Case report

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Paracentral acute middle maculopathy in the setting of central retinal artery occlusion following COVID-19 diagnosis

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Abstract

Background: Since its emergence in Wuhan, China, COVID-19 has disseminated across many other countries worldwide. In this report, we firstly presented a patient with mild COVID-19 disease who developed paracentral acute middle maculopathy (PAMM) due to CRAO.

Case presentation: A 54-year-old male patient who reported a contact with a COVID-19 patient applied to the hospital and tested positive for SARS-CoV-2 by polimerase chain reaction testing. He had no significant past medical history. Chest computed tomography was not notable. He had a mild COVID-19 course during hospitalization. Two weeks following COVID-19 diagnosis, he reported profund vision loss (counting fingers) in his right eye where central retinal artery occlusion (CRAO) was detected on fundoscopic examination. Coagulation profile was within normal limits. Hypercoagulable work up was also not notable. Treatment was given for CRAO. Visual acuity was counting fingers at 30 cm. Five days following treatment. Optical coherence tomography analysis showed increased diffuse reflectance and thickening at the level of inner nuclear layer consistent with PAMM. Fluorescein angiography illustrated no perfusion defect.

Conclusion: This is the first case that reports PAMM in the setting of CRAO following COVID-19 diagnosis. Viral induced microangiopathy may involve in the development of CRAO in our patient without a hypercoagulable state and additional risk factors. Physicians should be vigilant to seek for retinal evaluation in patients with significant visual loss even after a mild COVID-19 history.

Keywords

Central retinal artery occlusion, COVID-19, optical coherence tomography, paracentral acute middle maculopathy

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Introduction

By the end of December 2019, outbreak of the novel corona virus or severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) has emerged in Wuhan, China. Since then, the disease has disseminated across many other regions worldwide. The World Health Organization (WHO) officially declared this disease as coronavirus disease 2019 (COVID-19) on February 11, 2020. The symptoms of COVID-19 are usually fever, cough, sore throat, breathlessness, and fatigue. The disease has been reported to be mild in most people, but it can progress to pneumonia, acute respiratory distress syndrome, and multi organ dysfunction particularly in the elderly people and those with comorbidities.[1]

Paracentral acute middle maculopathy (PAMM) has been defined with the presence of a hyperreflective parafoveal band at the level of the inner nuclear layer (INL) on spectral-domain optical coherence tomography (SD-OCT) indicating ischemia at the level of deep capillary system including the deep and the intermediate capillary plexuses. This clinical entity has been shown to be associated with several retinal vascular diseases, including diabetic retinopathy, central retinal vein occlusion,

