

# COVID-19 Associated Cilioretinal Artery Occlusion

## COVID-19 İlişkili Silioretinal Arter Tıkanıklığı

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**ABSTRACT** A 49-years old woman patient presented with acute central loss of vision, with the diagnosis of cilioretinal artery occlusion was hospitalized. She had a history of close contact with a coronavirus disease-2019 (COVID-19) patient and her polymerase chain reaction test was positive. Topical and systemic treatments were used to reduce intraocular pressure. In addition, anticoagulant treatment was applied. After excluding other prothrombotic etiologic factors, the patient was diagnosed with cilioretinal occlusion with associated COVID-19. Thromboembolic complications associated with COVID-19 have a high incidence and may affect the retinal vascular structure. We described a case of cilioretinal artery occlusion associated with COVID-19 infection. We might suggest a pharmaceutical prophylaxis for COVID-19 associated ocular vascular thromboembolic complications not only in symptomatic patients but also in asymptomatic patients. We hope that this case report will contribute to a different perspective on thrombophilia and related conditions in COVID-19.

**Keywords:** COVID-19; retinal artery occlusion; thromboembolism

**ÖZET** Kliniğimize, akut santral görme kaybı ile başvuran 49 yaşındaki kadın hasta, silioretinal arter tıkanıklığı tanısı konularak hastaneye yatırıldı. Bir koronavirüs hastalığı-2019 [coronavirus disease-2019 (COVID-19)] hastasıyla yakın temas öyküsü vardı ve polimeraz zincir reaksiyonu testi pozitif. Göz içi basıncını düşürmek için topikal ve sistemik tedaviler kullanıldı. Ayrıca sistemik olarak antikoagülan tedavi uygulandı. Diğer protrombotik etiyolojik faktörler dışlandıktan sonra hastaya COVID-19 ile ilişkili silioretinal oklüzyon tanısı konuldu. COVID-19 ile ilişkili tromboembolik komplikasyonların insidansı yüksektir ve retinal vasküler yapıyı etkileyebilir. COVID-19 enfeksiyonu ile ilişkili bir silioretinal arter tıkanıklığı vakasını tanımladık. Sadece semptomatik hastalarda değil, asemptomatik COVID-19 geçiren olgular için de farmakolojik profilaksi gibi bir yaklaşımı önerebiliriz. Bu olgu sunumunun, COVID-19'daki trombofil ve ilişkili durumlara farklı bir bakış açısına katkıda bulunacağını umuyoruz.

**Anahtar Kelimeler:** COVID-19; retinal arter tıkanıklığı; tromboembolizm

Coronavirus disease-2019 (COVID-19) was first recognized and reported in China in January 2020 that causes severe acute respiratory syndrome-coronavirus-2.<sup>1</sup> This infection presents with different clinical presentations, typically affecting respiratory tracts; however, recent reports also showed other systems manifestations (nervous, digestive and cardiovascular systems).<sup>2,3</sup> This novel viral disease is now well described as a prothrombotic disease too.<sup>2</sup> These mechanisms lead to thromboembolic events and include multiple processes including coagulation and fibrinolytic network, platelets, endothelial cells and

inflammatory cells. But the specific mechanism(s) has not been fully dissolved.

In the literature, ophthalmic pathologies associated with COVID-19 have been reported.<sup>4</sup> Ozsaygılı et al. previously reported a case who developed cilioretinal artery occlusion 2 weeks after asymptomatic COVID-19 infection.<sup>5</sup> However, best of our knowledge, there is no isolated case of cilioretinal artery occlusion during the course of asymptomatic COVID-19 infection in the literature. Therefore, we are reporting a case of a cilioretinal artery occlusion in an asymptomatic COVID-19 patient.

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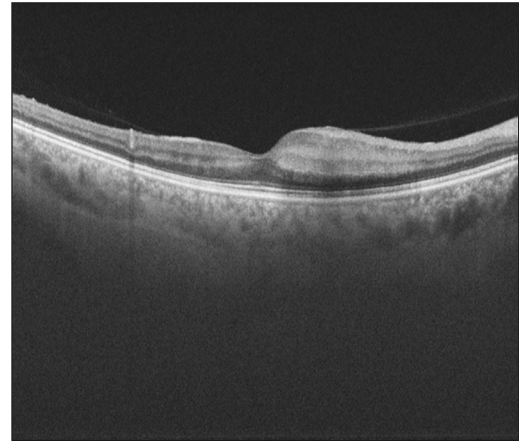


