



Case series bacillary layer detachment associated with acute central serous chorioretinopathy in patients with COVID-19

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1. Introduction

An outbreak of coronavirus disease (COVID-19) that emerged in China resulted in a global pandemic, and the new severe acute respiratory syndrome is caused by a type of coronavirus, SARS-CoV-2.¹ COVID-19 is contagious, and most patients are either asymptomatic or have mild symptoms. Its progression can lead to acute respiratory distress syndrome and even death, and the most common symptoms are fever, cough, fatigue, and dyspnea.¹ Ocular findings have been associated with COVID-19 infection, and vitritis, inner and outer retinal lesions, and retinal vascular occlusions represent the retinal features already reported in the literature.²⁻⁵

Central serous chorioretinopathy (CSC) is a multifactorial chorioretinal disease related to several clinical manifestations mainly in its acute phase, where we find macular neurosensory detachment associated with subretinal fluid, with or without retinal pigment epithelial detachment (PED).^{6,7}

Following the start of the COVID-19 pandemic, the incidence of anxiety disorders has increased in the worldwide population.^{8,9} In addition, patients with COVID-19 have been treated with corticosteroids since they decrease the need for mechanical ventilation in those with respiratory function deterioration.¹⁰ Endothelial dysfunction and generalized tissue stress occur in patients with COVID-19, and, therefore, the use of a high dose of steroids becomes critical for these patients' recovery.¹⁰ Corticosteroid exposure and anxiety disorders are known risk factors for CSC development.^{6,7}

We report two patients with COVID-19 who were treated with corticosteroids and developed typical clinical features of CSC seen on optical coherence tomography (OCT) associated with bacillary layer detachment (BALAD) and fibrin accretion. In both cases, the patients were tested for SARS-CoV-2 and underwent other serologic tests at the onset of the systemic clinical picture of COVID-19 and not at the onset of

visual symptoms. These patients had no remarkable past medical or ocular history, and no contact with animals, including cats.

2. Findings

2.1. Case 1

Case 1 was that of a 41-year-old Caucasian man who presented with unilateral acute visual loss on the 13th day of a SARS-CoV-2 infection, shortly after the introduction of a daily dose of 8 mg of oral dexamethasone.

The best-corrected visual acuity (BCVA) was 20/20 in the right eye and 20/40 in the left eye. Biomicroscopy of the anterior segment, pupillary reactions, and intraocular pressure were normal, and no vitreous cells were observed in both eyes. Fundus examination was unremarkable in the right eye and showed pigmentary changes and a serous macular detachment associated with a yellowish discoloration beneath the neurosensory elevation in the left eye. Within the macular area, B-scan spectral-domain OCT (Cirrus 6000, Carl Zeiss Meditec, Jena, Germany) of the left eye showed a large volume of subretinal fluid, a pigment epithelium detachment (PED) in the foveal area, and hyperreflective material accretion within the subretinal space and intraretinal cavity corresponding to BALAD (Fig. 1). The choroidal thickness was increased in both eyes.

Laboratory tests showed a normal complete blood count (CBC), and chest and sinus X-rays were unremarkable. The patient's C-reactive protein (CRP) level (2.26 mg/L) was increased.

During the follow-up and after corticosteroid discontinuation, the imaging features of CSC progressively resolved along with BALAD on OCT, and a large volume of hyperreflective material accretion appeared in the subretinal space of the left eye. By 3 months follow-up, the subretinal fluid spontaneously and completely resorbed (Fig. 2), and the

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BCVA of the left eyes improved to 20/25.

2.2. Case 2

Case 2 was that of a 43-year-old Caucasian woman who presented with visual loss in her right eye 20 days after diagnosis of COVID-19 and 5 days after completion of treatment for pneumonia secondary to the SARS-CoV-2 infection. Her therapy included chest computed tomography performed in another service and use of antibiotics and high doses of dexamethasone intravenously (10 mg/day) and orally (8 mg/day).

