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Cavernous Sinus Thrombosis and Blindness After Simple Tooth Extraction in Patient Who Recovered From Coronavirus 2019: A Case Report

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The pandemic Coronavirus 2019 is a disease transmitted either by droplets from a person's sneeze or cough or direct spread; also known as severe acute respiratory syndrome coronavirus-2. Although the morbidity of the disease is mainly related to respiratory distress, the associated inflammatory response can induce various coagulopathies despite an anticoagulant therapy. The authors are documenting a case of a diabetic patient who recovered from Coronavirus 2019 and is on prophylactic anticoagulant therapy after routine extraction of a maxillary second molar that progressed to unilateral cavernous sinus thrombosis and loss of vision.

J Oral Maxillofac Surg 80:709-713, 2022

The now-termed Coronavirus 2019 (COVID-19) was first identified by the Chinese Center for Disease Control and Prevention on January 7, 2020, from a nasopharyngeal swab of a patient diagnosed with atypical pneumonia in Wuhan.[1]

The disease causes severe influenza-like symptoms with respiratory distress and acute cardiac and renal injury. It induces a hypercoagulable state that yields defective endothelium, inhibits fibrinolysis, and causes thrombin invasion.[2] In addition, the related hypoxemia promotes intravascular coagulation.[3,4] This complex state of coagulopathy may lead to venous thrombosis, pulmonary embolism, disseminated intravascular coagulation, or cerebral venous thrombosis with various neurologic symptoms that further worsen where thrombotic hazards, or diabetes mellitus (DM), coexist.[4,5]

The authors are documenting a case report of a well-controlled diabetic patient who recently recovered from COVID-19 on anticoagulant therapy; however, he suffered cavernous venous thrombosis and progressive vascular, neurogenic manifestations that exaggerated to a unilateral loss of vision after a maxillary second molar was extracted.

The Case Report

A 69-year-old male patient suffering from DM and hypertension was admitted to the hospital with fever and hypoxia. The physical examination showed signs of dehydration, a blood pressure of 150/90 mm Hg, a random blood sugar of 214 mg/dL and 9% HbA1c, a temperature of 37.9 °C, a respiratory frequency of 18 cycles/min, and oxygen saturation of 88%. The

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Conflict of Interest Disclosures: None of the authors have any relevant financial relationship(s) with a commercial interest.

Consent: The authors obtained informed consent from the patient.

Data availability: The data are available per request.

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Received October 1 2021
Accepted December 22 2021

0278-2391/21/01519-6
https://doi.org/10.1016/j.joms.2021.12.015

patient was fully conscious with a normal neurological examination. The biological analysis showed 2.6-μg/mL D-dimer and leucopenia. Computed tomography images of the chest illustrated bilateral subpleural patchy areas of ground-glass opacities. A positive nasal swab polymerase chain reaction test confirmed the diagnosis of COVID-19 infection. The patient's laboratory investigations are illustrated in Table 1.

The treatment protocol consisted of hospitalization, oxygen therapy, intravenous (IV) fluids, IV antibiotics, antiviral drugs, steroids, and anticoagulants. After 7 days, the patient markedly improved. Five days later, the polymerase chain reaction test turned negative, and the patient was dismissed from the hospital after being instructed on the administration of an anticoagulant (Xarelto 10 mg oral daily, Rivaroxaban, Janssen, Egypt).

Twelve days after home quarantine, the patient felt pain in a fractured right maxillary second molar and was examined by a general dentist in a private clinic. Although the dentist acquired the patients' entire medical history and diagnosed a right maxillary retained root, he decided that it only demanded routine extraction, neglecting to prescribe a prophylactic antibiotic coverage or checking the patients' D-dimer. After the extraction, the patient presented to our hospital suffering from severe headaches and disturbed consciousness levels.

The patient was admitted to the intensive care unit (ICU) and immediately underwent radiographic and laboratory investigations. A brain magnetic resonance venography with a contrast medium revealed the presence of a transverse and sigmoid venous thrombosis (Fig 1A). The magnetic resonance images illustrated cavernous sinus thrombosis and sinusitis in the right maxillary and sphenoidal air sinuses (Figs 1B, C).

