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Monocular visual loss as the presenting symptom of COVID-19 infection

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1. Case presentation

A patient in his fifth decade was evaluated in the Wills Eye Emergency Room for acute onset of right, painless visual loss the prior day. The patient denied any past episodes of transient visual loss, diplopia, headache, weakness, sensory changes, facial weakness, or slurred speech. The patient’s past medical history is significant for hypertension, tobacco use, and occasional marijuana use. He had stopped smoking 2 weeks prior to presentation. He denied the use of any systemic medications. On review of systems, he confirmed mild pharyngitis and diarrhea for 2–3 days but denied fever, cough, changes in smell or taste, confusion, or respiratory complaints.

On examination, blood pressure was 174/107 mm Hg, pulse oximetry was 97% on room air, and he was afebrile (36.8°C). Vision was 20/20 on the right and 20/20 on the left. A prominent afferent pupillary defect was present on the right. His extraocular motility was normal and the anterior segment was unremarkable except for nuclear sclerotic cataracts. A central retinal artery occlusion (CRAO) was present on the right (Fig. 1). No embolic plaques were present. On the left, arteriovenous nicking was present with one questionable cotton wool spot and a flame hemorrhage. His neurologic exam was otherwise normal.

Based on neuroscience hospital policies, the patient underwent quantitative RNA testing for the SARS COVID-19 and was confirmed positive. The patient was admitted to the neurology service for further workup. His telemetry was unremarkable. On brain MRI, there was no evidence of acute ischemic stroke or hemorrhage. A long segment filling defect involving the mid and distal portions of the right common carotid artery extending to the communicating segment of the right internal carotid artery (ICA) was noted on CT angiography (CTA) (Fig. 2). On high resolution CTA images, decreased flow was also noted in the right ophthalmic artery (Fig. 2B). Poor flow was also noted on MR angiography (MRA) (Fig. 3). Flow in the ICA reconstituted distal to this point via filling from the right posterior communicating artery (Fig. 3). No significant calcifications were noted.

Pertinent laboratory results included a mildly elevated prothrombin time (14.6, normal 9.4–13.0 sec) and international normalized ratio (INR) (1.29, normal 0.83–1.14), with a normal partial prothrombin time. The low density lipoprotein and hemoglobin A1c were normal at 90 mg/dL and 5.4, respectively. Abnormal studies included elevated levels of D-dimer (450, normal <230 ng/mL DDU), fibrinogen (545, normal...
normal 170–460 mg/dL), lactate dehydrogenase (272, normal 125–240 IU/L), and C-reactive protein (2.10, normal ≤0.80 mg/dL).

Upon review of imaging, the patient was immediately started on therapeutic low molecular weight heparin (LMWH) and transferred to the neurocritical care unit for closer monitoring. He remained stable with no new ophthalmologic or neurologic symptoms. The patient remained afebrile and his oxygen saturation remained >95% on room air throughout his admission. LMWH was continued with a plan for repeat imaging and transition to direct oral anticoagulant.

2. Discussion

Additional time is needed to determine the exact impact of COVID-19 on acute cerebrovascular disease incidence, but recently published data has correlated COVID-19 to large vessel occlusion strokes [1]. Viruses, including COVID-19, can penetrate the central nervous system (CNS) (neuroinvasion), infect neurons and glial cells (neurotropism), and contribute to or cause neurological disease (neurovirulence) [2]. Access may be achieved via two main routes: hematogenously or transneuronally through the olfactory bulb. COVID-19 can also bind the angiotensin converting enzyme 2 (ACE-2) receptors that are present in the CNS, which are also involved in the autoregulation of the cerebral
perfusion pressure [3]. In addition to common cardiovascular comor-
biddities in the elderly COVID-19 positive population, mechanisms for
ischemic stroke in infected patients of all age groups include hyperco-
agulability from pro-inflammatory state, infection-induced dissemi-
nated intravascular coagulation, and embolism from virus-related
cardiac injury. These mechanisms may contribute to the development of
variable pathologies that could result in either unilateral or bilateral
vision loss, including, including ophthalmic artery occlusion, [4] central
retinal artery occlusion [5], central retinal vein occlusion [6], optic
neuropathy [7], occipital cortical infarct [8], or acute macular neuro-
retinopathy [9]. In our patient, the hypercoagulable state caused by
virus-induced cytokine storm likely triggered the formation of the in-
ternal carotid artery thrombus that led to a CRAO [10].

