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Original Article

# Bacillary Layer Detachment in Acute Vogt-Koyanagi-Harada Disease

Ferdane Ataş, Mahmut Kaya, Ali Osman Saatci

Dokuz Eylül University Faculty of Medicine, Department of Ophthalmology, İzmir, Turkey

## Abstract

**Objectives:** To evaluate the frequency and treatment response of eyes with bacillary layer detachment (BLD) in acute Vogt-Koyanagi-Harada (VKH) disease using spectral-domain optical coherence tomography (SD-OCT).

**Materials and Methods:** We retrospectively reviewed the medical records of 58 eyes of acute VKH patients with at least 6 months of follow-up between January 2009 and March 2021. SD-OCT, color fundus photographs, and fluorescein angiography images were analyzed in all patients.

**Results:** The study included 58 eyes of 29 patients. BLD was detected in 33 of the 58 eyes (56.9%) at baseline. Mean serous retinal detachment (SRD) height was 918.50±336.64 µm in the BLD group and 215.33±167.83 µm in the group without BLD ($p<0.05$). A positive correlation was found between SRD height and the presence of BLD ($r=0.783$, $p<0.05$). BLD was significantly more common in patients with a baseline SRD height greater than 500 µm ($p<0.05$). As subfoveal central choroidal thickness (CCT) could not be measured by enhanced depth imaging-OCT at baseline due to extreme choroidal thickness in all eyes, the earliest post-treatment CCT measurements were analyzed. At the completion of pulse steroid therapy, mean CCT was 425±82.87 µm in the BLD group and 385.58±82.87 µm in the group without BLD ($p=0.04$). The mean time to BLD resolution was 12.88±6.5 days (range: 2-26).

**Conclusion:** BLD is a common tomographic finding in eyes with acute VKH disease and can be differentiated from the associated SRD through careful SD-OCT analysis. Though it is mostly observed in patients with more serious disease, the presence of BLD has no negative effect on long-term visual function.

**Keywords:** Bacillary layer detachment, optical coherence tomography, serous retinal detachment, uveitis, Vogt-Koyanagi-Harada disease

**Address for Correspondence:** Ali Osman Saatci, Dokuz Eylül University Faculty of Medicine, Department of Ophthalmology, İzmir, Turkey
E-mail: osman.saatci@yahoo.com **ORCID-ID:** orcid.org/0000-0001-6848-7239

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## Introduction

Vogt-Koyanagi-Harada (VKH) disease is an autoimmune disease involving bilateral granulomatous panuveitis characterized by exudative retinal detachment that may be accompanied by neurological, auditory, and cutaneous findings.[1,2] Ocular signs have been classified as occurring in the acute or late stages of the disease. Choroidal inflammation/thickening and multiple serous retinal detachment (SRD) in the posterior pole are typically observed in acute VKH.[3] Multimodal imaging, especially spectral-domain optical coherence tomography (SD-OCT), plays a key role in the diagnosis of VKH disease.

In acute VHD, SD-OCT findings are typical and diagnostic. The presence of SRD, subretinal fluid compartments separated by septa, and undulations in the retinal pigment epithelium (RPE) are important findings for the diagnosis of acute VHD.[4,5] With advances in OCT technology, these septa are generally thought to be hyperreflective membranous structures that separate from the retina anterior to the RPE-Bruch's membrane complex and form a bridge with the retina. This anatomical finding on SD-OCT is referred to using the term "bacillary layer detachment" (BLD).[6] The presence of BLD is not unique to acute VKH and has been reported in many conditions, including acute VKH disease,[7,8] toxoplasmosis retinochoroiditis,[6] peripapillary pachychoroid syndrome,[9] acute posterior multifocal plaque pigment epitheliopathy,[10,11] central serous retinopathy,[12] neovascular age-related macular degeneration,[13] macular telangiectasis type 2,[14] acute idiopathic maculopathy,[15,16] sympathetic ophthalmia,[17] and trauma.[18,19]

This study investigated the frequency of BLD in patients with acute VKH disease using SD-OCT and evaluated the relationship between SRD height and choroidal thickness and visual prognosis.

## Materials and Methods

The records of 33 patients who were followed for at least 6 months for acute VKH disease between January 2009 and March 2021 were reviewed retrospectively. The study was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki and after obtaining approval from the Ethics Committee of Dokuz Eylül University.

