Retinal arterial macroaneurysms in patients recovered from COVID-19

Macroaneurismas arteriais retinianos em pacientes recuperados da COVID-19

Epitácio Dias da Silva Neto[1], Taurino dos Santos Rodrigues Neto[1], Lívia da Silva Conci[1], Rony Preti[1], Mário Luiz Ribeiro Monteiro[1], Leandro Cabral Zacharias[1]

[1] Department of Ophthalmology, Universidade de São Paulo, São Paulo, SP, Brazil.

How to cite:
Silva Neto ED, Rodrigues Neto TS, Conci LS, Preti R, Monteiro ML, Zacharias LC. Retinal arterial macroaneurysms in patients recovered from COVID-19. Rev Bras Oftalmol. 2023;82;e0034.

doi:
https://doi.org/10.37039/1982.8551.20230034

Keywords:
Anatomy; Biochemistry; Physiology; Microbiology; Retinal arterial macroaneurysm; COVID-19; Coronavirus infections

Descritores:
Anatomia; Bioquímica; Fisiologia; Microbiologia; Macroaneurisma arterial retiniano; COVID-19; Infecções por coronavirus

Received on:
July 18, 2022

Accepted on:
Apr 4, 2023

Corresponding author:
Lívia da Silva Conci
Avenida Dr. Enéas de Carvalho Aguiar, 255 – Cerqueira César
CEP: 05403000 – São Paulo, SP, Brasil
E-mail: livia.conci@gmail.com

Institution:
Department of Ophthalmology, Universidade de São Paulo, São Paulo, SP, Brazil.

Conflict of interest:
the authors declare no conflict of interest.

Financial support:
the authors received no financial support for this work.

ABSTRACT

This is a case series about retinal arterial macroaneurysms in three patients recovered from COVID-19. None of them had previous past ocular and systemic history. The first patient was a 47-year-old man, with best-corrected visual acuity of 20/20 in both eyes. He presented a cotton wool spot in the right eye and two peripheral exudative retinal arterial macroaneurysms in the left eye. Laser photocoagulation was performed and best-corrected visual acuity remained stable. The second one was a 62-year-old-woman with acute visual loss in the right eye (best-corrected visual acuity of 20/400). There was vitreous hemorrhage and a peripheral retinal arterial macroaneurysm in the right eye. Laser photocoagulation was performed and best-corrected visual acuity improved to 20/20. The third patient was a 54-year-old woman, with best-corrected visual acuity of 20/20 in the right eye and 20/600 in the left eye. Fundus examination showed multiple layer hemorrhage in the macular region and retinal arterial macroaneurysms in the superior temporal branch. The cases underwent fluorescein angiography, which confirmed the diagnosis of retinal arterial macroaneurysms.

RESUMO

Esta é uma série de casos sobre macroaneurismas arteriais da retina em três pacientes recuperados da COVID-19. Nenhum tinha história ocular e sistêmica prévias. O primeiro era um homem de 47 anos, com melhor acuidade visual corrigida de 20/20 em ambos os olhos. Apresentava mancha algodonosa em olho direito e dois macroaneurismas arteriais da retina exsudativos periféricos em olho esquerdo. Foi realizada fotocoagulação a *laser*, e a melhor acuidade visual corrigida permaneceu estável. A segunda era uma mulher de 62 anos com perda visual aguda em olho direito (melhor acuidade visual corrigida de 20/400). Havia hemorragia vítrea e um macroaneurisma periférico em olho direito. O *laser* foi realizado, e a melhor acuidade visual corrigida melhorou para 20/20. A terceira paciente era uma mulher de 54 anos, com melhor acuidade visual corrigida 20/20 em olho direito e 20/600 olho esquerdo. A fundoscopia mostrou hemorragia em múltiplas camadas na região macular e um macroaneurisma arterial da retina no ramo temporal superior. Os casos foram submetidos à angiofluoresceinografia, que confirmou o diagnóstico de macroaneurismas arteriais da retina.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an entity caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection that predominantly affects the respiratory system. The severe infection leads to an excessive host inflammatory reaction, responsible for a hypercoagulable state and serious cardiopulmonary manifestations, such as acute respiratory distress syndrome.[1] Furthermore, endothelial cell involvement has been shown in several organs (e.g., lung, heart, kidney, intestine, and brain), with histopathological evidence of endotheliitis and vasculitis.[2]