After 9 days of treatment in the ICU, a brain magnetic resonance venography showed improvement in both the transverse and sigmoid venous thrombosis, and the patient was discharged from ICU. However, the patient complained of a large firm swelling in the right cheek, along with an all-directional limitation of the right eye movement. The clinical examination demonstrated right intraoral canine space infection with an extraoral buccal space swelling (Figs 2A, B).

The patient was referred to the ophthalmology and ENT departments for consultation. The ophthalmology consultant reported the presence of a relative afferent pupillary defect, ptosis with all-directional eye movement limitation, a central retinal artery occlusion with the inspection of a cherry-red spot. She confirmed the diagnosis of cavernous sinus thrombosis.

Although the anesthesia department's protocol prevents elective surgical intervention 3 months after COVID-19 infection, the case was classified urgent and exempted from the routine protocol.

The surgical treatment constituted a functional endoscopic sinus surgery executed by an ENT consultant, coupled with incision and drainage of the canine space, which evacuated the concealed pus (Fig 2C). Along with IV fluids (Ringer's lactate and dextrose 5% solutions), IV antibiotics (metronidazole 500 mg infusion/8 hours for 7 days, garamycin 80 mg/12 hours for 7 days [Gentamycin, Shering-PLough, Egypt], and meropenem 500 mg/12 hours for 7 days), anticoagulants (Xarelto 15-mg tablet/12 hours for 15 days), the patient's routine drugs for hypertension and DM (Concor 10 mg once daily [Amlo, Merek, Egypt], Tareg 160-mg tablet once daily [Co-Tareg, Novartis, Egypt], Plendil 10-mg tablet once daily [Felodipino, Astrazeneca, Egypt], Insulin Lantus Flexop 15 units daily, Sanofi, Egypt), as well as (Controlic 40-mg tablet before breakfast for 15 days [Pantoprazole, Mycomi, Egypt]), (Atrovent Inhaler; inhalation/12 hours for 30 days [Boehringer Ingelheim, Egypt]), and (Systane Ultra Drops once daily for 15 days), as well as supplementary gastrointestinal tract, nasal, and ophthalmic treatment.

Although all the signs and symptoms of the cavernous sinus thrombosis subsided and the patient was discharged from the hospital with improved eye and lid movement, the right eye's vision was lost.

Table 1. THE PATIENT'S LABORATORY INVESTIGATIONS WHEN DIAGNOSED WITH COVID-19

Day (Date)	1 (25/12)	2 (26/12)	3 (27/12)	4 (28/12)	5 (29/12)	6 (30/12)	7 (31/12)	8 (1/1)	9 (1/2)	10 (1/3)	11 (1/4)	12 (1/5)
Ferritin	1,056			973					821			
DD	2.6			0.9	1.2							1.1
CRP	167.3		149	84.8	87.5	54.2	38.8		33.7			10
Lymphocytes	0.6	0.4	1	0.57	0.4	0.49	0.57	0.62	0.47	0.49	0.48	0.9
TLC	13.8	14.3	19.9	14.3	7.9	9.8	8.19	6.9	7.4	6.6	5.9	6.9

Abbreviations: CRP, C-reactive protein; DD, D-dimer; TLC, total leucocyte count.

Abdelmoiz, Alghandour, and Gibaly. Morbid Complications After Tooth Extraction and COVID-19. J Oral Maxillofac Surg 2022.