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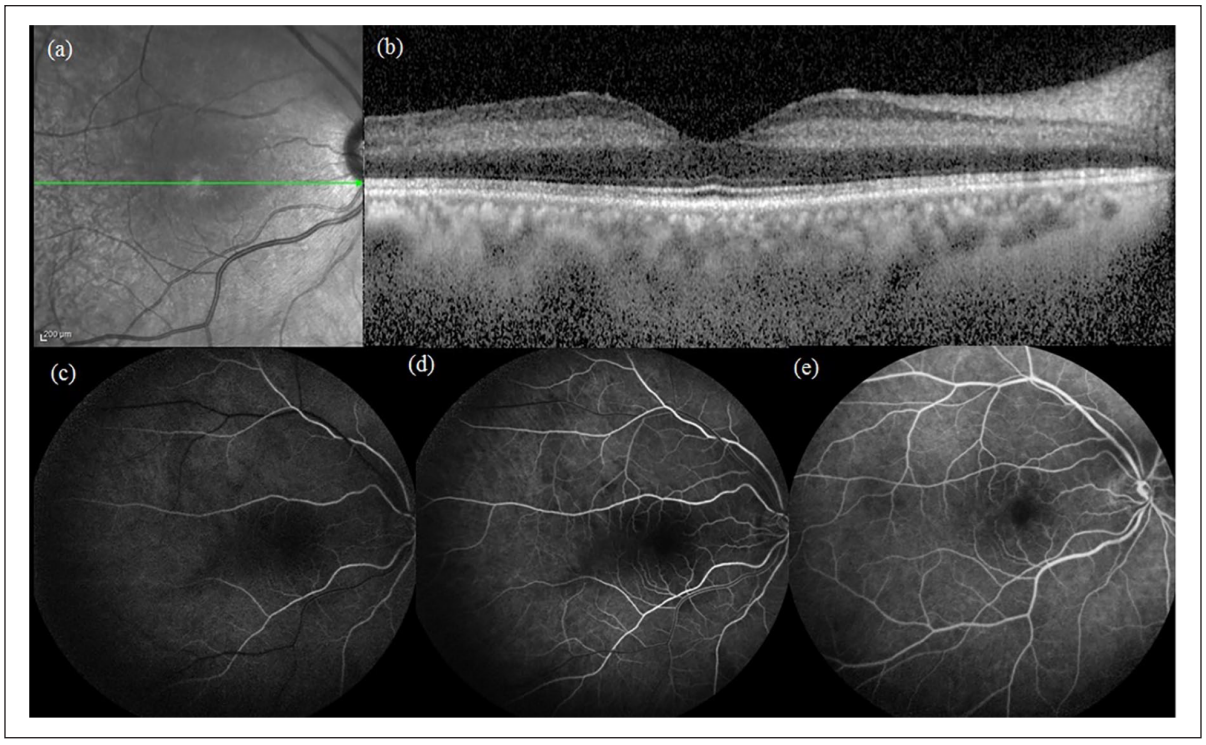

Figure 1. (a) A large hyporeflective area over the affected region with paracentral acute middle maculopathy can be seen. This is more noticeable when comparing with infrared imaging of the fellow healthy eye in Figure 3(a), (b) prominent diffuse hyperreflectivity of inner nuclear layer on optical coherence tomography, and (c–e) fluorescein angiography demonstrates no visible perfusion defect except for mild parafoveal leakage.

and retinal artery occlusion (CRAO).[2] Interestingly, a case of CRAO secondary to severe COVID-19 disease has recently been reported. The authors has attributed CRAO to the hypercoagulability namely "sepsis-induced coagulopathy (SIC)" state which can occur during COVID-19 disease.[3]

In the current report, we presented a patient without any hypercoagulability status who developed PAMM in the setting of CRAO following the diagnosis of COVID-19.

Case presentation

A 54-year-old male patient with no significant past medical history applied to the hospital with suspicion of COVID-19 disease. He reported a contact with a COVID-19 patient. He tested positive for SARS-CoV-2 by polimerase chain reaction testing. Chest computed tomography was not notable. He stayed in hospital for 1 week. He only had myalgia and mild fever during hospitalization. No supplemental oxygen was required. He received a therapy including hydroxychloroquine, low molecular weight heparin (Enoxaparine), and pantoprazole. This regime was based on standard treatment protocol for hospitalized COVID-19 patients established by Turkish Ministry of Health. He was discharged from the hospital with recovery and recommended home isolation for additional 1 week. Fourteen days later following the initial diagnosis of COVID-19, he presented to the emergency department with a complain of painless vision loss in the right eye for the last 8 h and an ophthalmology consultation was sought. Ophthalmologic examination revealed a visual acuity of counting fingers (CF) with relative afferent pupillary defect. Indirect fundoscopic examination showed a pale, white retina and "cherry-red spot appearance" in fovea which are typical findings of CRAO. Additional retinal imaging could not be performed in emergency department. Ocular massage was recommended and topical antiglaucoma drops were given to increase retinal perfusion pressure and restore retinal blood flow. A single session of hyperbaric oxygen therapy was applied. The patient was also assessed by a neurologist and head magnetic resonance with diffusion-weighted imaging was obtained. Neuroimaging was unremarkable for any cerebrovascular disease. Laboratory values were within normal limits. Hypercoagulable work up was also not notable.

