Case Report

Transient Visual Obscurations as the Presenting Symptom of Papilledema from COVID-19-Related Cerebral Venous Sinus Thrombosis

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Keywords
Transient visual obscurations · Papilledema · Coronavirus disease-19 · Cerebral venous sinus thrombosis

Abstract
Coronavirus disease-19 (COVID-19) patients are at an increased risk of cerebral venous sinus thrombosis (CVST). Rapid diagnosis and treatment are vital to ensure a favorable outcome for CVST, so clinicians need to be aware of all its potential presentations. We describe a unique case where transient visual obscurations (TVOs) from papilledema were the presenting symptoms of COVID-19-related CVST. A 43-year-old woman, who had tested positive for severe respiratory syndrome coronavirus-2 1 month earlier, developed holoccephalic headache, TVOs, and bilateral disc edema. She did not seek medical attention until she developed TVOs. Visual acuity was 20/20 and Humphrey visual field testing showed enlarged blind spots in both eyes. She was diagnosed with papilledema and underwent magnetic resonance imaging and magnetic resonance venography of the brain, which revealed right transverse sinus thrombosis. Lumbar puncture was performed, showing elevated opening pressure and normal cerebrospinal fluid contents. Her optic disc edema resolved and visual function remained normal 6 weeks following warfarin and topiramate therapy. Recanalization of the right transverse sinus occurred after 3 months. Although rare, TVOs are important presenting symptoms of COVID-19-related CVST. Ophthalmologists, who may be the first physicians to assess patients with this presentation, should be aware of TVOs as potential presenting symptoms of CVST, so diagnoses can be made in a timely manner.
Introduction

Neurological complications, including stroke, have been frequently described in coronavirus disease-19 (COVID-19) patients [1]. Cerebral venous sinus thrombosis (CVST) is a rare form of stroke due to obstruction of dural venous sinuses that occurs in the general population at rates of 5–20 per million per year [2, 3]. Reports estimate that CVST prevalence is higher in patients with COVID-19, with rates reaching 0.02%–1% in hospitalized COVID-19 patients [2]. CVST is more common in young, female patients, and is related to additional risk factors such as trauma, oral contraceptive use, malignant neoplasms, dehydration, and a hypercoagulable state [3]. COVID-19 has been suggested to lead to a hypercoagulable state as the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) binds to endothelial cells, causing dysfunction and activation of a cytokine cascade, which produces a prothrombotic condition [4]. The most common presenting signs and symptoms of COVID-19-related CVST are headache, seizures, encephalopathy, and focal neurological signs [2]. Visual symptoms from COVID-19-related CVST are rare and we describe a rare case where transient visual obscurations (TVOs) prompted the patient to seek medical attention. Since early recognition and treatment are essential for a favorable outcome in CVST [3], it is important that clinicians are aware of all possible presenting symptoms of COVID-19-related CVST.

Case Report/Case Presentation

A 43-year-old woman tested positive for SARS-CoV-2 after developing symptoms of rhinorrhea and fever. She had no known medical problems and did not take any regular medications. She was not on oral contraception and had no history of iron-deficiency anemia. One week later, she developed new onset headache that was holocephalic in nature and moderate in intensity. It improved with acetaminophen, and she did not seek medical attention for the headaches. One month later, she developed bilateral TVOs as her vision “blacked out” for seconds with position changes. Due to these TVOs, she saw an optometrist and was found to have bilateral optic disc edema and referred to the emergency room. In the emergency room, she had an unenhanced CT scan of the head that was reported as normal.

She was referred to neuro-ophthalmology and found to have a visual acuity of 20/20 in both eyes, pupils were equal and reactive to light, and there was no relative afferent pupillary defect. Humphrey 24-2 SITA-Fast visual fields showed enlarged blind spots in both eyes. Dilated fundus examination showed moderate-to-severe optic disc edema in both eyes (shown in Fig. 1). Ocular motility was normal. Due to her new symptoms and bilateral optic disc edema with preserved visual function, she was thought to have papilledema. She underwent magnetic resonance imaging and magnetic resonance venography of the brain, and was found to have right transverse sinus thrombosis (shown in Fig. 2). She also had a lumbar puncture in the left lateral decubitus position that showed an opening pressure of 44 cm of water with normal cerebrospinal fluid contents. In particular, angiotensin-converting enzyme levels were normal, varicella zoster virus PCR, herpes simplex virus PCR, and venereal disease research laboratory test were negative, and bacterial and fungal cultures showed no growth. Workup for a hypercoagulable state was negative. Hemoglobin and ferritin levels were normal. She was diagnosed with papilledema related to CVST and started on warfarin and acetazolamide. She did not tolerate acetazolamide, and this was changed to topiramate. Her symptoms resolved within 1 month and at the 6-week follow-up appointment, her optic disc edema resolved, and visual function remained normal. Follow-up magnetic resonance venography 3 months after diagnosis showed recanalization of the right transverse sinus.
Discussion/Conclusion

Our report describes a unique case of TVOs from papilledema being the presenting symptom of COVID-19-related CVST. Previous cases of COVID-19-related CVST commonly present with headache, seizures, encephalopathy, and focal neurological signs [2]. It is important that visual symptoms are recognized as potential presenting symptoms for CVST related to COVID-19, so cases are not missed.