On examination, the BCVA was 20/40 in the right eye and 20/20 in the left eye. Biomicroscopy of the anterior segment, pupillary reactions, and intraocular pressure were normal, and no vitreous cells were observed in both eyes. The fundus examination was normal in the left eye and showed pigmentary changes and a serous macular detachment in the right eye. A color fundus photograph of the right eye showed a yellowish discoloration beneath the neurosensory detachment. Within the macular area, B-scan spectral-domain OCT (Spectralis, Heidelberg Engineering, Germany) of the right eye showed a large volume of subretinal fluid associated with a small and shallow parafoveal PED and BALAD. Hyperreflective material accretion was depicted within the subretinal space and intraretinal cavity corresponding to the BALAD (Fig. 1). The choroidal thickness was increased in both eyes.

Laboratory tests showed a normal CBC, and chest and sinus X-rays were unremarkable, since the patient had been treated previously for pneumonia. The patient's CRP level (6.95 mg/L) was increased.

During the follow-up and after corticosteroid discontinuation, the imaging features of CSC progressively resolved along with BALAD and hyperreflective material accretion (Fig. 3). At 1-month follow-up, the BCVA of the right eye improved to 20/20.

3. Discussion

COVID-19 disease caused by the SARS-CoV-2 virus is a contagious

disease, and most patients are either asymptomatic or have mild symptoms. However, the progression of COVID-19 can lead to severe forms of disease, resulting in acute respiratory distress syndrome and even death.¹ The disorder infects host cells in the lung parenchyma, where the virus spreads, causing lesions and an intense immune response as systemic symptoms such as fever, cough, fatigue, and dyspnea appear.^{11,12} In severe COVID-19, corticosteroid therapy is recommended to control systemic manifestations, including the cytokine storm. However, corticosteroid therapy may induce micro-thrombus formation and increases blood viscosity by inducing platelet aggregation and vasoconstriction.^{13,14}

CSC occurs or is aggravated by corticosteroid administration regardless of its route of administration, and this drug is considered an important risk factor for disease development. Impaired vascular autoregulation by increased adrenergic receptor transcription, steroid-induced systemic hypertension, and a prothrombotic effect are possible mechanisms related to CSC development in patients treated with corticosteroid therapy.¹⁵⁻¹⁸ CSC is characterized by congestion, hyperpermeability, and thickening of the choroid leading to dysfunction of the retinal pigment epithelium (RPE), responsible for the blood-retinal barrier. The loss of its integrity leads to subretinal fluid accumulation and consequently marked loss of central macular vision.¹⁹ In its acute form, CSC is characterized by sudden loss of central vision, neurosensory macular detachment with or without a PED, focal or multifocal RPE changes, and increased thickness and hyperpermeability of the choroid.¹⁹⁻²¹

Few previously reported studies have described the development of CSC in COVID-19. Abrishami et al. reported three cases of bilateral CSC²² and Amulya and Thanuja one unilateral case,²³ all not associated with corticosteroid use. In the first report, all three cases improved after treatment, two cases with steroidal anti mineralocorticoid and one case by photodynamic therapy.²² In the second article, the patient improved without treatment.²³