Five days after initial diagnosis of CRAO, patient was reassessed at ophthalmology department and retinal imaging was obtained. Visual acuity was CF at 30 cm. Infrared imaging in Figure 1(a) demonstrated a large hyporeflective area over the affected region with PAMM which was more noticeable when comparing with infrared imaging of the fellow healthy eye in Figure 3(a). SD-OCT analysis showed increased diffuse reflectance and thickening at the level of INL consistent with PAMM (Figure 1(b)). Fluorescein angiography (FA) illustrated mild parafoveal

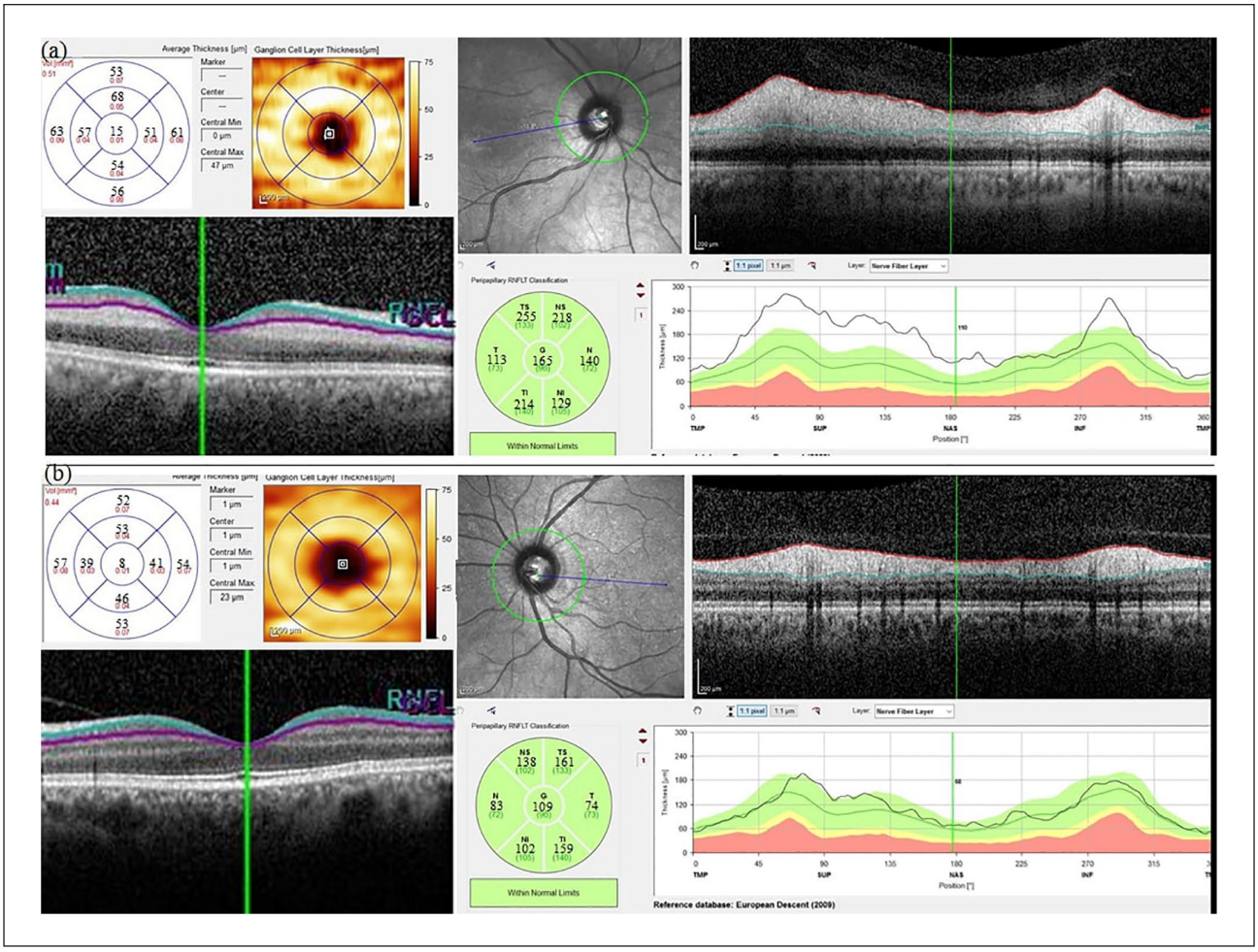

Figure 2. Retinal nerve fiber layer (RNFL) thickness and ganglion cell layer (GCL) thickness shows relative increase: (a) in the right eye compared to the (b) left eye.

