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Case Report

SARS-CoV-2 associated septic venous cavernous sinus thrombosis: A case report ☆,☆☆

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ABSTRACT

Cavernous sinus thrombosis (CST) is a life-threatening condition occurring due to an active infection, coagulation abnormalities, and trauma. Thromboembolic events are known complications secondary to novel coronavirus disease-19 (COVID-19) due to dysfunction in endothelial function and clotting factor dysfunction. We report a case of cavernous sinus thrombosis and delayed ophthalmic vein thrombosis associated with a preceding COVID-19 infection confirmed with a facial computed tomography (CT) scan. Clinicians should have a broad differential in patients with hypercoagulable states, as complications secondary to COVID-19 can be life-threatening.

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Introduction

Cavernous sinus thrombosis (CST) is a life-threatening condition requiring immediate medical treatment. Often due to sinusitis, orbital cellulitis, odontogenic infections, otogenic infections, coagulation disorders, or even trauma, CST can be further complicated by systemic infection due to septic

cavernous sinus thrombosis (SCST) [1]. Prior to the widespread use of antibiotics in the early 1940s, SCST had mortality rates as high as 80%-100%; however, antibiotics significantly reduced mortality rates to 20%-30%. SCST develops due to embolization. Because the cavernous sinuses are separated bilaterally by meningeal and periosteal layers of the dura mater, this allows for hematogenous spread to the cerebrum and neurological complications [2]. Symptoms include signs

Glossary of Terms: CST, cavernous sinus thrombosis; SCST, septic cavernous sinus thrombosis; COVID-19, Coronavirus disease-19; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; HIFs, hypoxia-inducible transcription factors; TBI, traumatic brain injury; CT, computed tomography; MRSA, methicillin resistant staphylococcus aureus; MRI, magnetic resonance imaging; MICU, medical intensive care unit; TEE, transesophageal echocardiogram.

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of sepsis and severe infection, such as tachycardia, confusion, and hypotension. Severe fever is observed in 90% of cases, while headache and subsequent facial pain are reported in 50%-90% of patients. Changes in vision, photophobia, diplopia, and loss of vision are secondary to the compression of cranial nerves from the emboli [3].

As previously discussed, infection is a common cause of SCST. Since the introduction of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), various studies have focused on the etiology associated with the novel coronavirus disease 2019 (COVID-19), including acute hypoxic respiratory distress syndrome, acute cardiac and renal injuries, among others [4]. Studies indicate COVID-19 predisposes patients to hypercoagulable states due to endothelial cell dysfunction, excess thrombin production, and inhibition of clot breakdown. Hypoxemia associated with COVID-19 has been linked to hypocoagulability. Studies have shown hypoxia induces production of hypoxia-inducible transcription factors (HIFs) leading to upregulation of thrombus formation. In addition, sepsis from COVID-19 predisposes patients to CST, septic pulmonary emboli, and disseminated intravascular coagulation. To date, studies have demonstrated development of thrombotic events from onset of COVID-19 infections to be 2-7 days [3]. Here, we present delayed thrombosis secondary to positive COVID-19 serology.

Case presentation

The patient is a 61-year-old male with a past medical history of type 2 diabetes, traumatic brain injury (TBI), hypertension, hyperlipidemia, and recent COVID-19 infection (July 26, 2022) who presented to the medical intensive care unit (MICU) for right-eye and facial swelling secondary to acute bacterial sinusitis, orbital cellulitis, and septic shock. The patient was started on norepinephrine bitartrate, broad-spectrum antibiotics and intubated upon admission for airway protection. Initial facial computed tomography (CT) scan (Fig. 1) revealed orbital cellulitis, ophthalmic vein thrombosis, and cavernous venous sinus thrombosis thought to be secondary to invasive fungal or necrotizing infection. Blood cultures were positive for methicillin-resistant *Staphylococcus aureus* (MRSA). Heparin thrombotic protocol was initiated due to bilateral cavernous sinus and right ophthalmic vein thrombosis. The patient was successfully weaned off pressor support and extubated the following day; however, he was re-intubated later in his hospital course. Nasal endoscopy with intraoperative frozen sections were negative for acute invasive fungal sinusitis. Acute bacteria sinusitis was likely due to an unknown source. Lumbar puncture on the same day revealed pleocytosis with negative cultures due to a para-meningeal focus of infection. The patient was re-intubated due to failure to protect the airway. Oral and maxillary facial surgery (OMFS) removed 23 of the patient's teeth. Repeat CT sinuses showed interval worsening opacification of right frontal, maxillary, sphenoid, and ethmoid sinuses from the previous scan with dilated right superior ophthalmic vein of known thrombosis. Magnetic resonance imaging (MRI) of cervical, thoracic, and lumbar spine on August 21, 2022 showed no evidence of discitis or epidural

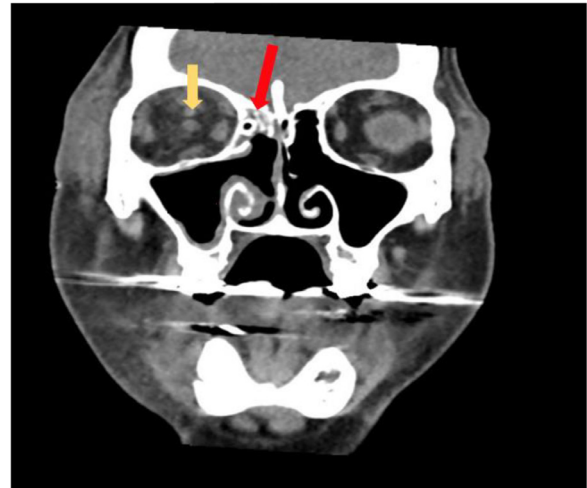


Fig. 1 – Initial facial CT showing ophthalmic vein thrombosis (yellow arrow) and sinus cavernous thrombosis (red arrow) with associated soft tissue swelling.

