A Case Of COVID-19 Who Developed Cilioretinal Artery Obstruction Associated With Impending Central Retinal Vein Occlusion After COVID-19 Infection

Eyupcan Sensoy[1], *Berrak Sekeryapan Gediz*[1]

ABSTRACT

COVID-19 is a disease accompanied by severe coagulopathy secondary to inflammation and multi-organ involvement. The frequency of thromboembolic complications in COVID-19 and its relationship with the severity of the disease has still not been determined. In this article, we present a case of cilioretinal artery occlusion associated with impending central retinal vein occlusion after severe COVID-19 infection.

Keywords: Cilioretinal artery obstruction, Impending central retinal vein occlusion, Paracentral acute middle maculopathy, SARS-COV-2, Thrombosis

INTRODUCTION

New Coronavirus Disease-2019, caused by Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-COV-2), has rapidly spread worldwide immediately after onset in China and was declared as global pandemics at March 12, 2020 by World Health Organization.[1] The homeostatic alterations secondary to inflammation caused by COVID-19 infection lead severe coagulopathy and multi-organ involvement.[2,3] Procoagulant state resulting from infection may also affect retinal vascular system.[4,5]

Cilioretinal artery originates from posterior ciliary arteries and presents in 32% of eyes.[6,7] The cilioretinal arteries show variations in size, calibration and distribution and provide blood supply of macula in approximately 19% of eyes. Cilioretinal artery occlusion (CAO) can be either isolated or together with central retinal vein occlusion (CRVO).[6-9] Paracentral acute middle maculopathy (PAOM) is a recently defined optical coherence tomography (OCT) finding which shows acute retinal ischemia.[10] It has been reported that PAOM also accompanies retinal vascular occlusions.[11-13] Here, it was aimed to present a CAO cases accompanied by CRVO and PAOM following COVID-19 infection.

CASE REPORT

A 70-years old male patient presented with loss of vision in the right for one day. In his history, it was found out that the patient underwent surgery due to colon cancer one year ago and that he was admitted to intensive care unit due to COVID-19 infection 3 months ago and were not on anticoagulant therapy. In the examination, best-corrected visual acuity was finger count at 1 meter in the right eye and 8/10 in the left eye. Intraocular pressure measurements and anterior segment examination were normal in both eyes. In the fundus examination, there was retinal whitening at papillomacular bundle and central fovea which corresponded to cilioretinal artery trace, thinning of cilioretinal artery, increased venous tortuosity and small intraretinal hemorrhage at posterior pole in the right eye; the left eye was normal (Figure 1a and 1b). On OCT (OCT Spectralis, Heidelberg Engineering, Germany), there was increased hyper-reflectivity at inner central retinal segments and hyper-reflective line at inner segment of outer plexiform layer [marked middle limiting membrane (MLM) appearance] as well as subfoveal and intraretinal fluid, characteristic hyper-reflective band appearance of PAOM at parafoveal area which showed skipping pattern

1- MD, Ulucanlar Eye Training and Research Hospital, Ankara, Türkiye
2- MD, Prof, Ulucanlar Eye Training and Research Hospital, Ankara, Türkiye

Received: 22.07.2022
Accepted: 21.11.2022
J Ret-Vit 2023; 32: 199-204
DOİ: 10.37845/ret.vit.2023.32.33

Correspondence Adress:
Eyüpcan Şensoy
Ulucanlar Eye Training and Research Hospital, Ankara, Turkey
Phone: +90 546 417 7538
E-mail: dreyupcansensoy@yahoo.com