There is an increasing number of articles on ophthalmic disorders in the COVID-19 pandemic. An update showed that most COVID-19 ophthalmic manifestations are related to anterior segment, including conjunctivitis, conjunctival hyperemia and chemosis.[3] Nevertheless, SARS-CoV-2 RNA has been detected in retina and optic nerve biopsies of affected patients.[4] Some publications provide evidence of retinal microangiopathy by analyzing optic coherence tomography angiography (OCTA) images.[5] Cotton wool spots, hemorrhages, vascular occlusions, paracentral acute middle maculopathy (PAMM), neuroretinopathy, and panuveitis are some of the previously reported posterior segment findings.[3]

It is well known that retinal arterial macroaneurysm (RAM) is an acquired vascular disorder and the most common risk factors for its development are hypertension, female sex, and older age.[6] In this report, we describe three cases of healthy patients presenting RAM after recovery from COVID-19.

This study was approved by the Hospital das Clínicas of the Medical School of the University of São Paulo, opinion no. 4.834.601, CAAE: 47157821.0.0000.0068.

CASE 1

A 47-year-old Brazilian man, asymptomatic, came for a routine ophthalmic evaluation. He had had a mild form of COVID-19 one month before. He denied any history of systemic or ocular diseases. His best-corrected visual acuity (BCVA) was 20/20 in both eyes (OU). Anterior segment examination was unremarkable. In the right eye (RE), fundus examination revealed a cotton wool spot at the posterior pole (Figure 1A), with clear vitreous and without retinal lesions. There were no retinal abnormalities in the left eye (OS) (Figure 1B).

After 2 months, the patient remained without complaints. Fundus exam showed cotton wool spots reduction

Figure 1. Imaging of retinal arterial macroaneurysms in a patient recovered from COVID-19. Baseline color fundus photography shows cotton wool spots at the posterior pole, close to the superior temporal arcade and optic disc in the right eye (A); the posterior pole of the left eye was unremarkable (B). After 2 months of the initial eye exam, fundus photography showed a reduction of the cotton wool spot in the right eye (C) and the presence of two retinal arterial macroaneurysms of the inferior temporal retina of the left eye (D and E). The fluorescein angiography confirmed the diagnosis (F).