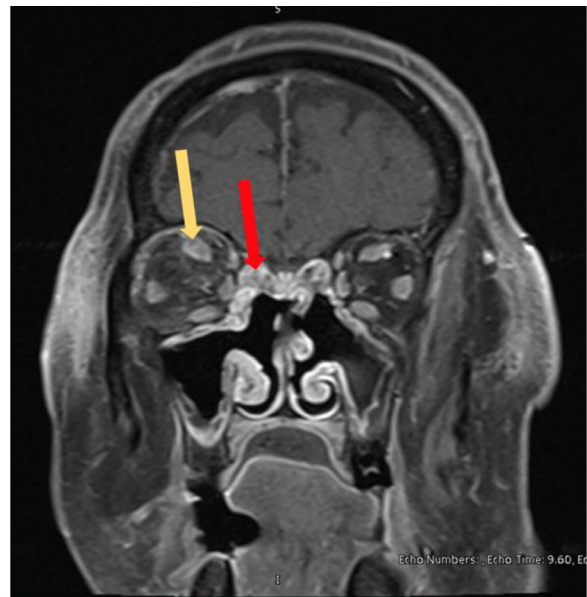


Fig. 2 – MRI orbits w/wo contrast. Thrombosis of the right superior ophthalmic vein (yellow arrow) with subsequent right cavernous sinus thrombosis (red arrow).

abscess. Transesophageal echocardiography (TEE) performed on same date was negative for septic emboli. CT chest performed on same date show multifocal infectious/septic emboli related to pneumonia and pulmonary thrombi embolism. To this date, the patient still has bacteremia secondary to MRSA and increasing leukocytosis. MRI was ordered to rule out hematogenous spread (Fig. 2). Results re-demonstrated right superior ophthalmic vein thrombosis with extension to bilateral cavernous venous sinuses. Endotracheal tube placed after 2 prior failed extubation attempts. The patient was transferred to a long-term acute care hospital for a 6-week course of IV vancomycin therapy. The patient continued to

improve after completion of his antibiotic therapy and is working towards returning to his baseline functional status.

Discussion

CST and SCST are life-threatening conditions with high morbidity and mortality requiring prompt identification and treatment. Prior to novel coronavirus, causes of SCST included bacteria such as *Ss aureus* and *Streptococcus* [5]. However, this case highlights the importance of vigilance for CST and SCST with COVID-19 infection, particularly those in the intensive care unit (ICU). Interestingly, SARS-CoV-2 does not appear to behave like a typical virus pertaining to thromboembolic events. For instance, thromboembolic events due to influenza are roughly 2%, whereas thromboembolic events related to COVID-19 are as high as 31% in an ICU setting [6,7]. This further outlines the importance vigilance for thromboembolic events, such as CST and SCST with COVID-19 infection.

Thromboembolic events such as deep vein thrombosis (DVT), CST, and SCST are commonly associated with COVID-19 infection, whereas ophthalmic vein thrombosis, as seen here, is more rare with an incidence of 3-4 cases per million patients per year [8]. Clinical features include proptosis, ophthalmoplegia, and visual disturbances. Risk factors include sepsis, hypercoagulability, and even neoplasms. In our case presentation, COVID-19 and sepsis predisposed this patient to develop ophthalmic vein thrombosis. Independently, both sepsis and COVID-19 are known risk factors for hypercoagulability and together they further increase hypercoagulability [8]. This patient presentation highlights the importance of including rare conditions in the differential diagnosis, in this case, ophthalmic vein thrombosis with a known COVID-19 infection. As previously discussed, COVID-19 is known to predispose patients to develop a hypercoagulable state through upregulation of the clotting cascade and inhibition of fibrinolysis [9].

Hypercoagulability due to COVID-19 raises the question regarding prophylactic anticoagulation. Several studies have highlighted the use and success of prophylactic steroids, especially in the ICU setting. More robust use of prophylactic steroids and/or anticoagulants may prevent the development of CST, SCST, and ophthalmic vein thrombosis and improve outcomes.

Conclusion

Our case highlights the importance of provider vigilance for rare conditions, such as CST, SCST, and ophthalmic vein

thrombosis with COVID-19 infection, especially for patients in an ICU setting. With early identification and treatment of these conditions, clinical outcomes may be improved.

Patient consent

The patient has consented to his medical course being used for a case report and educational purposes.

Data availability

All data pertinent to the case report can be found within the manuscript.

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