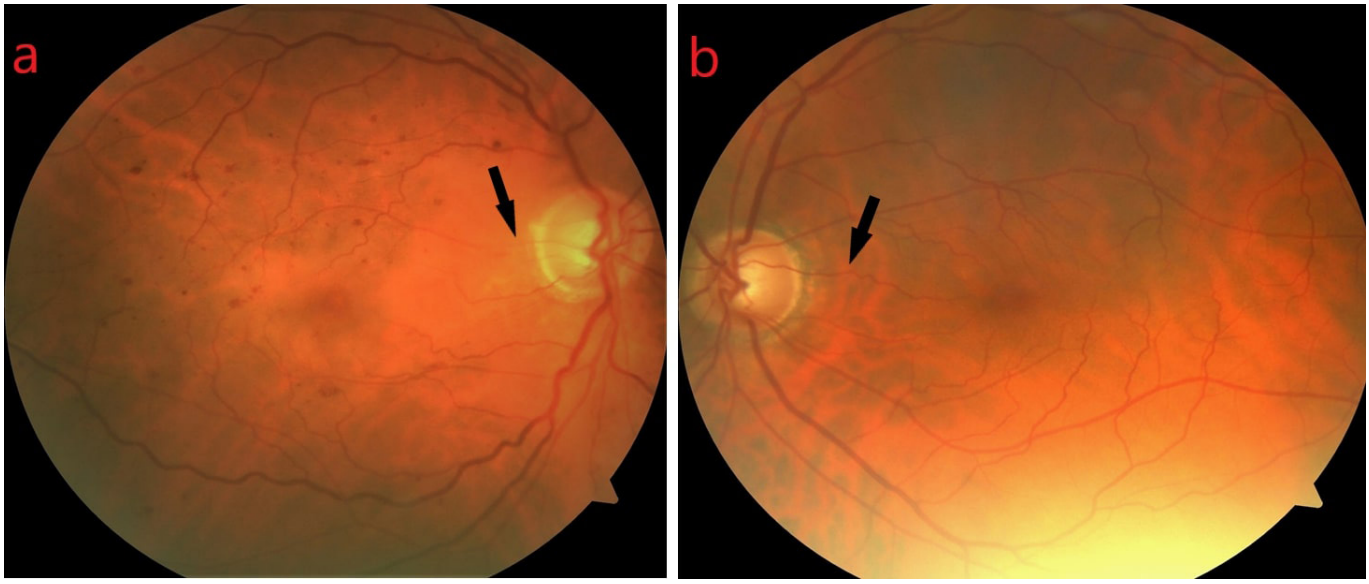

Figure 1: a) *On color fundus image of right eye, there was retinal whitening at papillomacular bundle and central fovea which corresponded to cilioretinal artery trace, thinning of cilioretinal artery, increased venous tortuosity and small intraretinal hemorrhage at posterior pole;* **b)** *Color fundus image of left eye was normal.*

at inner nuclear layer (Figure 2a and 2b). The patient underwent fundus fluorescein angiography with initial diagnosis of CAO together with baseline CRVO and it was found that, although there was no permanent occlusion in the blood flow of cilioretinal artery, the cilioretinal artery filling was associated with pulsation and there was no hyper-fluorescence at macula in the right eye; the left eye was normal (Figure 3a and 3b). Thus, it was seen that subfoveal and intraretinal fluid was resolved in control OCT scan on the same day (Figure 4). On OCT angiography, there was perivenular fern appearance at deep capillary plexus (Figure 5). Complete blood count, biochemistry, ESR and CRP tests were normal in the patient; a plaque (11x2.5 mm in size) was detected at right carotid bifurcation on carotid artery Doppler sonography. The patient was prescribed anticoagulant therapy. On month 4, it was found that BCVA was finger count at 2 meters in the right eye with marked regression in the fundus findings. On OCT, there was retinal thinning at inner segments and derangement and thinning at inner nuclear layer corresponding to PAOM (Figure 6a and 6b). The patients is still attending control visits.

DISCUSSION

Although it has been initially thought that COVID-19 disease causes mortality due to severe pneumonia, many subsequent case reports and studies have shown that it leads thrombosis in both venous and arterial system and resultant multi-organ failure by causing a hyper-inflammatory state.[2,3] In post-mortem analysis, it was shown that endothelial cells were directly infected with virus and that diffuse endothelial inflammation led endothelial dysfunction and procoagulant state.[14,15] The prolonged prothrombin time, elevated D-dimer levels and increased level of pro-inflammatory cytokines demonstrated in COVID-19 patients, are considered as most possible cause of disseminated intravascular coagulation and thrombotic microangiopathy. Although venous thromboembolism is predominant in the majority of reported cases, there is a rapid increase in the arterial thromboembolic complications due to COVID-19.[2-5]