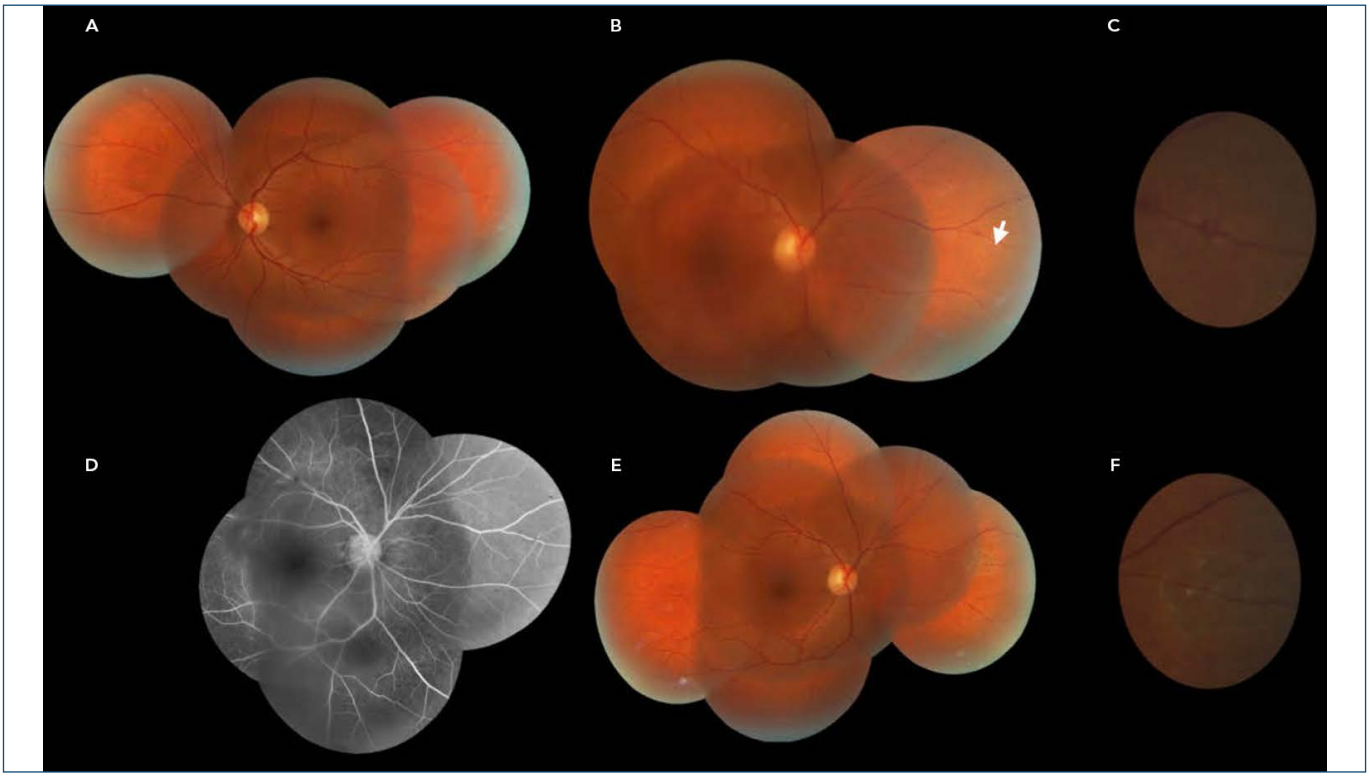

Figure 2. Image of retinal arterial macroaneurysms in a patient with sudden visual loss after recovery from COVID-19. Normal color fundus photography of the left eye (A). Moderate vitreous hemorrhage and a nasal peripheral retinal arterial macroaneurysms observed in the right eye (white arrow) (B and C). Fluorescein angiography exam shows a typical fill in the early arterial phase and late stain of the vessel walls (D). After one month, laser marks in the retinal arterial macroaneurysms region and clear vitreous are noted (E and F).

in RE (Figure 1C) and two RAM with hard exudates forming a circinate, with some adjacent ghost vessels at the equator of the inferior temporal retina in OS (Figures 1D and 1E). Fundoscopic findings were more evident in the fluorescein angiography exam (Figure 1F). Laser photocoagulation was performed in the region of the macroaneurysms, to reduce exudation and the risk of vitreous hemorrhage. Patient was referred to the cardiologist, but no systemic disease was identified.

CASE 2

A 62-year-old woman reported sudden visual loss in RE few days before admission. She had had a mild form of COVID-19 7 months before. No history of trauma, comorbidities or ophthalmic treatments were reported. She underwent a complete eye examination a year ago, in which no retinal abnormalities were identified. Best-corrected visual acuity was 20/400 RE and 20/20 OS. Anterior biomicroscopy and intraocular pressure were normal in OU. Fundus exam was normal in OS (Figure 2A) and showed moderate vitreous hemorrhage and a RAM in the nasal peripheral retina in RE (Figure 2B and 2C), without other vascular changes.

Fluorescein angiography confirmed the presence of the RAM (Figure 2D), with no other vascular changes. Laser photocoagulation was performed. After one month, BCVA improved to 20/20 RE. Fundus exam showed clear vitreous and laser marks in the RAM region (Figures 2E and 2F). The patient was referred to the cardiologist for further investigation, but no comorbidities were identified.

CASE 3

A 54-year-old woman with unilateral negative scotoma over the past 21 days presented with decreased visual acuity in OS. She did not have any significant past medical history. She reported a history of mild COVID-19 a month prior to ocular symptoms. Her BCVA was 20/20 (RE) and 20/600 (OS). Anterior segment examination was unremarkable. Fundus exam showed vitreous hemorrhage, deep and superficial retinal hemorrhages, with grayish fibrotic aspect at the central macula. RE had no signs of vascular abnormality.

The optical coherence tomography (OCT) showed dense subretinal and pre-retinal hematoma, with major disruption of the retinal layers due to a hemorrhagic RAM, visible at the superior temporal branch (Figure 3).

Figure 3. Optical coherence tomography shows dense subretinal and preretinal hemorrhage due to retinal arterial microaneurysm visible at the superior temporal branch in a patient after recovery from COVID-19.