## CASE REPORT

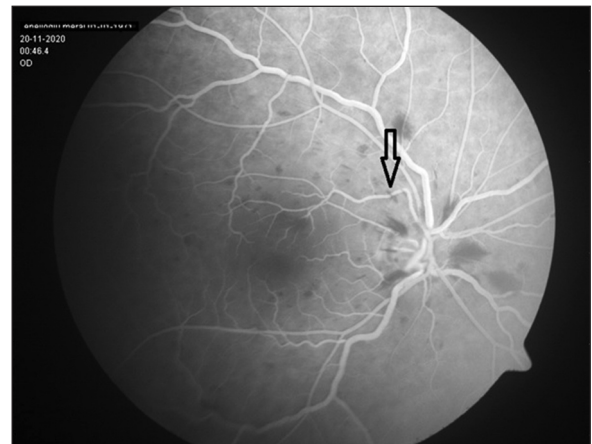
In November 2020, a 49-year-old female patient presented at the ophthalmology department of Selçuk University Medical Faculty Hospital complaining of acute central visual loss in the right eye. She did not have any systemic disease such as diabetes mellitus or hypertension, and she didn't smoke. Also, there was no history of oral contraceptive pill use. After the case was informed about the study written informed consent form was obtained. Our case report was approved by COVID-19 Scientific Research Evaluation Commission of the Ministry of Health with reference number 2022-04-19T10\_56\_09. Visual examination of both eyes showed visual acuity was 10/10 with the Snellen chart. Intraocular pressure was 18 mmHg in right eye and 16 mmHg in left eye. In the detailed biomicroscopic examination, no pathological findings were detected in both eyes. However, in the funduscopy examination, macular paleness, cherry-red spot on the macula, enlarged veins with some hemorrhagic spots were observed in the right eye (Figure 1). Optical coherence tomography showed increase in thickness and hyper-reflectivity of the inner retinal layers in the affected area with intracellular edema in the right eye (Figure 2). In the right eye, delayed filling of the cilioretinal artery was detected on fluorescein angiography (Figure 3). In addition, fluorescein angiography examination revealed dilatation of the veins and mild diffuse retinal hemorrhages in four quadrants of the retina. It was



**FIGURE 1:** The color fundus photography of the right eye shows the cherry-red spot on the macula, swollen veins and multiple hemorrhagic spots.



**FIGURE 2:** Optical coherence tomography of the right eye showed increase in thickness and hyper-reflectivity of the inner retinal layers in the affected area with intracellular edema.



**FIGURE 3:** Fluorescein angiography shows delayed filling of the cilioretinal artery in the right eye.

observed that there was hypofluorescence consistent with these areas in the form of a patch accompanied by retinal hemorrhage. Findings in fluorescein angiography were consistent with impending retinal vein occlusion.

The patient was diagnosed with cilioretinal artery occlusion in the right eye and was hospitalized. Treatment with topical and systemic therapy (brimonidine timolol combination eye drop, intravenous 300 mL mannitol) was initiated to reduce intraocular pressure. Also, ocular massage was described and practiced. She was referred to the hyperbaric oxygen therapy center. In her detailed anamnesis, it was learned that her husband was hospitalized with the diagnosis of COVID-19 three days ago. She was

asymptomatic, had no fever, shortness of breath. Nasopharyngeal swab sample was tested using polymerase chain reaction and was positive for COVID-19. The patient was checked for rheumatologic, cardiologic diseases and other systemic examinations that can cause artery occlusion. Routine laboratory examinations (complete blood count, lipid profile, renal and hepatic function test) were within the normal range (Table 1). The workup for thrombophilia (prothrombin time, activated thromboplastin time, antiphospholipid antibodies, and serum protein for coagulopathies), carotid Doppler ultrasonography, and echocardiography were normal. There was not an abnormality on the chest X-ray. She was treated with hyperbaric oxygen therapy (2.5 atm and 2 hours daily; total 40 hours) and also given favipiravir and enoxaparin 4.000 IU for 10 days.

In a final follow-up after 2 weeks, visual acuity was 10/10 and perimetry showed arcuate defect in 10-2 central visual field test. (Figure 4). Blood parameters were normal. After 2 months prothrombin G20210A, factor V leiden G1691A, MTHFR C 677T

couldn't be detected by the genetic tests. But MTHFR A1298C heterozygous polymorphism was detected.

## DISCUSSION

Cilioretinal arteries arise from the short posterior ciliary arteries and can be found in about 32% of eyes.<sup>6</sup> There are great variations in the size, number, and distribution of cilioretinal vessels.<sup>6</sup> In cases of central retinal artery occlusion, the presence of an additional cilioretinal blood supply to the macula can help to preserve central vision. Occasionally in these patients, the cilioretinal artery can be obstructed. These situations are the only 5% percentage of all retinal artery occlusions. There are numerous risk factors for this, such as hypercoagulopathy by increasing hyper-inflammatory response.<sup>7</sup> And novel COVID-19 is added to these etiologic causes list. So there is an important issue to use an anti-thrombotic agent for COVID-19 diagnosed patients who have elevated inflammatory markers.

