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Bacillary layer detachment (BALAD) in neovascular age-related macular degeneration — three years' follow-up of a case study

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ABSTRACT

The study aimed to present a case of bacillary layer detachment (BALAD) in a patient with neovascular age-related macular degeneration (nAMD) treated with brolucizumab.

An 85-year-old patient with nAMD underwent a comprehensive clinical examination and multimodal imaging analysis. The patient received a series of injections with initial retinal layers and visual acuity (BCVA) improvements. After five injections, there were notable improvements in the retinal appearance and BCVA (enhanced from 1.3 to 0.22 logMAR). However, it later decreased to 1.0 logMAR due to the development of fibrosis and ellipsoid zone (EZ) disruption.

The study highlights the resolution of BALAD after the initial brolucizumab treatment but also emphasizes the difficulties in handling nAMD. Later fibrotic changes and disruptions in the EZ negatively impacted the long-term visual outcome.

KEYWORDS: bacillary layer detachment; brolucizumab; age-related macular degeneration; OCT-A; macular neovascularization

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INTRODUCTION

Bacillary layer detachment (BALAD) is a rare finding in optical coherence tomography (OCT) images. Mehta et al. first identified it in toxoplasma retinochoroiditis, describing it as a retinal detachment linked to the separation of photoreceptor inner segment myoid from inner segment ellipsoids [1]. Different terms, like "outer retinal cystic spaces", "septate neurosensory detachment", and "subretinal fluid with fibrin" have been used to describe this OCT feature [2]. Ramtohul et al. recently defined BALAD as a split in the inner myoid segment of photoreceptors, forming an intraretinal cavity [2].

BALAD is a nonspecific feature observed in various choroidal conditions, such as acute Vogt-Koyanagi-Harada (VKH) syndrome, acute posterior multifocal placoid pigment epitheliopathy (APMPPE), posterior scleritis, tubercular choroidal granuloma, panuveitis, choroidal metastases from lung and breast tumors, or acute nonpenetrating ocular trauma [3–7]. It has also been reported in

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central serous chorioretinopathy after photodynamic therapy (PDT) [3], acute idiopathic maculopathy [4], or nAMD [8–10].

BALAD can change during treatment, often improving as clinical conditions improve. It is usually seen inside the photoreceptor's cell body, raising concerns about long-term effects on photoreceptor function. Earlier, Ramtohul et al. reported a resolution of BALAD followed by a restoration of the ellipsoid zone (EZ) [5]. Despite the initial improvement, best corrected visual acuity (BCVA) decreased and finally returned to baseline. After a four-year follow-up, it was concluded that BALAD was linked to poor functional outcomes due to the high likelihood of subretinal fibrosis [5]. However, only the effects of ranibizumab, aflibercept, and bevacizumab were assessed. Now, the impact of brolucizumab has been reported. Brolucizumab, a small antibody fragment, offers potential advantages leading to more effective treatment [6]. However, there are some reported severe side effects, including occlusive retinal vasculitis and macular fibrosis [7]. This study explores the use of brolucizumab in treating neovascular age-related macular degeneration (nAMD) with BALAD. By documenting the clinical and imaging aspects of this rare condition, we assess the effectiveness of brolucizumab in treating nAMD with BALAD and potentially provide better patient outcomes.

CASE PRESENTATION

An 85-year-old man presented to our care with a sudden decreased vision in the left eye. The BCVA was 0.4 and 1.3 logMAR in the right and left eye, respectively. A slit-lamp evaluation of the left eye revealed an incipient cataract, which impacted fundus photography. Ophthalmoscopy showed a well-circumscribed, yellowish oedema in the macula (Fig. 1A). Funduscopic examination of the right eye revealed a macular pigmentary alteration.

OCT and OCT-angiography (OCT-A) were performed using Angio Retina QuickVue, Angio Retina and Cross line scans (RTVue, Optovue, Fermont, USA).

OCT scans of the left eye showed a dome-shaped hyporeflective cavity with subretinal hyperreflective material (SRHM) and subretinal fluid in the macular region (Fig. 1D). The OCT-A scan confirmed the presence of macular neovascularization (MNV) within the outer retina and choriocapillaris layer, classified as MNV type 2 (Fig. 1C, G).

Treatment utilizing brolucizumab (6 mg/0.05 mL) was initiated promptly, adhering to a T&E (treat and extend) regimen. Between the second and third injections, the patient underwent cataract surgery on the left eye. After 26 months, a resurgence of MNV without the presence of BALAD was observed. To date, ten intravitreal injections of brolucizumab have been administered.

The cystic retinal space was partially resolved two weeks after the first injection. BALAD was entirely resolved by the fourth week. The effect was sustained throughout the subsequent 35 months of follow-up. Meanwhile, a peripapillary MNV was identified in the right eye, and anti-vascular endothelial growth factor (anti-VEGF) therapy was instantly initiated.