Here, we reported a case who developed CAO following COVID-19 infection. Cilioretinal artery may account for both blood supply of all fovea and part of fovea; in addition, it may supply retinal arteries other than fovea. Although CAO is a rare entity, it may manifest in 3 distinct pattern: isolated, in combination with CRVO and in combination with ischemic optic neuropathy. In a study by Brown et al., [6] it was reported that the incidences of isolated and CAO plus CRVT were comparable but the incidence of CAO plus ischemic optic neuropathy was lower. Arteriosclerosis of carotid artery is the most common cause of CAO. In CAO in association with CRVT, it is thought that the increased intraluminal pressure at retinal capillaries caused by acute occlusion of central retinal vein is extremely high for cilioretinal artery, leading hemodynamic blockade of cilioretinal artery.[8]

Central retinal artery and cilioretinal artery originate

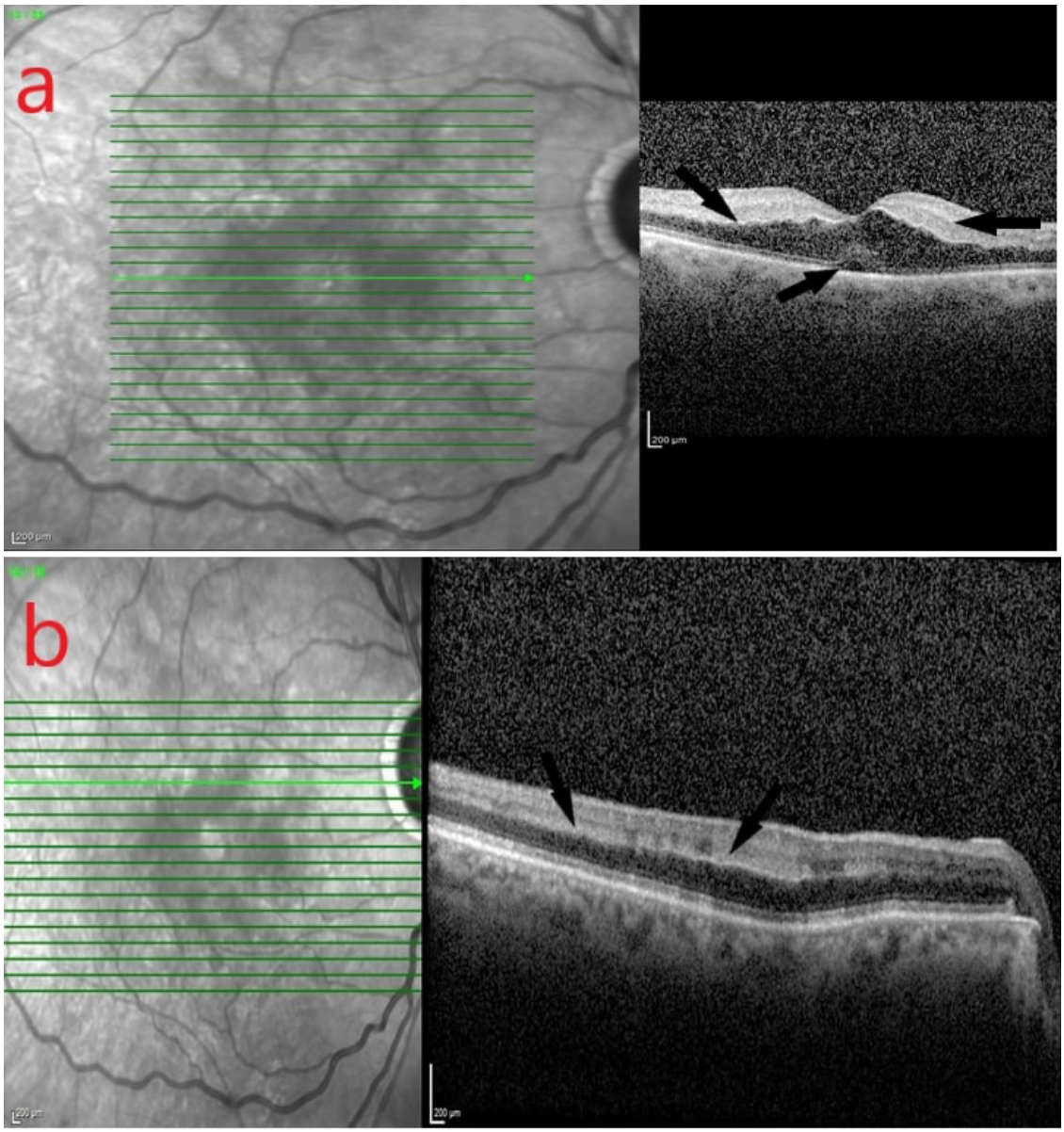

Figure 2: *a) On OCT image of right eye, there was increased hyper-reflectivity at inner central retinal segments and hyper-reflective line at inner segment of outer plexiform layer [marked middle limiting membrane (MLM) appearance] as well as increased subfoveal and intraretinal fluid. All three findings are marked in the areas shown by black arrows; b) hyper-reflective band appearance of PAOM at parafoveal area which showed skipping pattern at inner nuclear layer (black arrows).*

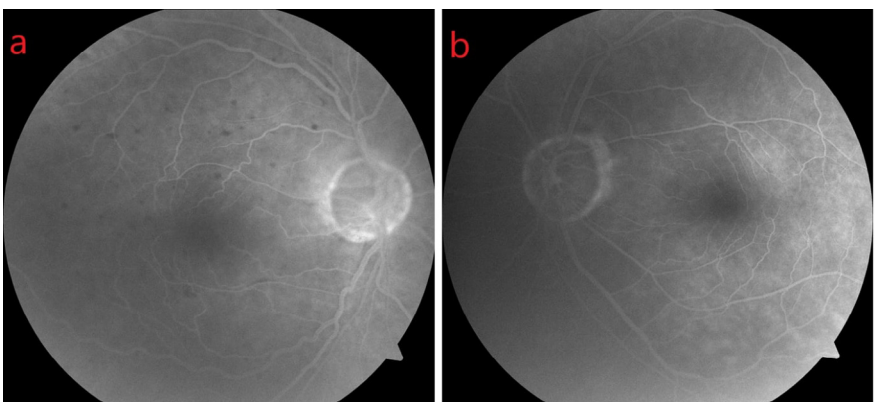

Figure 3: *On fundus fluorescein angiography* **(a)** *right cilioretinal artery was stained;* **(b)** *thinned when compared to left cilioretinal artery.*