leakage during late phase of the study (Figure 1(c)–(e)). Retinal nerve fiber layer (RNFL) thickness and ganglion cell layer (GCL) thickness increased in the right eye compared to left eye which were thought to be related to CRAO development (Figure 2). Left eye showed no abnormality on SD-OCT and FA (Figure 3). Because the patient was then lost to follow-up, no further documentation was available.

Conclusion

Central retinal artery occlusion is a rare condition and presents with complete and severe vision loss. Occlusion of the central retinal artery is related to impaired blood flow in cerebral and ocular circulation, hence cerebrovascular and cardiovascular morbidity and mortality remains higher. CRAO has been shown to be significantly associated with hypertension, diabetes mellitus, ischemic heart disease, hyperlipidemia, and cardiac arrhythmia (atrial fibrillation).[4] Typical fundoscopic appearance during early period of CRAO includes retinal whitening and a cherry-red spot in foveal region. Incidence of visual improvement in CRAO patients is relatively low. Spontaneous recanalization can occur within 48–72 h, but this may have a partial impact on visual improvement.[5]

Current evidence suggests that patients with mild COVID-19 symptoms can present with arterial thromboembolism in the absence of advanced disease. Viral induced endothelial damage has been proposed for the development of increased risk of thrombus formation in these patients.[6] Compatible with this, herein we described a SARS-Cov-2 infected patient who developed CRAO as his additional illness following COVID-19 diagnosis in the absence of significant past medical history. Acharya et al.[3] firstly demonstrated isolated CRAO during hospitalization in a COVID-19 patient with several comorbidities including hypertension, dyslipidemia, coronary artery disease, and chronic obstructive pulmonary disease. Unlike our case, that patient also required intubation for severe COVID-19.

Optical coherence tomography examination has demonstrated increased thickness of the internal retinal layers in the affected retina in CRAO.[4] Consistently, we detected