BCVA of the left eye improved concomitant with the resolution of BALAD, from 1.3 to 0.7 logMAR, within the first two weeks. Post-cataract extraction, BCVA improved to 0.4 and reached 0.22 logMAR after five injections. Unfortunately, it declined to 1.0 logMAR due to fibrosis and EZ layer disruption.

DISCUSSION

The hypothesis suggests that BALAD might occur when the tensile strength in the photoreceptors' inner segment myoid is exceeded during exudation. This process, combined with outward forces, is believed to make the outer segments of the photoreceptors stick to the RPE/BM (retinal pigment epithelium/Bruch's membrane complex) complex [8]. Previous studies have shown that a rapid proteinaceous fluid influx caused by fulminant type 2 MNV can pass through a defect in the RPE/BM complex into the space in front of the EZ [8]. There is significant evidence linking type 2 MNV and BALAD [8, 9]. Palmieri et al. suggested intense exudation and inflammation in certain MNVs might pull on the photoreceptors' myoid, causing a split [10]. Additionally, SRHM observed in this case could be a mix of inflammatory fibrin and photoreceptor debris, potentially contributing to subretinal fibrosis [1, 2, 5]. Ramtohul et al. have suggested a possible connection between BALAD and the development of subretinal fibrosis [5].

However, BALAD has been observed in uveitis cases, acute VKH syndrome, APMPPE, posterior scleritis, tubercular choroidal granuloma, panuveitis, choroidal metastases from lung and breast tumors, acute nonpenetrating ocular trauma,