DISCUSSION

COVID-19 is caused by a coronavirus that uses the angiotensin-converting enzyme-related carboxypeptidase (ACE2) receptor to infect cells. ACE2 receptor is present in many cell types, including retina. It is a vital element in the renin-angiotensin-aldosterone system pathway that regulates processes such as blood pressure, wound healing and inflammation.[7] The ACE2 receptor is also involved in the diabetic and hypertensive retinopathy. Microvascular injury and thrombosis in patients with severe COVID-19 appear to highlight the importance of evaluating vascular involvement concomitant to this disease.[8]

The inflammatory cytokine storm could be associated with retinal findings related to COVID. Retinal lesions, such as microhemorrhages, nerve fiber infarcts, PAMM, and neuroretinopathy, have been reported in outpatients after confirmed COVID-19 with mild to moderate symptoms.[3,9]

We described three cases of RAM after COVID-19 in healthy adults. As the virus is enrolled with vascular injury, cases of local arterial damage and aneurysms can occur. A study conducted by Whittaker et al. reported two giant coronary artery aneurysms in children with multiple systemic inflammations during the COVID-19 pandemic.[10]

Retinal arterial microaneurysm and focal dilations of retinal arterial branches are acquired, most often found along the supero-temporal arteriole, which can be classified as hemorrhagic or exudative. The possible pathophysiology is a localized ischemia in the arterial walls from vascular disease, which can predispose vessels to focal dilation. Older age, female sex, and systemic hypertension (seen in 75% of patients) have a strong association.[6] However, none of our patients had advanced age or comorbidities. Casagrande identified SARS-COV-2 RNA in the retina of affected patients. Given the presence of ACE2 receptors in various layers of the retina vasculature and choroid, pathoanatomical abnormalities in these ocular tissues may be expected.[4]

The causes of the macroaneurysms in this case report are unclear. Although direct coronavirus infection of the retina vasculature is possible, secondary effects of inflammation cannot be excluded. Exacerbation of underlying systemic diseases is unlikely, given the young age of the patients and the absence of pre-existing systemic disorder.

Vascular retinal disease may be presented even in asymptomatic patients. Prospective studies are necessary to better understand the spectrum of ophthalmologic manifestations in COVID-19, in order to better treat and avoid visual loss in these patients.

REFERENCES

1. Harapan H, Itoh N, Yufika A, Winardi W, Keam S, Te H, et al. Coronavirus disease 2019 (COVID-19): A literature review. J Infect Public Health. 2020;13(5):667-73.
2. Becker RC. COVID-19-associated vasculitis and vasculopathy. J Thromb Thrombolysis. 2020;50(3):499-511.
3. Jevnikar K, Jaki Mekjavic P, Vidovic Valentincic N, Petrovski G, Globocnik Petrovic M. An Update on COVID-19 Related Ophthalmic Manifestations. Ocul Immunol Inflamm. 2021;29(4):684-9.
4. Casagrande M, Fitzek A, Spitzer M, Püschel K, Glatzel M, Krasemann S, et al. Detection of SARS-CoV-2 genomic and subgenomic RNA in retina and optic nerve of patients with COVID-19. Br J Ophthalmol. 2022;106(9):1313-7.
5. Cennamo G, Reibaldi M, Montorio D, D'Andrea L, Fallico M, Triassi M. Optical coherence tomography angiography features in post-covid-19 pneumonia patients: a pilot study. Am J Ophthalmol. 2021;227:182-90.
6. Panton RW, Goldberg MF, Farber MD. Retinal arterial macroaneurysms: risk factors and natural history. Br J Ophthalmol. 1990;74(10):595-600.
7. Scholz JR, Lopes MA, Saraiva JF, Colombo FC. COVID-19, renin-angiotensin system, angiotensin-converting enzyme 2, and nicotine: What is the interrelation? Arq Bras Cardiol. 2020;115(4):708-11.
8. Magro C, Mulvey JJ, Berlin D, Nuovo G, Salvatore S, Harp J, et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: A report of five cases. Transl Res. 2020;220:1-13.
9. Virgo J, Mohamed M. Paracentral acute middle maculopathy and acute macular neuroretinopathy following SARS-CoV-2 infection. Eye (Lond). 2020;(34)2352-3.
10. Viner RM, Whittaker E. Kawasaki-like disease: emerging complication during the COVID-19 pandemic. Lancet. 2020;395(10239):1741-3.