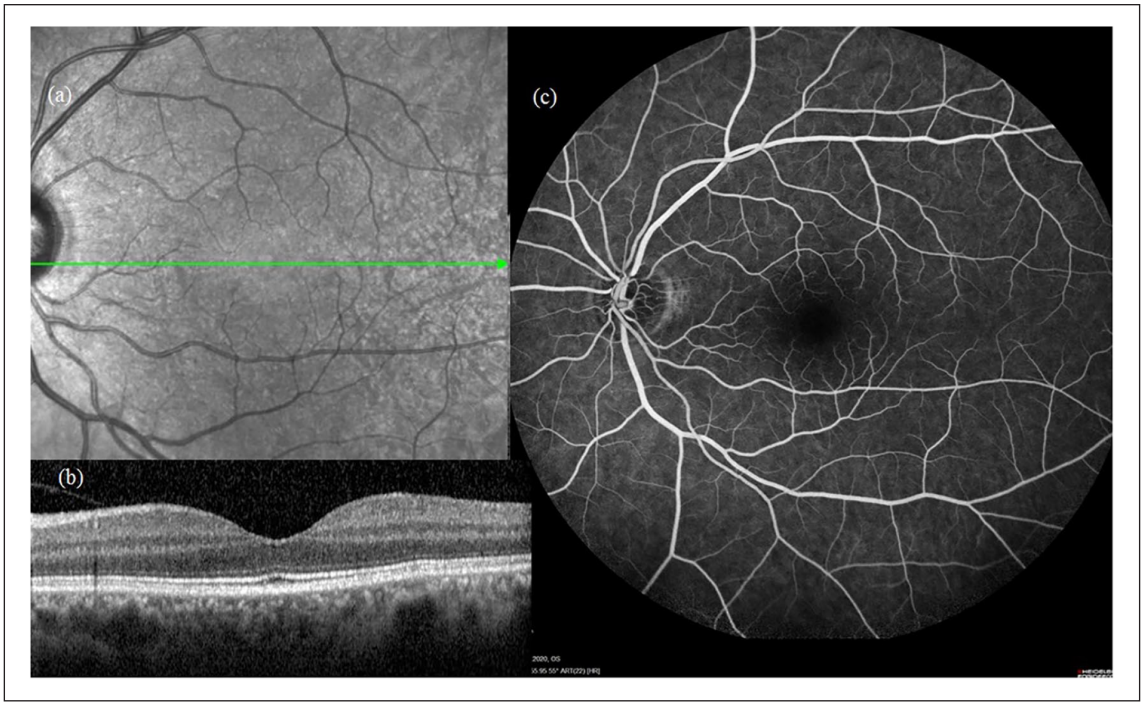

Figure 3. No abnormality on: (a) infrared imaging, (b) optical coherence tomography, and (c) fluorescein angiography in the left eye.

increased RNFL thickness and GCL thickness on SD-OCT in the involved eye compared to the fellow eye in our patient supporting the diagnosis of CRAO. We could not identify a vascular perfusion abnormality except for a mild parafoveal leakage on FA.

Another striking finding was diffuse hyperreflectivity in the INL which we thought to be related to PAMM. Paracentral acute middle maculopathy is a SD-OCT description comprising the middle layers of the retina at the level of the INL. Ischemia of the intermediate and deep retinal capillary plexuses is thought to be the mechanism behind the development of PAMM.[7] Bakhoum et al.[7] have described an ischemic cascade that starts at the level of the deep capillary plexus (DCP) closer to the perivenular pole (perivenular fern-like PAMM) and progresses laterally to diffusely involve the entire INL (globular PAMM) and then ascends anteriorly to involve the inner retina at the level of the superficial capillary plexus (SCP). In our case, we could obtain OCT images 5 days later following CRAO diagnosis with hyperreflectivity limited to middle retinal layers as occurred in PAMM, while both middle and inner layers are usually affected in the setting of CRAO. Here, it is plausible to think that recanalization of SCP might have reversed the abovementioned ischemic cascade in the present case at the time of OCT analysis. Hyperreflective band like lesions in the INL may be the only presenting sign in the absence of typical fundoscopic and fluorescein angiographic appearance in patients with PAMM in the setting of CRAO. Follow-up SD-OCT analysis of PAMM lesions were also associated with subsequent thinning of the INL.[8] Unfortunately, as our patient was lost to follow-up, we were not able to detect further SD-OCT alterations in the present study.

Recently, several articles have reported on COVID-19 associated retinopathy.[9,10] Virgo and Mohamed[9] have presented two cases with PAMM/acute macular neuroretinopathy (AMN) following COVID-19 diagnosis. Gascon et al.[10] have also demonstrated an association between acute SARS-CoV-2 infection and PAMM/AMN lesions. They proposed microvascular ischemia of the SCP and DCP to be reason for development of PAMM and AMN in COVID-19.

Our main goal in presenting the current case is to emphasize possible occurrence of CRAO even after a mild COVID-19 course. We detected PAMM on SD-OCT as an additional finding during examination. It would be plausible to think that viral induced microangiopathy may involve in the development CRAO in our patient without a hypercoagulable state and additional risk factors. Physicians should be vigilant to seek for retinal evaluation in patients with significant visual loss even after a mild COVID-19 history.

Author contributions

BOG drafted the manuscript and reviewed the literature. NT and BOG were involved in the study design, manuscript correction, and interpretation of the data. BOG participated in the study design. All authors read and approved the final manuscript.

Declaration of conflicting interests

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Informed consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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