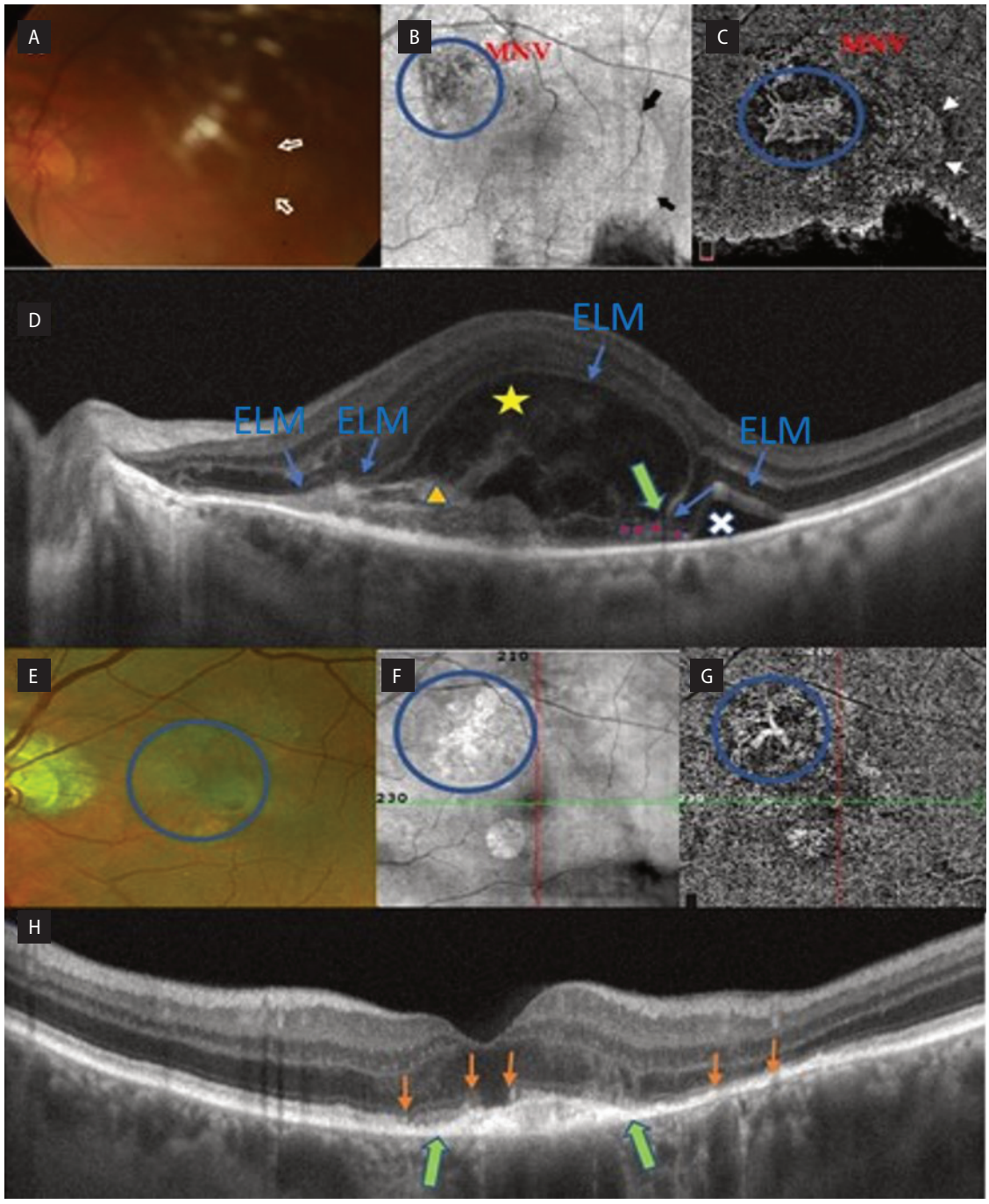

FIGURE 1. Multimodal imaging features of bacillary layer detachment. **A.** Color fundus photography — white, arrowheads indicate yellowish margin of cystic, intraretinal cavity. Light reflections caused by lens opacities. **B.** SLO ((Scanning Laser Ophthalmoscopy) fundus scan reveals hyporeflective active macular neovascularization (MNV) type 2 and less hyporeflective line of bacillary layer detachment (BALAD) cavity (dark arrows). **C.** En face optical coherence tomography-angiography (OCT-A) shows an active MNV type 2 (blue oval), margin of BALAD (white arrows). **D.** Scan B OCT shows bacillary layer detachment — intraretinal cystic (yellow star), hyperreflective band constituting the ellipsoid zone (EZ) (red dots), which is partially obscured by subretinal hyperreflective material (SRHM) — orange triangle, split between the EZ (elipsoid zone) and ELM (external limiting membrane) (green arrow). Subretinal fluid (white ×). **E.** Color fundus photography at last visit — blue oval surrounds yellowish subretinal fibrosis. **F.** SLO fundus scan at last visit shows hyperreflective area of non active MNV (blue oval). **G.** En face OCT-A reveals nonactive MNV (blue oval). **H.** Scan B OCT shows subretinal fibrosis (between green arrows), EZ and ELM disruption (orange arrows)

and also DME [3–7, 15]. Interestingly, this occurrence did not consistently relate to subretinal fibrosis in treated and untreated cases. Therefore, these studies may suggest reconsidering the in-

flammatory factors linked to BALAD. We believe a significant fluid influx into the neuroretina, causing a split in the photoreceptor layer, is crucial in developing BALAD.

Previous studies show that BALAD responds well to intravitreal injections of anti-VEGF agents [2, 5, 8]. Our observation showed significant improvement in BALAD and BCVA after the first brolucizumab injection. However, signs of fibrosis appeared one month later, leading to disruptions in the EZ and the ELM (external limiting membrane), causing decreased visual acuity. These findings align with results from other similar studies [2, 5, 8]. While recent reports discussing nAMD with BALAD are limited, existing literature indicates that, in almost all cases, ranibizumab, aflibercept, or bevacizumab rapidly resolved BALAD and significantly improved vision in most patients [2, 5, 8–10]. Notably, most of these cases involved MNV type 2, similar to our patient's condition.

However, a retrospective study found that BCVA often returns to its initial levels after four years [5]. Our result aligns with this observation. Additionally, it has been observed that MNV type 2 is often associated with poorer long-term visual outcomes, primarily because of the higher occurrence of subretinal fibrosis than other MNV types [8]. Therefore, similar to other studies, we could not definitively confirm the role of BALAD in fibrosis development.

The effectiveness and role of anti-VEGF agents in treating BALAD are unclear. Historically, common treatments have involved ranibizumab, bevacizumab, and aflibercept. In significant studies, the average number of anti-VEGF injections administered to patients was around 14 to 15 doses [5, 8]. Ramtohul et al. found a similar frequency of fibrosis development in patients treated with these three anti-VEGF agents [5]. In our clinical experience, a single brolucizumab injection effectively resolved BALAD, although we continued with the T&E regimen. However, further research is needed to determine the optimal dosage of brolucizumab to maintain its therapeutic effect, considering potential macular fibrosis development [7]. It is important to note that while BALAD resolved after the first brolucizumab injection, ongoing therapy was required for managing MNV type 2. This observation emphasizes the complexity of treating these conditions and the need for customized therapeutic approaches.

We hope the information shared in this report enhances our understanding of BALAD and aids in shaping future treatments. However, the case study has limitations, including a 36-month observation period and challenges attributing the role of BALAD or brolucizumab in macular fibrosis development. Using a T&E regimen further complicates pinpointing the specific effects of a single brolucizumab dose. Future research is crucial to clarify the relationship between BALAD or brolucizumab and subretinal fibrosis, contributing to improved clinical management of these conditions.

CONCLUSIONS

The study shows that BALAD improved with the first brolucizumab injection but also emphasizes the difficulties in handling nAMD. Unfortunately, later fibrotic changes and disruptions in the EZ layer negatively impacted the long-term visual outcome, highlighting the complexity of managing nAMD.

Ethics statement

The patient has provided informed consent to present test and treatment results.

Author contributions

Conceptualization: M.L. and A.W..; methodology: ML.; software: ML.; validation: ML and AW; formal analysis: AW., investigation: AW., ML.; resources: ML.; data curation: ML., AW.; writing — original draft preparation: ML.; writing — review and editing, AW, ML.; visualization: ML.; supervision: AW.; project administration: AW.; funding acquisition: AW. All authors have read and agreed to the published version of the manuscript.

Conflict of interest

The authors declare no conflict of interest.

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