COVID-19 is believed to lead to CVST by inducing a hypercoagulable state. Patients with COVID-19 have been shown to have higher levels of D-dimer, fibrinogen, and fibrin degradation products than healthy controls [5]. SARS-CoV-2 activates the inflammatory cascade and thrombotic pathways by binding to angiotensin-converting enzyme 2 receptors of endothelial cells [6]. This leads to hyperproduction of angiotensin II, and thus generalized endothelial damage, which induces a hypercoagulable state and promotes thromboembolic events such as CVST [7]. As many patients in the literature develop CVST weeks to months after COVID-19 diagnosis, similarly to the patient we present in this report, it has been suggested that this prothrombotic state can persist even after acute infection [8]. Except for female sex, our patient did not have any other risk factors for CVST such as trauma, oral

Fig. 1. Optic disc photographs from the presentation showing bilateral optic disc edema in both eyes.

Fig. 2. a Magnetic resonance imaging of the brain, T1-sagittal image showing an empty sella (yellow arrow), and descent of the cerebellar tonsils (white arrow). b Magnetic resonance venography demonstrating a filling defect in the right transverse sinus (red arrow). c Magnetic resonance venography demonstrating recanalization of the right transverse venous sinus.
contraceptive use, malignant neoplasms, or dehydration [3], further emphasizing that COVID-19 may have been the precipitating factor in her case.

Early recognition of CVST is crucial for a favorable outcome. This diagnosis may be difficult to make in COVID-19 patients, since COVID-19 can present with nonspecific neurological symptoms that are common in CVST as well, such as a headaches [9]. Hence, it has been suggested that CVST should be suspected in COVID-19 patients with symptoms overlapping with CVST, including headaches, seizures, and encephalopathy, even in the absence of focal neurological signs [9]. Our case report highlights that TVOs should be added to that list of symptoms, as our patient’s sole presenting symptoms were headaches and TVOs.

Out of more than 60 cases of CVST related to COVID-19 in the literature, few reports have described ocular signs and symptoms at presentation. We found 5 cases of patients presenting with papilledema at CVST diagnosis following COVID-19 infection [8–12], one of which also describes disc hemorrhage [11]. Two of these cases presented with blurred vision [8, 12], one described blurred vision accompanied by horizontal diplopia [9], and one described recurrent episodes of transient vision loss and diplopia [11]. These cases were all accompanied by other presenting symptoms, such as headache, seizures, nausea, vomiting, fever, and/or hand tingling, unlike our case where TVOs and headaches were the only presenting symptoms. Hence, visual symptoms are rare, yet important presentations of COVID-19-related CVST [2].

Visual signs and symptoms in CVST in the general population have been more widely reported. In a retrospective study of 118 CVST patients, 21.2% of patients presented with ocular symptoms at diagnosis, and 30.5% presented with ocular symptoms in conjunction with other CVST symptoms, including headache, dizziness, nausea, vomiting, convulsions, disturbance of consciousness, tinnitus, hearing loss, and limb movement disorder [13]. Ocular symptoms included blurred vision, vision loss, transient monocular vision loss, diplopia, ophthalmalgia, metamorphopsia, and abnormal vision [13]. In addition, 70.3% of patients had abnormal ocular examination with limitation of eye movements, conjunctival hyperemia, exophthalmos, nystagmus, and fundus changes (papilledema, optic atrophy, optic disc hemorrhage, retinal hemorrhage, retinal vein abnormalities, and macular edema) [13]. Papilledema was the most common ocular finding, reported in 48.3% of patients, and large prospective studies suggest that it occurs in 30–60% of CVST patients [3]. TVOs have also been previously reported as presenting symptoms of CVST not related to COVID-19 [14]. Thus, visual symptoms may be rarer or not as commonly reported in COVID-19-related CVST than in CVST in the general population.

TVOs are a common symptom of papilledema. While most cases of papilledema are caused by idiopathic intracranial hypertension, especially in women and patients presenting with headaches, such as our patient, papilledema can also be caused by life-threatening conditions like CVST, intracranial masses, or granulomatous meningitis [15]. Our report thus emphasizes the need for imaging workup in patients presenting with TVOs and papilledema, even if they have characteristics that might make idiopathic intracranial hypertension the more likely diagnosis.

In conclusion, TVOs are rare, yet important presenting symptoms of COVID-19-related CVST. As rapid diagnosis and treatment are vital for a favorable outcome, it is important that clinicians are aware of TVOs as potential presenting symptoms of CVST, especially ophthalmologists who may be the first physicians to assess patients with this presentation.

**Statement of Ethics**

Research Ethics Approval was not required for this paper as per University of Toronto Research Ethics Board. The study complies with the guidelines for human studies and was conducted in accordance with the World Health Organization Declaration of Helsinki.
Informed written consent was obtained directly from the patient for publication of the details of their medical case and any accompanying images.

**Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

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**Author Contributions**

Conception and design: M.C., J.A.M., and P.J.R. Data collection: M.C., J.A.M., and P.J.R. Preparation of manuscript: M.C. Critical revisions: J.A.M. and P.J.R. Final approval: M.C., J.A.M., and P.J.R.

**Data Availability Statement**

All data that support the findings of this study are included in this article.

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