Other studies have reported two cases of bilateral CSC after

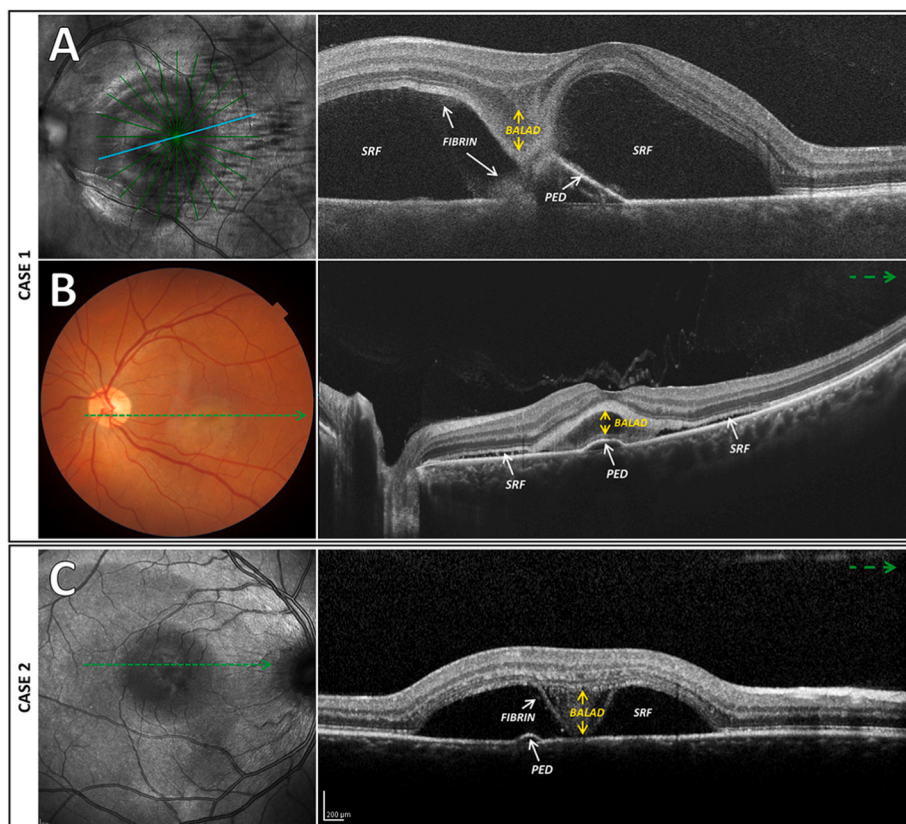


Fig. 1. Case 1. (A) B-scan spectral-domain optical coherence tomography of the left eye shows a large volume of subretinal fluid (SRF), a pigment epithelial detachment (PED) in the foveal area, fibrin, and bacillary layer detachment (BALAD). (B) Case 1. After 10 days, more defined BALAD, PED, and SRF are seen in the respective color fundus photographs. Case 2. (C) After 20 days of COVID-19, BALAD, PED, and SRF are well-defined. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

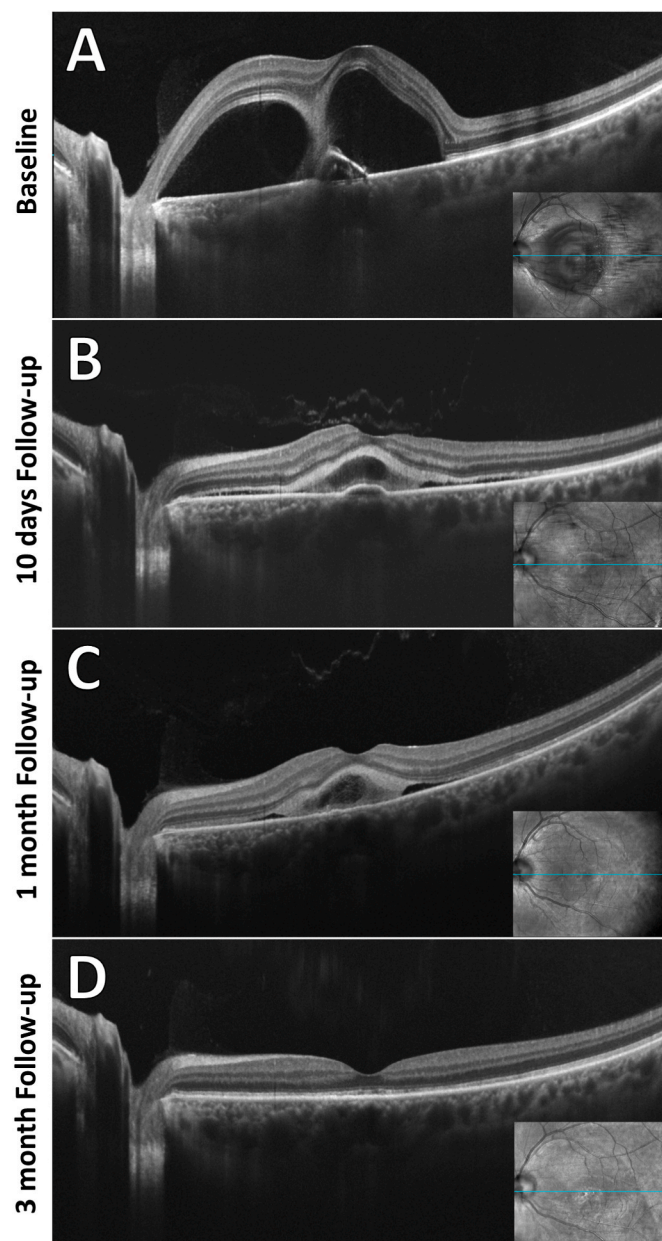


Fig. 2. Case 1 Follow-up. (A, B, C, D) B-scan spectral-domain optical coherence tomography images of the left eye show progressive resolution of BALAD, PED, subretinal fluid, and hyperreflective material accretion in the subretinal space at (B) 10-days, (C) 1-month, and (D) 3-months.