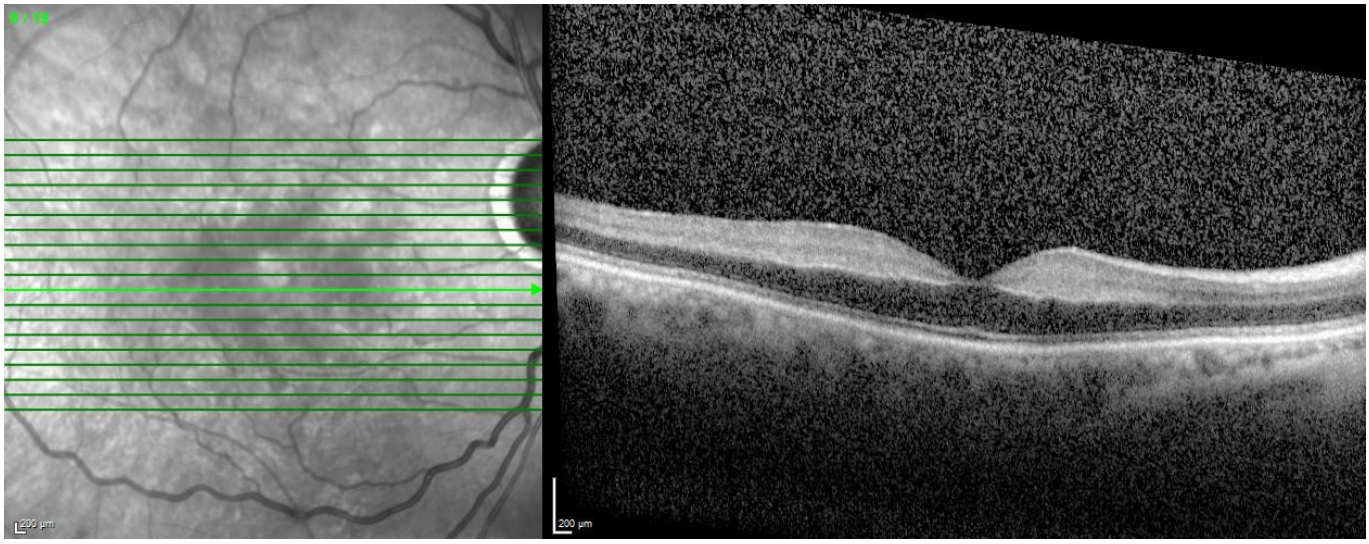

Figure 4: *subfoveal and intraretinal fluid was resolved in control OCT scan on the next day.*

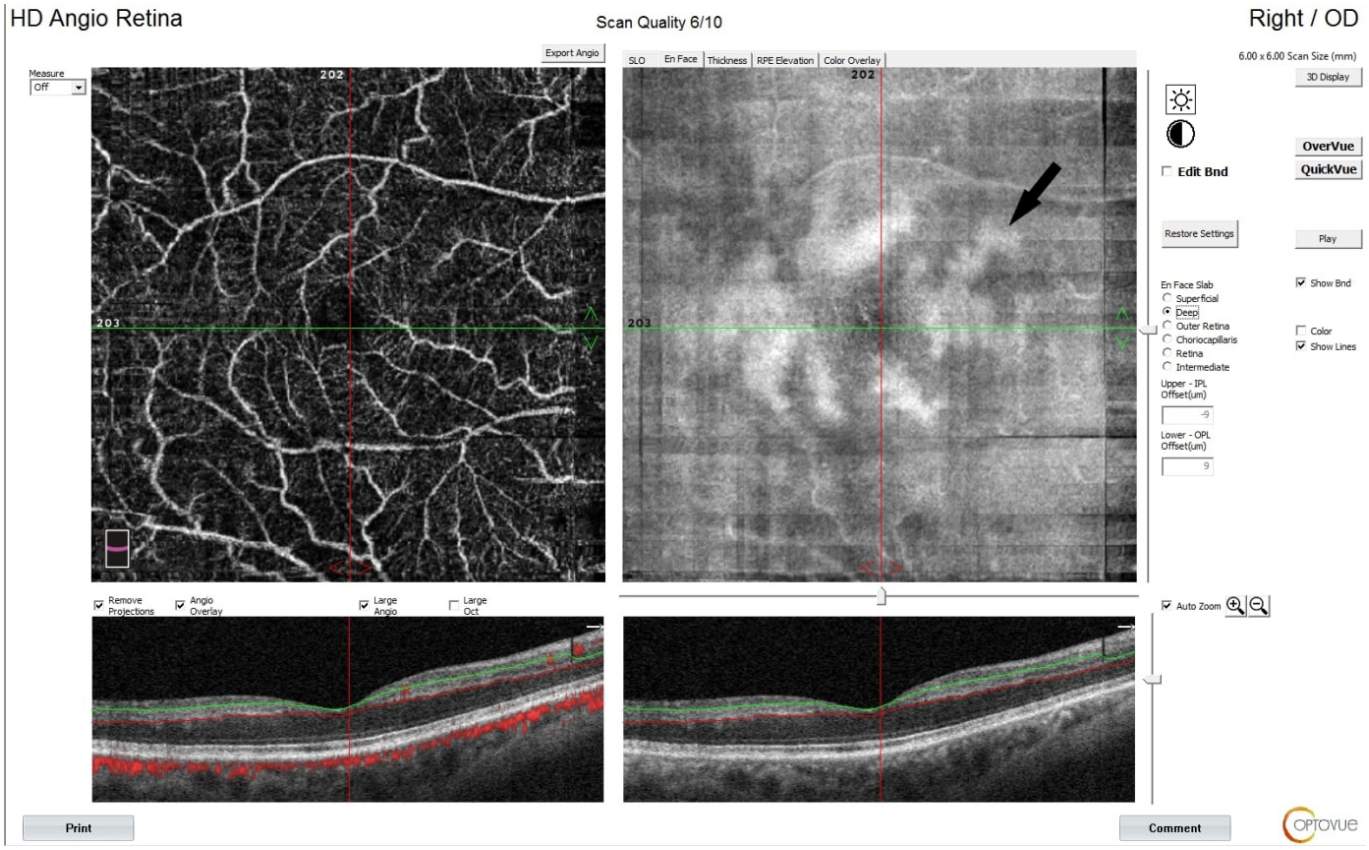

Figure 5: *On en face OCT angiography, there was perivenular fern-like appearance at deep capillary plexus (black arrow)*