The International Society on Thrombosis and Hemostasis recommends regular monitoring of D-dimer, prothrombin time, platelet, and fibrinogen levels.<sup>8</sup> Prophylactic doses of low-molecular-weight heparin (LMWHs) are recommended unless there is active bleeding or a very low platelet count ( $25 \times 10^9/L$ ).<sup>9</sup> Elevated D-dimer levels are associated, although not specifically, with mortality in patients. The biological half-life of LMWHs is much longer and LMWHs have fewer side effects. These agents also exhibit anti-inflammatory effects unlike unfractionated heparin and can downregulate inflammatory cytokines.<sup>2</sup> In our case, enoxaparin 4000 IU treatment was given for 10 days since there were no contraindications. The COVID trial is being planned to study whether prophylactic-dose enoxaparin may reduce early all cause mortality and hospitalizations in adult symptomatic ambulatory patients aged 50 or older diagnosed COVID-19.<sup>10</sup>

In the case reported by Ozsaygılı et al., they reported cilioretinal artery occlusion that developed after symptomatic COVID infection 2 weeks ago.<sup>5</sup> During active COVID infection, this patient did not receive anticoagulant prophylaxis treatment. In line with these data, it is seen that post-COVID hyperco-

**TABLE 1:** Blood test results of the patient.

TEST	Patient's value	Normal range
Sedimentation	3 mm/hour	-
CRP	1.99 mg/L	0-8
RF	<20 iu/mL	0-20
ANA	Negative	-
p-ANCA	Negative	-
c-ANCA	Negative	-
Urea	22 mg/dL	17-43 mg/dL
Creatinine	0,71 mg/dL	0,51-0,95 mg/dL
ALT	29 u/L	0-35
AST	21 u/L	0-35
LDH	231 u/L	126-222 U/L
Fibrinogen	403 mg/dL	200-400 mg/dL
D-dimer	263 ng/mL	0-500 ng/mL
PT	12 sec	9.2-14.0 SEC
APTT	29 sec	26-40 SEC
Protein C	82	70-140%
Protein S	74.8%	54.7-123.7%
Antitrombin 3	94%	80-130%
Anticardiolipin	Negative	-
Anticardiolipin IgG	Negative	-

CRP: C-reactive protein; RF: Rheumatoid factor; ANA: Antinuclear antibody; ANCA: Antineutrophil cytoplasmic antibodies; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; LDH: Lactate dehydrogenase; PT: Prothrombin time; APTT: Activated partial thromboplastin time.