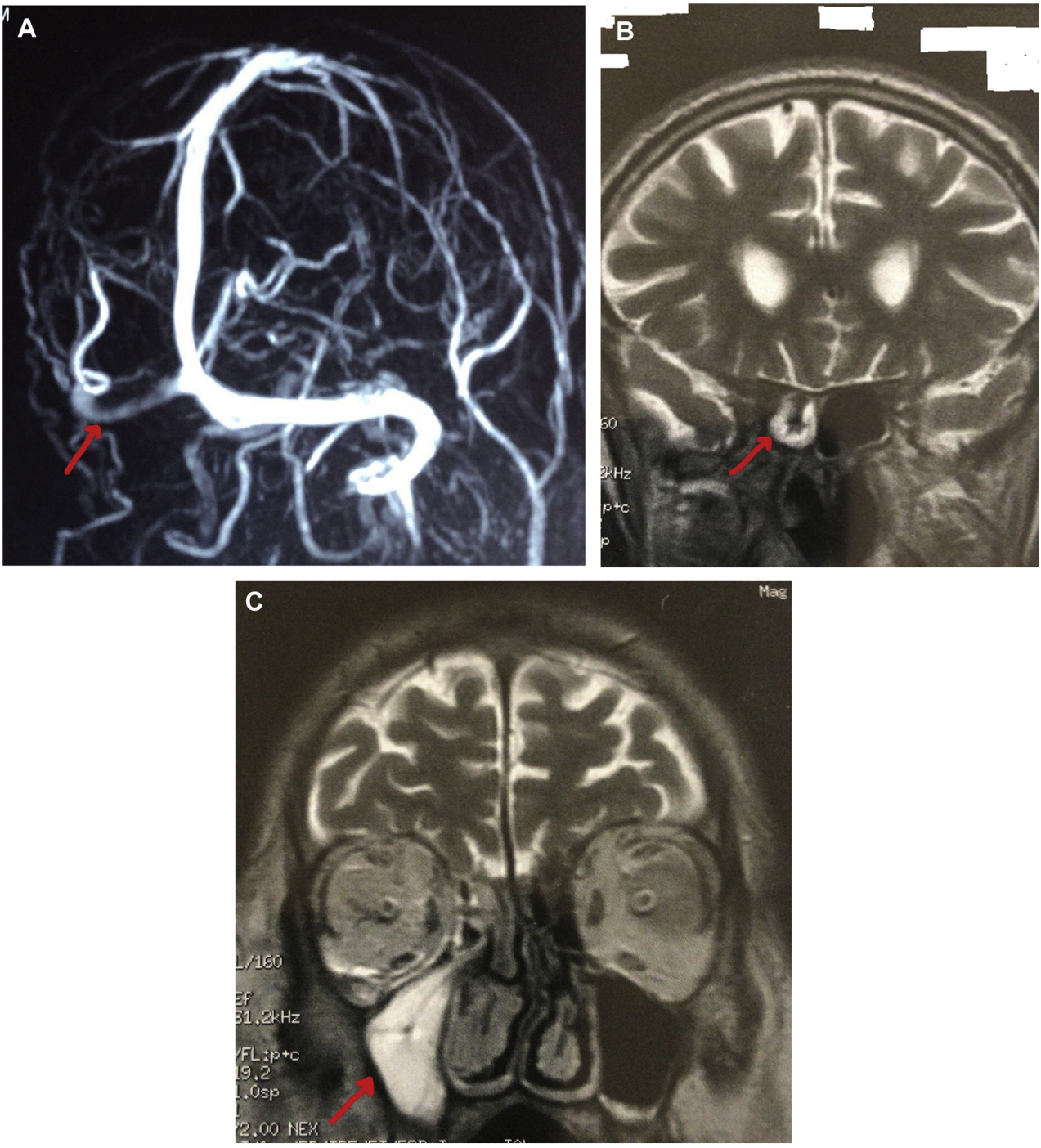

FIGURE 1. *A*, Brain magnetic resonance venography with a contrast medium showing prominent transverse and sigmoid venous thrombosis (*red arrow*). *B*, magnetic resonance image showing cavernous sinus thrombosis (*red arrow*). *C*, MRI showing right maxillary and sphenoidal air sinuses (*red arrow*).

Abdelmoiz, Alghandour, and Gibaly. Morbid Complications After Tooth Extraction and COVID-19. J Oral Maxillofac Surg 2022.