from two distinct arterial system which have different physiological characteristics. Central retinal artery directly originates from ophthalmic artery and has an effective auto-regulation; thus, the decreased perfusion pressure in the retinal artery due to increased retinal venous pressure can be compensated by auto-regulation. On the other hand, cilioretinal originates from choroid artery; thus, two distinct mechanisms can impair cilioretinal artery mechanism in eyes with CRVO: lack of auto-regulation in choroidal vascularity and absence of obstruction in vortex veins. Thus, acute occlusion of central retinal vein leads decreased blood flow in cilioretinal artery due to lack of auto-regulation. Moreover, previous studies have shown that perfusion pressure of choroidal vascularity is normally lower than central retinal artery.[16]

Although there was no clinical manifestation of CRVO

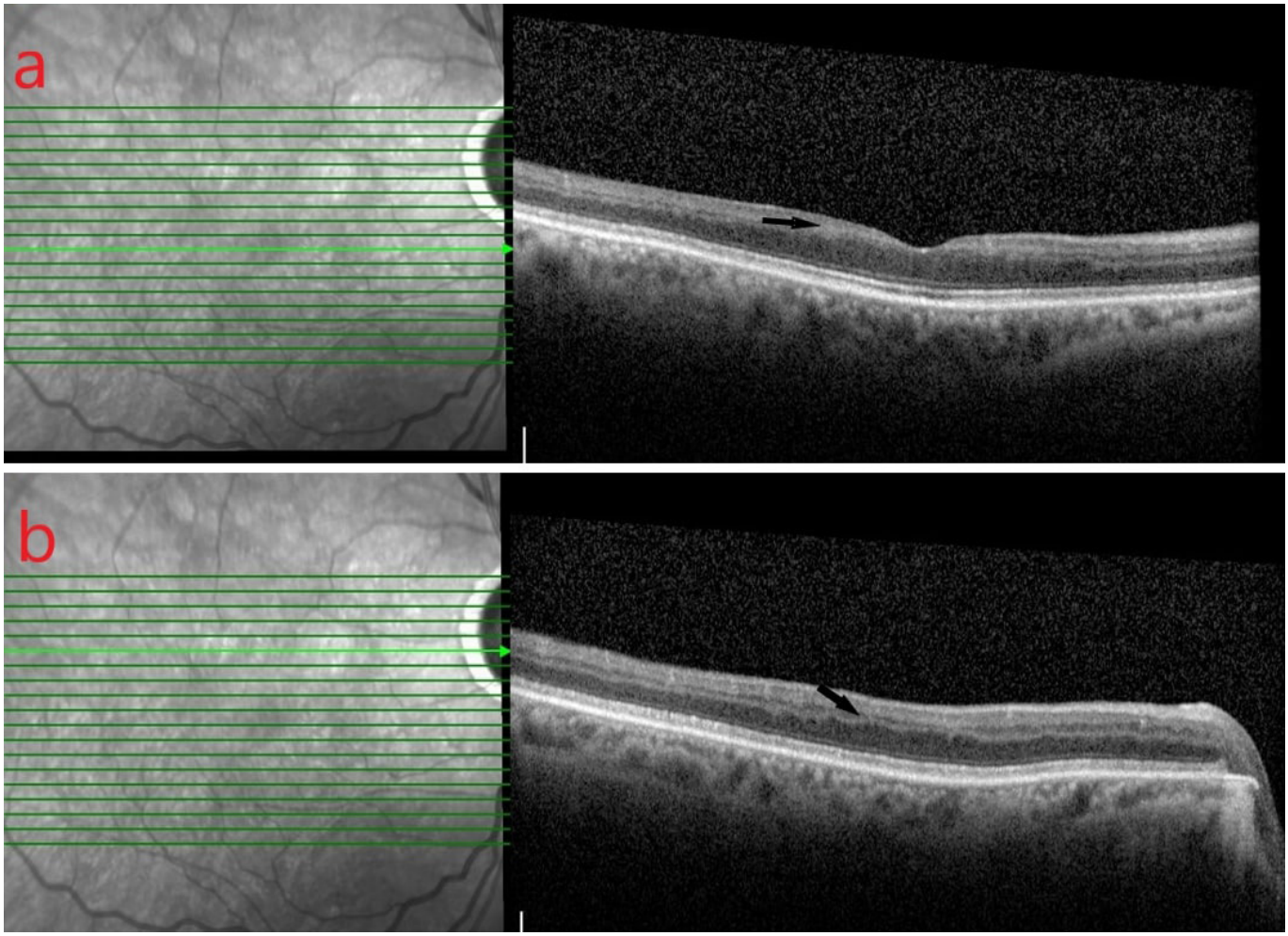

Figure 6: a) *On OCT image of right eye on month 4, marked OLM appearance disappeared and there was retinal thinning at inner segments (black arrow); derangement and thinning at inner nuclear layer corresponding to PAOM* **b)** *derangement and thinning at inner nuclear layer compatible with PAOM on parafoveal OCT image (black arrow).*

in our case, there were findings of venous stasis such as increased tortuosity in retinal veins and small intraretinal hemorrhage at posterior pole. Subretinal and intraretinal fluids detected on initial OCT were regressed on the next day and it was seen that the clinical presentation did not progress towards CRVO during follow-up. In the literature, there are varying definitions for retinal venous alterations seen without presence of fully CRVO. Hayreh et al.[17] defined the condition as venous stasis retinopathy while Gass et al.[18] defined as impending-CRVO. According to definition by Gass et al., the loss of vision in impending-CAO is smaller and fundus findings include venous dilatation and retinal hemorrhages alone. However, authors emphasized that impending-CRVO should be considered as risk factor for development of CRVO. Bottos et al. [19] defined a case with CAO in association with findings of venous stasis and reported that the findings of venous stasis regressed within one week and that vision was improved up to 10/10.In our case, procoagulant stated induced by previous COVID-19 might have led retinal venous stasis, which, in turn, caused increased pressure and cilioretinal artery occlusion. The greater extent of the area supplied by cilioretinal artery might be the reason for poor vision as similar to that resulted from central retinal artery occlusion.