treatment with a corticosteroid, one in a 38-year-old woman with blurred vision bilaterally after 1 month of infection with COVID-19²⁴ and the other, in a 38-year-old man with subacute onset of central visual loss.²⁵ In two other cases, the CSC was unilateral after COVID-19 treatment with inhaled and oral steroids, one in a 42-year-old woman²⁶ and another in a 27-year-old woman.²⁷ In all of these cases, subretinal fluid was observed but without fibrin formation or subretinal fibrin material (SRFM).^{22–27}

In a randomized, retrospective study, of 100 patients evaluated post-recovery from COVID-19, 19 had ocular manifestations, and 2 of them had CSC. However, there is no information on whether these patients were treated with corticosteroids or had a history of eye disease.²⁸

In contrast to all these studies, our cases are unique and demonstrated novel CSC OCT imaging in patients with COVID-19 as BALAD and fibrin accretion in the subretinal space. Fibrin or SRFM has been

identified previously in CSC,^{15,29} posterior uveitis cases such as Vogt-Koyanagi-Harada (VKH) disease,³⁰ age-related macular degeneration, acute posterior multifocal placoid pigment epitheliopathy, unilateral acute idiopathic maculopathy, pre-eclampsia, retinchoroiditis secondary to toxoplasmosis and ocular trauma, sympathetic ophthalmia,^{31,32} but nothing like these cases that we reported.

The excessive choroidal hyperpermeability and RPE ruptures associated with CSC may allow a large molecule from the sub-RPE space (such as fibrin) to enter the subretinal space.³² In CSC, SRFM has been described as overlying the RPE defects on OCT and corresponding to the leakage on fluorescein angiography.³² Conversely, in VKH disease, SRFM may represent inflammatory debris or macrophages encompassing shed outer segments.³⁰

The OCT imaging and natural history of the current cases indicate the occurrence of BALAD. It is postulated that the BALAD septum is composed of fibrin-like inflammatory products, since they promptly resolve following corticosteroid therapy.³²

In a recent literature review, of the 164 cases of BALAD described, two were associated with CSC, i.e., one case of fibrinous CSC and one case of CSC secondary to a complication from systemic lupus erythematosus with severe hypertension and renal failure.²⁹

Those authors also documented a high proportion of choroidal thickening associated with BALAD, as we observed, but different from the fibrinous CSC. This one is characterized by the presence of exudative detachment and subretinal fibrin deposition like as a ring- or doughnut-shaped area with a pellucid central area surrounded by grayish-white exudates and a yellowish lesion with a translucent dark spot, that has already been reported as retinal dipping and fibrinous exudation with a translucent lesion in OCT.³³ As in our case, there were no inflammatory signs in the anterior chamber and vitreous, but they differ in the fluidity of the retinal detachment. Our case had a great deal of fluidity, whereas in fibrous CSC there is little. Another sign refers to the presence of dark spotting within the subretinal fibrin exudate seen in eyes with fibrinous CSC and the presence of a hyporeflective vacuole amid the cloud-like hyperreflective fibrin.³³

In the current cases, a split at the level of the photoreceptor inner segment (IS) formation of an intraretinal cavity associated with choroidal thickening (present in 93.8% of BALAD cases) was identified.²⁹ In addition, the prompt functional improvement and structural recovery of the BALAD also were observed in our cases. As Cicinelli et al. reported, our patients also had rapid restoration of the outer retina and improvement in visual acuity.³¹

Furthermore, the development of BALAD may be related to the severe and acute choroidal exudation in the subretinal space that extended into and exceeded the photoreceptor IS tensile strength, which split the myoid layer and separated it from the ellipsoid zone.²⁹ Ledesma-Gil et al. reported a substantial increase in subretinal fluid and associated subfoveal BALAD in a case of CSC treated with half-fluence, half-dose verteporfin photodynamic therapy.³⁴ BALAD also was described in a case of peripapillary pachychoroid syndrome.³⁵ Nevertheless, our cases represent the first report of BALAD in typical treatment-naïve CSC cases.