Discussion

The Coronavirus is a ribonucleic acid (RNA) virus, usually incubated in birds and mammals. When transmitted to humans, variable signs and symptoms with multisystemic manifestations that range from mild respiratory distress to mortal hypoxia with severe inflammatory responses may arise. In addition, the COVID-19-associated coagulopathy includes arterial, venous, and pulmonary embolisms, deep venous thrombosis, retinal and renal microangiopathy, ischemic infarctions, and cerebral and cavernous

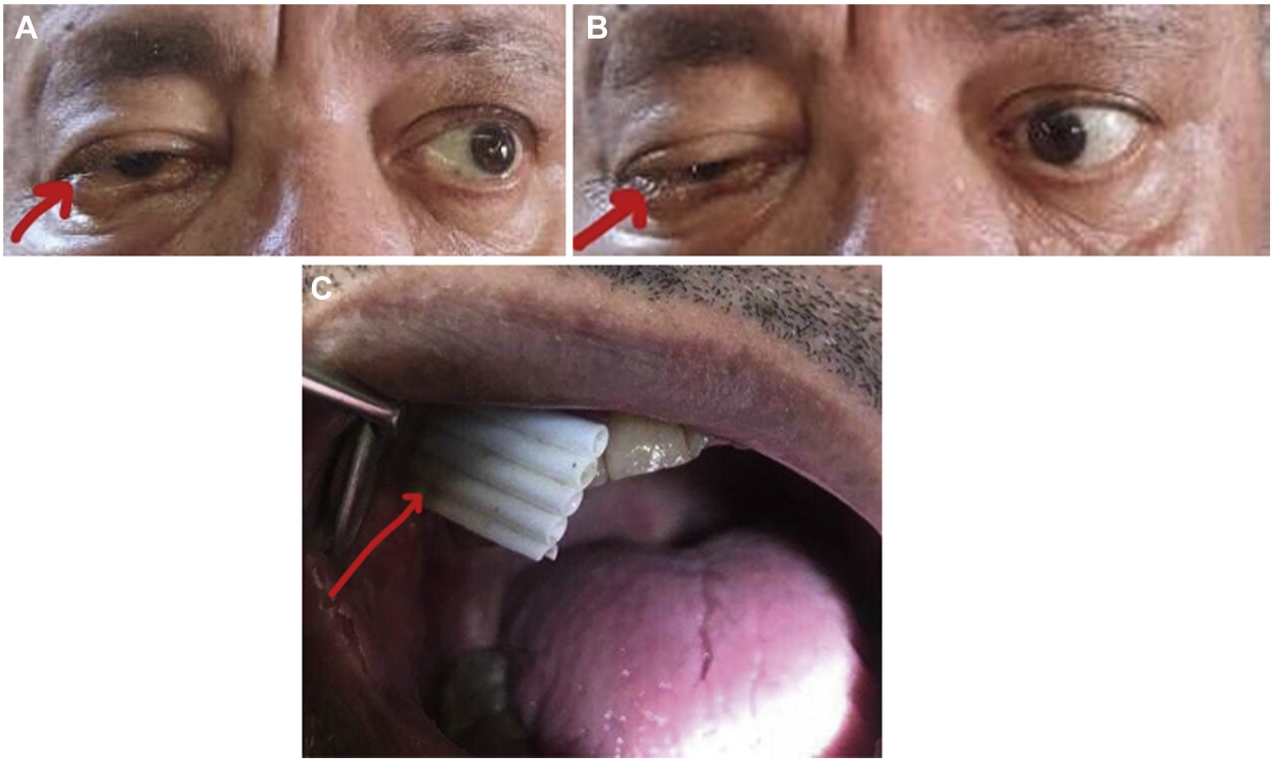

FIGURE 2. *A*, Ptosis in right eyelid and limitation in movement of the right eye (*red arrow*) when the patient looked to the left side; *B*, limitation in movement of the right eye (*red arrow*) when the patient looked to the right side; *C*, incision and drainage for the canine space using a corrugated drain (*red arrow*).

Abdelmoiz, Alghandour, and Gibaly. Morbid Complications After Tooth Extraction and COVID-19. J Oral Maxillofac Surg 2022.

venous thrombosis.[6,7] Unfortunately, these incidents are unpreventable in susceptible patients despite receiving the in-hospital thromboprophylaxis.[8]

Vallianou et al[9] demonstrated the coupled effect of COVID-19-associated coagulopathy and DM. The COVID-19-induced endothelial inflammation and hypercoagulability aggravates the existing endothelial dysfunction among diabetic patients and renders them more vulnerable to aggressive thrombosis. Furthermore, they declared that hyperglycemia-related immune suppression exaggerates the severity of the viral infection.