CRAO causes retinal ischemia, and prompt medical treatment is
warranted to prevent irreversible retinal cell death and ultimately
blindness. The retinal cells can sustain ischemic conditions for approx-
imately 2 h; beyond that window the damage may be irreversible [11].
Hyperbaric oxygen therapy (HBOT) may be used as an adjunct to
thrombolytic treatment [12].

In retrospective studies, critically-ill COVID-19 patients had
increased proinflammatory cytokines, including interleukin 2 (IL-2) and
tumor necrosis factor α (TNF-α), which can upregulate the coagula-
tion system [13].

In this case, visual loss occurred secondary to occlusion of the in-
ternal carotid artery extending into the skull base. The clinical findings
were consistent with a CRAO rather than ophthalmic artery (OA) oc-
cclusion, either because of partial backfilling of the OA from the posterior
communicating artery or secondary to an embolism from the carotid
artery thrombus lodged in the central retinal artery posterior to the
lamina cribrosa; in this case, partial occlusion of the OA cannot be rules
out. Hemispheric stroke was averted because of reperfusion of the ICA at
the level of the anterior clinoid process.

The neuroscience hospital policies at our institutions mandate rapid
SARS COVID-19 testing in any patient presenting with symptoms of an
acute cerebrovascular event. This policy also includes any patient pre-
senting with an ophthalmic or retinal artery occlusion based on recent
data.

Outcomes in available COVID-19 patient data do not suggest clear
benefit over risk of therapeutic anticoagulation for primary stroke pre-
vention. However, assuming low risk of hemorrhage conversion, ther-
apueutic anticoagulation is frequently initiated for secondary stroke
prevention in the critically ill with significantly elevated D-Dimer levels
and no other clear etiology of ischemic stroke.

Recent studies of infected patients with cerebrovascular disease
revealed the possibility of large vessel occlusion and significant throm-
bosis in the relatively asymptomatic patient with low D-Dimer levels.
When initiating anticoagulation in the COVID-19 patient for secondary
stroke prevention, low molecular weight heparin is often preferred to
unfractionated heparin given consistent immediate therapeutic levels,
reduced nursing and phlebotomy staff exposure, and anti-inflammatory
properties. Patients can later be transitioned to ideally a direct acting
oral anticoagulant if there are no contraindications.

This case illustrates the need to suspect COVID-19 infection in pa-
tients presenting with retinal arterial occlusion, including individuals
who are asymptomatic or minimally symptomatic for COVID-19
infection.

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Data sharing statement

The relevant anonymized patient-level data are available on
reasonable request from the authors.

Ethical approval

All procedures performed in the studies involving human partici-
pants were per the ethical standards of the Institutional Review Board
(IRB) or national research committee and with the 1964 Helsinki
Declaration and its later amendments or comparable ethical standards.

Fig. 3. A. Axial MRA image depicting supraclinoid carotid artery reconstitution through the posterior communicating artery (arrow). B. Axial MRA showing lack of
flow in the right ophthalmic artery (arrows), compared to left normal side. C. 3D MRA reconstruction depicting attenuated flow in the right hemisphere.
Informed consent

The study protocol was reviewed and approved by the Thomas Jefferson University Institutional Review Board. Following our institutional guidelines, all protected health information was removed, and individual patient consent was obtained.

CRediT authorship contribution statement

Ann P. Murchison: Conceptualization, Data curation, Methodology, Resources, Writing - original draft, Writing - review & editing. Ahmad Sweid: Data curation, Writing - original draft, Writing - review & editing. Robin Dharia: Data curation, Writing - original draft, Writing - review & editing. Thana N. Theofanis: Data curation, Writing - original draft, Writing - review & editing. Stavropoula I. Tjoumakaris: Conceptualization, Data curation, Methodology, Resources, Writing - original draft, Writing - review & editing. Pascal M. Jabbour: Conceptualization, Data curation, Methodology, Resources, Writing - original draft, Writing - review & editing. Jurij R. Bilyk: Conceptualization, Data curation, Methodology, Resources, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

The other authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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