SARS-CoV-2 acts on macrophages and other myeloid cells by triggering the assembly of a proinflammatory protein complex through interleukin activation. The synthesis of interleukin-6 induces an increase in CRP and is an important proinflammatory agent in the cytokine storm in COVID-19.¹² In the current cases, although no inflammation was seen during ocular examinations, such as the presence of both anterior chamber and anterior vitreous cells, flares, and vitreous opacities, laboratory workups showed increased levels of CRP. Increased CRP in the blood is a marker of inflammation that can result from several disorders ranging from infection to cancer.²⁹ Inflammation and elevated plasma levels of CRP have prothrombotic effects by enhancing tissue factor and fibrin expression. Fibrin is involved in inflammatory processes, and generation of a stable fibrin network is necessary for sufficient inflammation control.^{29,34}

Despite little evidence, we speculated that the occurrence of BALAD

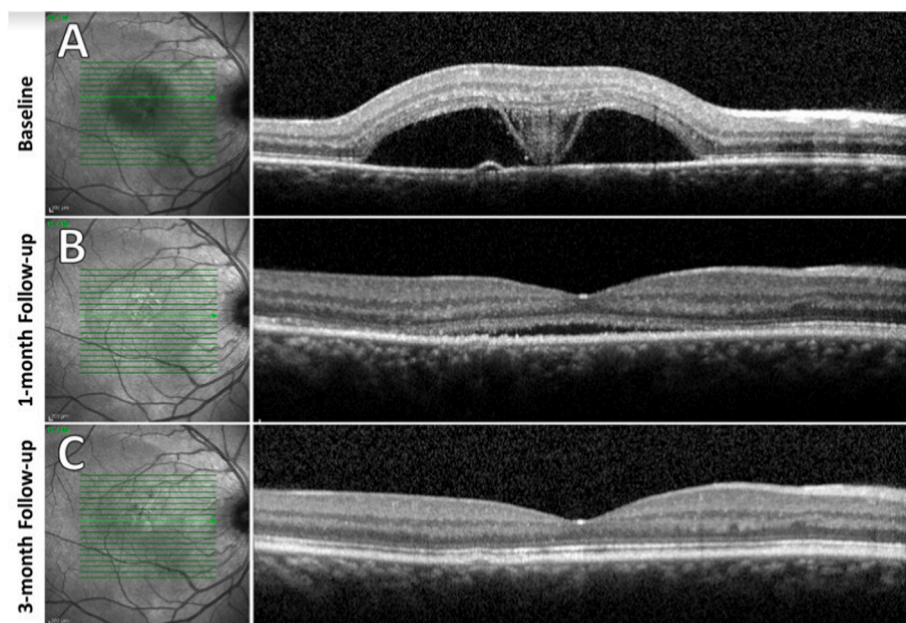


Fig. 3. Case 2 Follow-up. (A, B, C) B-scan spectral-domain optical coherence tomography images of the right eye show progressive resolution of the BALAD, PED, subretinal fluid and hyperreflective material accretion in the subretinal space at (B) 1 month and (C) 3 months.

and large amount of fibrin accretion in the current CSC cases may be related to the systemic inflammatory condition observed in patients with COVID-19. Additionally, both patients were treated with high levels of systemic steroids. The combination of the systemic inflammatory state and high steroid administration also can be related to these unique features.

4. Conclusions

We report two patients with COVID-19 treated with corticosteroids who developed typical acute CSC findings on imaging associated with BALAD and fibrin accretion. The development of BALAD and large amounts of fibrin in our cases may be related to the severe systemic inflammatory reaction that occurs in patients with COVID-19. These features broaden the causality spectrum of BALAD and vision losses that can follow acute CSC presentation.

Publication originality statement

We confirm this publication is original.

Patient consent

The patients provided written consent for publication of this case series. This study was granted a Certificate of Ethical Appraisal of the Federal University of São Paulo.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

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