PAOM is a novel finding of acute retinal ischemia which is diagnosed by the presence of hyper-reflective band appearance in middle retinal layers, particularly in inner nuclear layer, and is considered to develop due to deep capillary ischemia.[7] It has been reported that PAOM is associated with conditions which affect retinal micro-circulation such as retinal artery and vein occlusions, cilioretinal artery occlusion, diabetic retinopathy, hypertensive retinopathy, Purtcher's retinopathy and sickle cell retinopathy.[11-13] It is characterized by areas of hypo-perfusion in deep capillary plexus on OCT-angiography.[20] On En-face OCT images, 3 patterns have been identified for PAOM: arteriolar, globular and fern-like (perivenular)

appearance.[21] Again, a marked OLM finding has been recently defined as a marker of acute retinal ischemic injury, which is observed as a hyper-reflective line at synaptic segment of outer plexiform layer on OCT.[22,23] Although it was reported that it can be seen during acute phase in retinal artery occlusion, it commonly accompany retinal vein occlusions. The marked OLM is not a true membrane and develops due to cytoplasmic swelling caused by ischemia of bipolar cells.

Here, a case with CAO developed following COVID-19 infection is reported with retinal ischemia findings on OCT for the first time. In our case, presence of ipsilateral carotid plaque suggest that CAO might be developed due to embolism resulting from the carotid plaque. In addition, history of COVID-19 infection requiring intensive care, no history of anticoagulant use and retinal venous stasis findings suggest an underlying hyper-coagulant state.

In conclusion, it should be outlined that there is a correlation between retinal vascular occlusions and COVID-19 infection although no definitive association could be demonstrated. It should be kept in mind that inflammatory and procoagulant states secondary to COVID-19 may be a trigger for retinal vascular occlusion.