The patients were diagnosed with VKH according to the revised diagnostic criteria defined at the First International Workshop on VKH Disease (2001).[2] Patients underwent systemic screening and an extensive ophthalmologic examination including best corrected visual acuity (BCVA), slit-lamp examination, intraocular pressure measurement with Goldmann applanation tonometry, detailed fundus examination, colored fundus photography (Visucam® 500, Carl Zeiss Meditec AG, Germany and DRI OCT Triton Plus®; Topcon Corporation, Tokyo, Japan), fluorescein angiography (FA) (Heidelberg Retinal Angiography 2), SD-OCT and enhanced depth imaging-OCT (EDI-OCT) (Spectralis OCT®, Heidelberg Engineering, Heidelberg, Germany). Of the 33 patients whose records were examined, 3 patients were not included in the study because they did not have EDI-OCT images, and 1 patient was not followed up. In all eyes undergoing EDI-OCT imaging, subfoveal central choroidal thickness (CCT) was too high to be measured at baseline. Therefore, it was calculated based on the earliest post-treatment measurements that could be obtained. Patients with ocular conditions other than VKH disease and those with complications of VKH disease such as choroidal neovascularization were not included in the study.

All patients were treated with intravenous methylprednisolone (1 g/day) for a minimum of 3 and maximum of 10 days at the clinician's discretion based on improvement of the SRD, followed by oral corticosteroid (starting at 1 mg/kg, maximum 64 mg/day) tapering 8 mg/week and azathioprine (2 mg/day) or adalimumab (40 mg/2 weeks after an 80-mg loading dose).

### Image Analysis

All patients' SD-OCT and EDI-OCT images were evaluated for SRD height, the presence of intraretinal septa, and CCT. The RPE-Bruch's membrane complex, cone interdigitation zone, photoreceptor ellipsoid zone (EZ), and external limiting membrane (ELM) were determined according to the International Nomenclature for OCT consensus guideline.[20] The hyporeflective band between the ELM and EZ was defined as the myoid zone (MZ). SRD height was measured as the vertical line from the upper border of the RPE layer through the fovea to the outer border of the anteriorly detached retina. In eyes with BLD, SRD height was measured from the lower border of the ELM in the anteriorly displaced retina. In EDI-OCT images, CCT was measured as the vertical line drawn through the foveal center from the outer border of the hyperreflective RPE-Bruch's membrane complex to the choroid-sclera junction. BLD was defined as separation of the photoreceptor layer at the level of the MZ (between the ELM and EZ inner segment), as described by Mehta et al.[6] (Figure 1). Time to resolution of BLD was calculated as the time from its first detection on OCT to the examination in which it was no longer observed. SD-OCT images were analyzed by retinal specialists (M.K., A.O.S.).

### Statistical Analysis

Statistical analysis of all parameters was performed using IBM SPSS Statistics version 24.0 (IBM Corp, Armonk, NY, USA) software. Mean, percentage, and standard deviation were used to analyze quantitative variables. BCVA was converted to the logarithm of the minimal angle of resolution (logMAR) values. SRD height, presence of BLD, choroidal thickness, and BCVA data were analyzed. Wilcoxon's test was used to compare pre-treatment and post-treatment parameters. Groups with and without BLD were compared using the Mann-Whitney U test. A p value $<0.05$ was considered statistically significant.

## Results

A total of 58 eyes of 29 patients were included in the study. Of the patients, 23 (79.3%) were female and 6 (20.7%) were male. The mean age of all patients was 35.20±15.15 years (range: 8-66). The clinical characteristics of the patients are summarized in Table 1. All patients had bilateral SRD at the posterior pole.

In all eyes, multiple punctate hyperfluorescent leaks at the RPE level, pooling in the SRD regions, and hyperfluorescence of the disc were detected on FA. The mean follow-up time of the patients was 30±22 months (range: 8-132).

BLD was detected in 33 (56.9%) of the 58 eyes in the first examination. Involvement was bilateral in all patients found to have BLD. SRD height was 918.50±336.64 µm in the BLD group and 215.33±167.83 µm in the group without BLD (p<0.05). There was a positive correlation between SRD height and the presence of BLD (r=0.783, p<0.05). BLD was detected significantly more frequently in patients with an SRD height of 500 µm or greater at the time of diagnosis (p<0.05). Complete resolution of the SRD was first observed after 21.7±1.65 days in the BLD group and 17.66±1.26 days in the group without BLD. There was no significant difference between the two groups in terms of SRD resolution time (p=0.076) (Table 2).

At 1-month follow-up after complete SRD resolution, EZ disruption was detected in 6 eyes (18%) in the BLD group and 3 eyes (12%) in the group without BLD (p>0.05). RPE disruption was detected in 12 eyes (36%) in the group with BLD and 7 eyes (28%) in the group without BLD (p>0.05).