In a retrospective case series, Wu et al[10] investigated the conjunctiva's ocular manifestations and viral prevalence. They counted a third of 38 COVID-19 hospitalized patients who had ocular abnormalities consistent with conjunctivitis. The authors believed that ocular complications are more prominent among those patients with more severe systemic manifestations.

Although blindness secondary to cavernous sinus thrombosis is uncommon, according to Walsh and Hoyt[11] and Ahmadi et al[12], the loss of vision results from either the formation of the corneal ulcers that emerge by poor lid closure or the occlusion of the central retinal artery secondary to orbital apex compression, emboli, internal carotid arteritis, toxic neuritis, and ischemic optic neuropathy. This coincides with the authors' belief that the canine space infection, with the well-known capability of vulnerable intracranial spread accompanied by the intense inflammatory reaction and the patient's immunocompromised state, induced the visual affection.

A study that retrospectively analyzed 7,337 (COVID-19) patients, among which 952 had preexisting type 2 DM in Hubei Province, China, confirmed the association between preexisting DM and the rates of mortality, independent of known confounders. In this study, type 2 DM required more medical interventions and had significantly higher multiple-organ injury and mortality rates than those free from DM (7.8 vs 2.7%; adjusted hazard ratio, 1.49).[13]

Several mechanisms induce the accentuated clinical presentations of COVID-19 among diabetic patients. Glucotoxicity, endothelial damage by inflammation, oxidative stress, and cytokine production contribute to an increased risk of thromboembolic complications and damage to vital organs. In turn, the systemic corticosteroids, usually administrated during

hospitalization, might contribute to an increased state of hyperglycemia.[2]

With the worldwide pandemic spread of the disease, the literature still lacks clear guidelines for dentists and oral-maxillofacial surgeons that should be followed upon treating infected and recently recovered patients. The recent inquiry of the disease makes the medical modifications needed for safe minor oral surgical treatments uncertain. However, considering the tooth extraction, an elective minor surgical procedure allocated within the "Joint Statement on Elective Surgery, and Anesthesia for Patients after COVID-19 Infection",[14] it was declared by the American Society of Anesthesiologists and Anesthesia Patient Safety Foundations that "The timing of elective surgery after recovery from COVID-19 utilizes both symptom- and severity-based categories. The suggested wait times from the date of COVID-19 diagnosis to surgery are as follows:

- Four weeks for an asymptomatic patient or recovery from only mild, non-respiratory symptoms.
- Six weeks for a symptomatic patient (eg, cough, dyspnea) who did not require hospitalization.
- Eight to ten weeks for the symptomatic diabetic, immunocompromised, or hospitalized.
- Twelve weeks for a patient who was admitted to an ICU due to COVID-19 infection."

Furthermore, the clinician should investigate the presence of a standard range of D-dimer, partial thromboplastin time, and international normalized ratio before any elective surgical procedure for 3 months after COVID recovery. Meanwhile, any alteration of the patient's anticoagulant regimen must be addressed by the treating physician.[14,15] Zehani et al in 2017[16] considered that providing a prophylactic antibiotic cover before tooth extraction for uncontrolled diabetic patients is essential to guard against aggressive infections. This is consistent with the authors' belief. We relate the incidence of cavernous sinus thrombosis and blindness to not deferring the tooth extraction for safe timing and neglecting the safety precautions concerning the patients' immune and thrombotic states.

In conclusion, the COVID-19 infection and DM represent two worldwide pandemics, where, when combined, the patients are susceptive to aggressive inflammatory response and morbid thrombosis. The authors recommend that minor oral surgical procedures for COVID-19 diabetic patients be postponed for 8 to 12 weeks after recovery, extending to 12 weeks if the patient was admitted to an ICU. Meanwhile, fulfilling strict infection control, administering prophylactic antibiotics, and monitoring the patients' thrombotic state in collaboration with the patient's treating physician are mandatory.

The authors realize that their recommendations are based on expert opinions and suggestions, awaiting the outcome of clinical trials to provide evidence-based regulations.

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