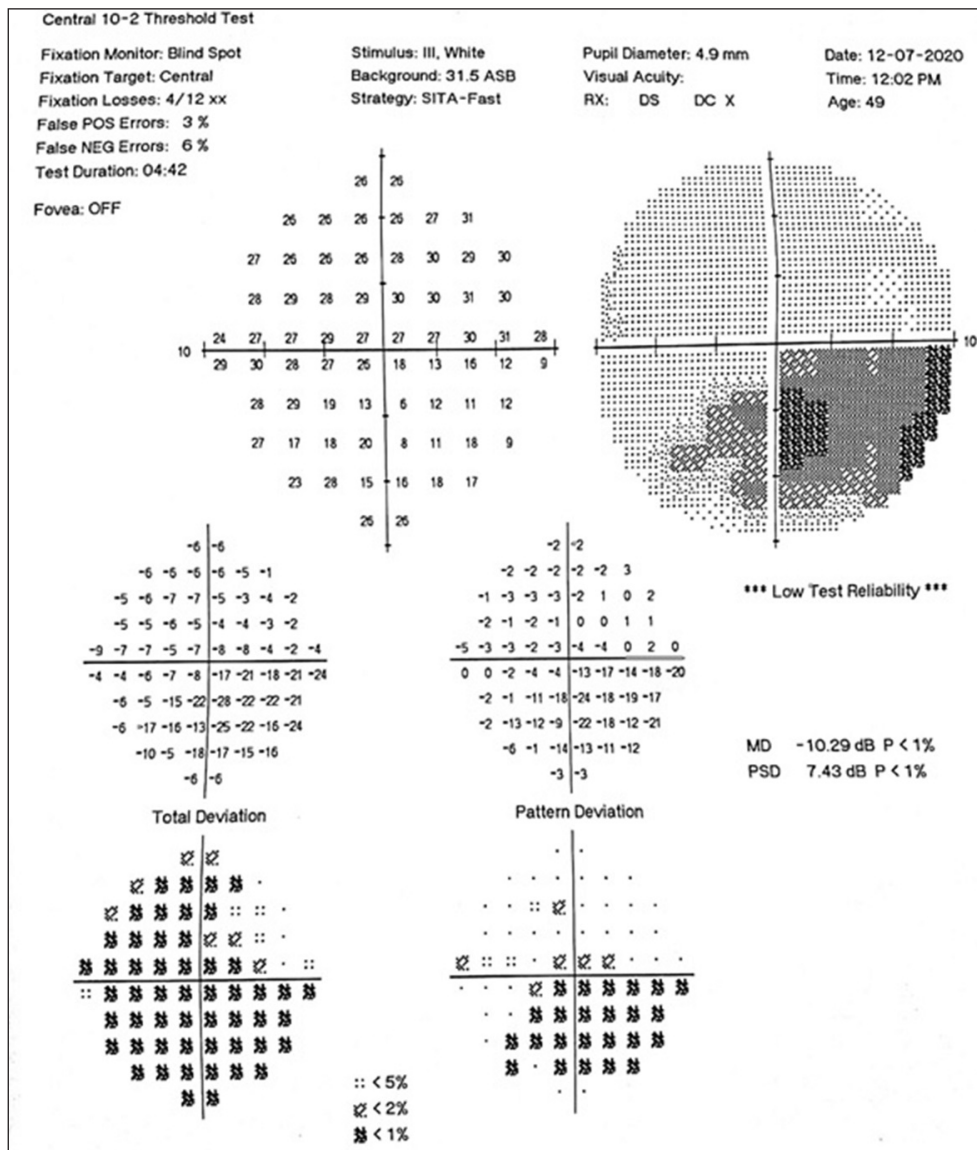


FIGURE 4: In a final follow-up after two weeks, central 10-2 central field test showed the arcuate defect.

agulation may occur even after a period of active infection. Especially risky cases should be reviewed in terms of anticoagulant therapy.

In our case, we detected MTHFR A1298C heterozygous polymorphism. High homocysteine levels are a common feature in thrombotic diseases. Zetterberg et al, in their study, explored the possible associations between the MTHFR A1298C and TC C776G genetic polymorphisms, hyperhomocysteinemia and arterial and venous thrombosis.<sup>11</sup> Neither the MTHFR A1298C nor the TC C776G polymorphism was not found to be a significant determinant of hy-

perhomocysteinemia, nor were they associated with increased risk for thrombosis. Also, Hotoleanu et al found the MTHFR A1298C polymorphism is not significantly associated with an increased risk of venous thromboembolism.<sup>12</sup>

From a public health perspective, it would be beneficial to have a COVID-19 strategy not only in epidemiology and immunology but also in the treatment of subsequent coagulopathy. COVID-19 is associated with hypercoagulability. Initial data point to high rates of thromboembolism in patients without pharmacological thrombosis prophylaxis. Most evi-

dence is limited to small retrospective studies, and an assessment of the true prevalence of thrombosis in COVID-19 in larger or even prospective studies will yield clearer results. We hope that this case report contributes to looking from different angle about thrombophilia and related situations in COVID-19.

Finally, we have to research more about thrombophilia association with COVID-19 and develop a strategy for thrombophilia complications, after that according to the further study we may suggest a prophylactic approach such as some special drugs, pre-medication or pharmatherapeutical prophylaxis for COVID-19 not only in symptomatic patients but also in asymptomatic patients.

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### Conflict of Interest

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

### Authorship Contributions

**Idea/Concept:** Sona Gorchuyeva, Semih Çakmak, Mustafa Tuğrul Uğur, Yalçın Karaküçük; **Design:** Sona Gorchuyeva, Semih Çakmak, Mustafa Tuğrul Uğur; **Control/Supervision:** Semih Çakmak, Yalçın Karaküçük; **Data Collection and/or Processing:** Sona Gorchuyeva, Semih Çakmak; **Analysis and/or Interpretation:** Sona Gorchuyeva, Semih Çakmak, Mustafa Tuğrul Uğur, Yalçın Karaküçük; **Literature Review:** Sona Gorchuyeva, Mustafa Tuğrul Uğur; **Writing the Article:** Sona Gorchuyeva, Semih Çakmak, Mustafa Tuğrul Uğur, Yalçın Karaküçük; **Critical Review:** Sona Gorchuyeva, Semih Çakmak, Mustafa Tuğrul Uğur, Yalçın Karaküçük; **References and Fundings:** Sona Gorchuyeva, Mustafa Tuğrul Uğur, Yalçın Karaküçük; **Materials:** Sona Gorchuyeva, Mustafa Tuğrul Uğur, Yalçın Karaküçük.

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