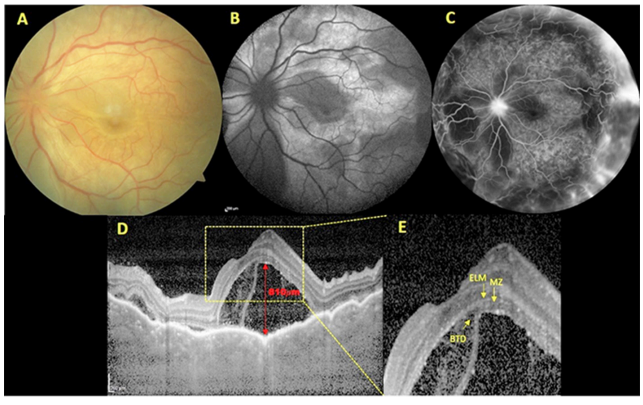


**Figure 1.** Left eye of a 45-year-old female patient. (A) Color fundus photograph showing multiple bullous serous retinal detachment (SRD) at the posterior pole. (B) Fundus autofluorescence imaging showing hypoautofluorescence in regions corresponding to the SRD and hyperautofluorescence in adjacent regions. (C) Fluorescein angiography shows numerous punctate hyperfluorescent leaks, pooling, and disc hyperfluorescence. (D) Spectral-domain optical coherence tomography (SD-OCT) shows high subretinal fluid (810 µm), septated fluid compartments within the subretinal detachment, and retinal pigment epithelium-choroidal folds. (E) An enlarged section from the SD-OCT image in panel D shows the bacillary layer detachment (yellow arrows) at the level of the inner myoid zone

ELM: External limiting membrane

The mean duration of pulse steroid therapy was 7.96±2.7 days (range: 3-10). After completion of pulse steroid therapy, CCT was measured as 425±82.87 µm in the BLD group and 385.58±82.87 µm in the group without BLD (p=0.04). Mean BCVA at baseline was 0.62±0.8 logMAR in the BLD group and 0.30±0.90 logMAR in the group without BLD (p<0.001). The final BCVA in the two groups was 0.08±1.0 and 0.07±0.90 logMAR, respectively (p=0.802). Final BCVA was significantly improved in both groups (p<0.001 for both). We detected no significant relationship between final BCVA and the presence of BLD. The mean time between first detection and resolution of BLD was 12.88±6.5 days (range: 2-26) (Table 2).

## Discussion

The bacillary layer was first described by neuroanatomist Polyak[21] in 1941 as the inner and outer segments of the photoreceptors. In current studies, BLD is defined as the bacillary layer (MZ, EZ, and outer segments) adjacent to the RPE remaining to the posterior, with separation and anterior displacement of the ELM and other retinal layers.[6,7,8,9,10,11,12,13,14,15,16,18,19]

In studies conducted with time-domain OCT, hyperreflective septa that create cystoid spaces by dividing the fluid in SRD into compartments have been reported in acute VKH patients.[22,23]Authors have referred to these hyperreflective structures as subretinal fibrosis,[24] inflammatory fibrin,[5] fibrous strands,[25] or membranous structures.[4] In their study comparing the OCT features of VKH disease, central serous chorioretinopathy, and posterior scleritis, Liu et al.[26] reported that the presence of these membranous structures had over 95% specificity and 97% positive predictive value in the

**Table 1. Clinical characteristics of patients with acute VHD**

| Clinical characteristic | Number of eyes, n (%) |
|---|---|
| SRD at posterior pole | 58 (100) |
| Eyes with BLD<br>Eyes without BLD | 33 (56.9)<br>25 (43.1) |
| Anterior chamber cells | 20 (34.4) |
| Vitritis | 12 (20.6) |
| FA: Punctate hyperfluorescent spots and disc hyperfluorescence | 58 (100) |

SRD: Serous retinal detachment, BLD: Bacillary layer detachment, FA: Fundus fluorescein angiography

**Table 2. Comparison of eyes with and without bacillary layer detachment**

| | Eyes with BLD | Eyes without BLD | *p* value |
|---|---|---|---|
| SRD height (µm), mean ± SD | 918.50±336.64 | 215.33±167.8 | **<0.05** |
| SRD resolution time (days), mean ± SD | 21.7±1.65 | 17.66±1.26 | 0.076 |
| CCT after pulse steroid (µm), mean ± SD | 425±82.87 | 385.58±82.87 | **0.04** |
| Initial BCVA (LogMAR), mean ± SD | 0.62±0.8 | 0.30±0.90 | **0.001** |
| Final BCVA (LogMAR), mean ± SD | 0.08±1.0 | 0.07±0.90 | 0.802 |