REFERENCES

1. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. J Med Virol. 2020;92:401-2.
2. Levi M, Thachil J, Iba T, et al. Coagulation abnormalities and thrombosis in patients with COVID-19. Lancet Haematol. 2020;7:438-40.
3. Levolger S, Bokkers RPH, Wille J, et al. Arterial thrombotic complications in COVID-19 patients. J Vasc Surg Cases Innov Tech. 2020;6:454-9.
4. Montesel A, Bucolo C, Mouvet V, et al. Case Report: Central retinal artery occlusion in a COVID-19 patient. Front Pharmacol. 2020 Dec 23;11:588384.
5. Gaba WH, Ahmed D, Al Nuaimi RK, et al. Bilateral central retinal vein occlusion in a 40-year-old man with severe coronavirus disease 2019 (COVID-19) pneumonia. Am J Case Rep. 2020 Oct 29;21:e927691.
6. Brown GC, Moffat K, Cruess A, et al. Cilioretinal artery obstruction. Retina. 1983;3:182-7.
7. Stoffelns BM, Laspas P. Cilioretinal artery occlusion. Klin Monatsbl Augenheilkd 2015; 232: 519-24.
8. Hayreh SS, Fraterrigo L, Jonas J. Central retinal vein occlusion associated with cilioretinal artery occlusion. Retina. 2008;28:581-94.
9. Kızıltoprak H, Özateş S, Teke MY, ve ark. Kombine santral retinal ven tıkanıklığı ve silyoretinal arter tıkanıklığı. Retina-Vitreus. 2018;27:94-97.
10. Sarraf D, Rahimy E, Fawzi AA, et al. Paracentral acute middle maculopathy: a new variant of acute macular neuroretinopathy associated with retinal capillary ischemia. JAMA Ophthalmol. 2013;131:1275-87.
11. Bakhoum MF, Freund KB, Dolz-Marco R, et al. Paracentral acute middle maculopathy and the ischemic cascade associated with retinal vascular occlusion. Am J Ophthalmol. 2018;195:143-53.
12. Pichi F, Fragiotta S, Freund KB, et al. Cilioretinal artery hypoperfusion and its association with paracentral acute middle maculopathy. Br J Ophthalmol. 2019;103:1137-45.
13. Chen X, Rahimy E, Sergott RC, et al. Spectrum of retinal vascular diseases associated with paracentral acute middle maculopathy. Am J Ophthalmol. 2015;160:26-34.
14. Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. Lancet. 2020;395:1417-8.
15. Yılmaz H, Topçuoğlu P. COVID-19 ilişkili koagülopati ve yönetimi. Türkiye'de Lösemi Lenfoma Miyelom Araştırmaları. 2020;4:55-60.
16. Blumenthal M, Best M, Galin M, et al. Ocular circulation: analysis of the effect of induced ocular hypertension on retinal and choroidal blood flow in man. Am J Ophthalmol. 1966;75:806-7.
17. Hayreh SS. So-called 'central retinal vein occlusion'. II. Venous stasis retinopathy. Ophthalmologica. 1976;172:14-37.
18. Gass JD. Stereoscopic atlas of macular disease: diagnosis and treatment. 4th ed. St Louis: Mosby; 1997. 546-55
19. Bottós JM, Aggio FB, Dib E, et al. Impending central retinal vein occlusion associated with cilioretinal artery obstruction. Clin Ophthalmol. 2008;2:665-8.
20. Nemiroff J, Kuehlewein L, Rahimy E, et al. Assessing deep retinal capillary ischemia in paracentral acute middle maculopathy by optical coherence tomography angiography. Am J Ophthalmol. 2016;162:121-32.
21. Sridhar J, Shahlaee A, Rahimy E, et al. Optical coherence tomography angiography and en face optical coherence tomography features of paracentral acute middle maculopathy. Am J Ophthalmol. 2015;160:1259-68.
22. Chu YK, Hong YT, Byeon SH, et al. Invivo detection of acute ischemic damages in retinal arterial occlusion with optical coherence tomography: a “prominent middle limiting membrane sign”. Retina. 2013;33:2110-7.
23. Ko J, Kwon OW, Byeon SH. Optical coherence tomography predicts visual outcome in acute central retinal vein occlusion. Retina. 2014;34:1132-41.