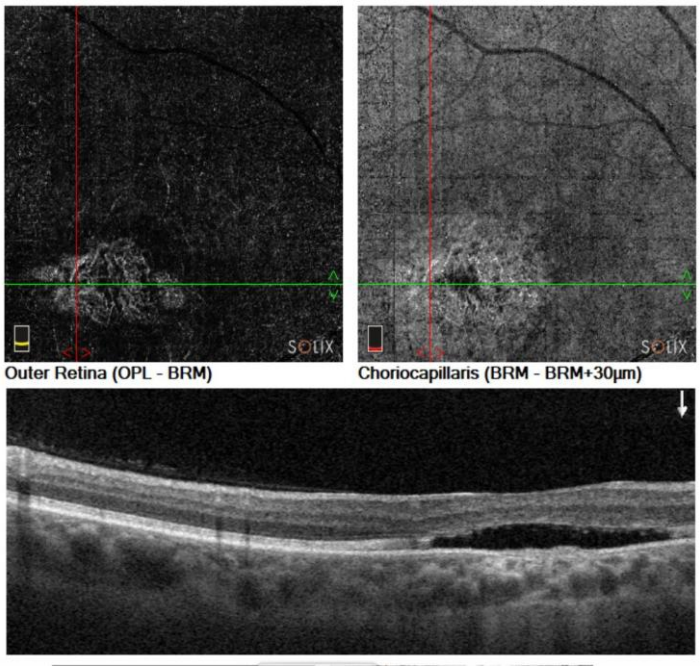
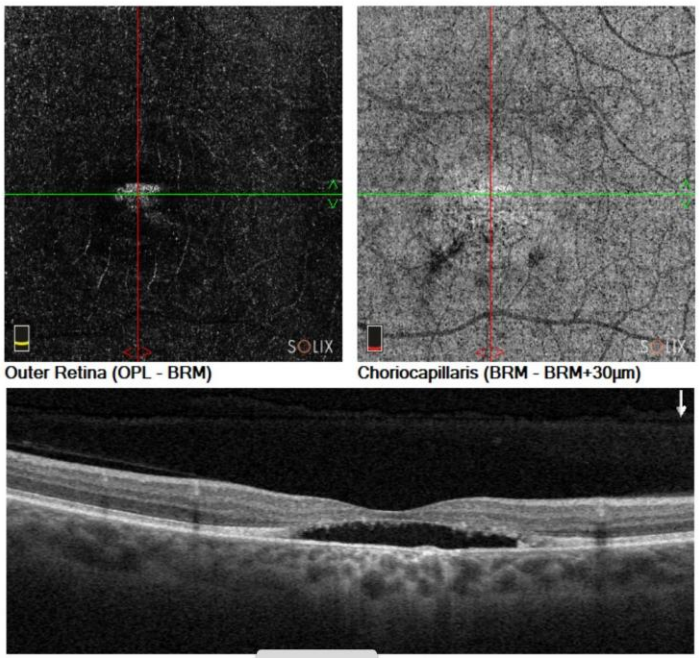


Fig. 4. *OCT-A (SOLIX, Zeiss), outer retina slab + B-scan (OS) — left eye. No flow signal in the outer retina on any serial examination. B-scan: hyperreflective subretinal deposit (vitelliform material) without neovascular component.*



III. DISCUSSION

This case is best read as a stabilization case, not as a visual recovery case. During 29 months of follow-up, BCVA stayed at 0.3 in both eyes. In an eye with long-standing BVMD and established dystrophic macular damage, this stability is clinically meaningful, even if it does not look impressive when judged only by acuity gain.

The first aflibercept course produced a modest but useful anatomical result. CST decreased from 247 to 237 µm and FLV from 2.23% to 2.15%, while visual acuity remained unchanged. The CNV signal on OCT-A did

not disappear, but it also did not enlarge. This is a realistic treatment endpoint in non-AMD CNV: suppression of activity and prevention of further structural damage, rather than restoration of normal retinal anatomy [4,8].

The recurrence seen 20 months after the last aflibercept injection should not be described as simple aflibercept failure. The more likely interpretation is reactivation of CNV in a chronically abnormal RPE-Bruch's membrane complex. The increase in FLV to 7.22%, together with worsening GCC-related parameters, shows why long-term OCT-A surveillance is important in BVMD, even after an initially quiet period [3,4].

Faricimab was selected at retreatment because it offered a plausible biological advantage, not because there is established evidence of superiority in BVMD. By targeting both VEGF-A and Ang-2, it may influence neovascular drive and vascular instability [7]. In this patient, FLV decreased from 7.22% to 4.22% after two injections, and the OCT-A flow signal was reduced. This is an anatomical response, but a single case cannot define the role of faricimab or compare it reliably with aflibercept.

The stable but unimproved visual acuity is also not surprising. BEST1-related disease damages the RPE-photoreceptor complex through accumulation of vitelliform material and progressive outer retinal degeneration [1,2,9]. Anti-VEGF therapy can reduce additional CNV-related injury, but it cannot recover photoreceptors that have already been lost because of the inherited dystrophy.

The fellow eye is a useful reminder of the diagnostic value of OCT-A. On structural OCT, a subfoveal hyperreflective lesion could easily raise concern for CNV or another subretinal lesion. Repeated absence of flow in the outer retina slab supported a non-neovascular vitelliform deposit. This distinction matters clinically, because anti-VEGF treatment is justified for active CNV, not for vitelliform material alone [3,4].

The family history also has practical consequences. With autosomal dominant BEST1 disease, first-degree relatives may be at risk and should not be reassured only because vision is still good. In this family, similar visual impairment in previous generations had been attributed to antibiotic toxicity, which delayed the correct interpretation of the disease. Genetic counseling and targeted ophthalmic surveillance are therefore part of the management, not an optional add-on.

IV. CONCLUSION

This case documents OCT-A-confirmed active CNV in genetically confirmed BVMD, treated sequentially with aflibercept and faricimab over 29 months. Aflibercept was followed by initial structural stability, and faricimab provided partial anatomical control after a late recurrence. BCVA remained 0.3 in both eyes throughout follow-up. In hereditary macular dystrophy, the response to anti-VEGF treatment should be judged mainly by control of neovascular activity and prevention of additional structural loss. Faricimab may be a reasonable retreatment option when recurrent activity is documented, but evidence in BVMD-related CNV is still limited. Genetic counseling remains mandatory in autosomal dominant BEST1 disease.

Compliance with Ethical Standards

Conflict of Interest: The authors declare no conflict of interest.

Ethical Approval: This report was prepared in accordance with the Declaration of Helsinki. Informed consent was obtained from the patient for publication of this case report.

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