SRD: Serous retinal detachment, CCT: Central choroidal thickness, SD: Standard deviation, BCVA: Best corrected visual acuity, LogMAR: Logarithm of the minimum angle of resolution

diagnosis of acute VKH disease. Mehta et al.[6] reported that in an eye with toxoplasma retinochoroiditis, the photoreceptor layer was detached from the inner segment myoid level, similar to the postmortem histological artifact seen in eyes with age-related macular degeneration, and their finding was the first tomographic definition of BLD. In this study, BLD was present in 56.9% of patients with acute VKH disease at initial presentation. BLD resolution on OCT was observed in a mean of 12.8 days with pulse steroid therapy. Agarwal et al.[8] reported the prevalence of BLD as 94.9% (n=112) in 118 eyes with acute VKH disease in their swept-source OCT study conducted between January 2015 and February 2019. Of the 112 eyes with BLD, focal defects in the ELM anterior to the BLD were observed in 8 (7.1%), disruption of the interdigitation zone at the base of the BLD was observed in 53 (47.3%), and the hyperreflective band representing the EZ could not be detected at the base of the BLD in 102 eyes (91.1%). In their study, the patients' mean CCT at the time of admission was 456.1 µm, and it was shown that BLD resolved with pulse steroid therapy in a mean of 3.4 days.[8] In all of the eyes in our study, CCT was too thick to be measured in the initial examination. Therefore, CCT measurements could only be obtained after pulse steroid therapy. The long BLD resolution time compared to the study by Agarwal et al.[8] suggests that the patients in our study were likely diagnosed later and had more severe disease. The difference in choroidal thickness at the time of diagnosis between the studies is consistent with this view.

The mechanism of BLD formation is still unknown. The most likely hypothesis is that decreased perfusion due to choroidal ischemia in the photoreceptor layer may cause BLD. After pulse steroid therapy, BLD regresses as inflammation resolves and choroidal perfusion improves.[4,16] In our study, both CCT and SRD height were significantly greater in eyes with BLD compared to those without BLD. These findings support the notion that increased choroidal thickness associated with intense inflammation may cause impaired photoreceptor perfusion and BLD formation. SRD height is believed to represent the degree of leakage in the choroid, which increases in thickness because of deterioration of the blood-RPE barrier and inflammation during the acute period of VKH disease.[27] It is also thought that in addition to the underlying inflammation, the sudden increase in hydrostatic pressure due to rapid fluid accumulation in the external retina may cause the development of BLD by splitting the photoreceptors.[14,28] In our study, SRD height in patients with acute VKH disease was significantly greater in eyes with BLD compared to the eyes without BLD. In addition, the prevalence of BLD increased to 94.2% among patients with SRD height of 500 µm or greater. These findings demonstrate the positive association between SRD height and the prevalence of BLD. Agarwal et al.[8] used swept source OCT to investigate the presence of BLD in acute VKH disease, whereas we used SD-OCT in our study. There are no studies in the literature comparing SS-OCT and SD-OCT devices for determining the frequency of BLD.

It is emphasized that the metabolic activity of the photoreceptor inner segment and its ability to renew the outer segment by producing new disc membranes persist in patients with VKH disease. As there is no permanent functional damage to the photoreceptors, improvement in visual acuity is reported to be rapid.[4] There are also studies indicating that the presence of SRD does not delay the functional recovery of photoreceptors in patients with VKH disease.[29] The results of histological and imaging studies suggest that rapid functional improvement can be expected in eyes with VKH disease. In our study, we observed that BLD resolved faster with pulse steroid therapy than SRD (mean 12.8 days vs. 21.7 days). In addition, rates of RPE and EZ disruption were 36% and 18%, respectively, in the eyes with BLD at 1-month follow-up after SRD resolution. In the eyes without BLD, these rates were 28% and 12%, respectively, with no significant differences between the groups. In addition, although BCVA was significantly lower at baseline in eyes with BLD compared to eyes without, both groups showed a significant increase in vision and there was no significant difference between them at final examination.

### Study Limitations

The main limitations of this study are the small number of patients, its retrospective nature, and the fact that not all patients could be monitored daily. If postmortem histopathological studies could be performed, they may improve our understanding of these findings.

## Conclusion

Although BLD is an OCT finding that has been described in many diseases in the literature, it is frequently observed in patients with acute VKH disease. BLD resolves quickly with treatment. The presence of BTD was not shown to have a favorable or unfavorable impact on visual prognosis in patients with acute VKH in this study.

### Ethics

**Ethics Committee Approval:** The study was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki and after obtaining approval from the Ethics Committee of Dokuz Eylül University.

**Informed Consent:** Obtained.

**Peer-review:** Externally peer revieved.

### Authorship Contributions

Surgical and Medical Practices: M.K., A.O.S., Concept: M.K., A.O.S., Design: F.A., M.K., A.O.S., Data Collection or Processing: M.K., F.A., Analysis or Interpretation: F.A., M.K., A.O.S., Literature Search: M.K., F.A., A.O.S., Writing: F.A., M.K., A.O.S.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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