

**COVID-19 associated cavernous sinus thrombosis: a case report of patient presented with necrosis of hard palate and glabella region of the face following by acute stroke**

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**Abstract**

Besides the typical respiratory symptoms, the coronavirus disease 2019 (COVID-19) is also known to have a high risk of thrombosis and thromboembolism. Currently, no literature exists about the risk of patients to develop cavernous sinus thrombosis, a rare life-threatening condition, in patients who were diagnosed with SARS-CoV-2 infection.

**Case presentation:** Here, we describe the case of a 67-year-old female with a history of type 2 diabetes, arterial hypertension and obesity who developed cavernous sinus thrombosis two weeks after the first symptoms onset of COVID-19 disease confirmed by RT-PCR, being 3 days after discharge from the COVID-19 hospital due to significant improvement of general status. Patient presented at the department of Adult ENT and Maxillofacial Surgery with necrosis of hard palate and glabella region of the face, following by

acute stroke. Brain and facial CT scan revealed right cavernous sinus enlargement and thrombosis, old pontine infarcts, right eye ptosis and orbital and periorbital swelling, pansinusitis. MRI Angiography confirmed findings of right cavernous sinus thrombosis, occlusion of intracranial right internal carotid artery, and ischemic stroke of the basins of right anterior and middle cerebral artery.

**Keywords:** COVID-19, SARS-CoV-2, cavernous sinus thrombosis, maxillar osteomyelitis, hard palate necrosis

**Introduction**

Since its start, the coronavirus disease 2019 (COVID-19) pandemic has spread across the world with over 1,37 million reported cases in 223 countries or territories<sup>1</sup>. Although the main characteristics of COVID-19 disease is respiratory symptoms, the coagulopathy with the increased incidence of

thrombotic and thromboembolic complications is a common finding<sup>2</sup>.

Cavernous sinus thrombosis is a very rare, life-threatening condition. Typically, it caused by an infection that has spread beyond the face, sinuses, teeth, pharynx, ears or eyes, or have post-traumatic origin<sup>3-5</sup>. The incidence of cavernous sinus thrombosis comprises approximately 2-4 cases per million people per year<sup>6</sup>. Currently, no literature exists about the risk to develop cavernous sinus thrombosis among patients who were diagnosed with SARS-CoV-2 infection. Here, we report the case of a patient with cavernous sinus thrombosis who manifested symptoms 3 days after being discharged with significant improvement of the general condition being 8 days at the COVID-19 hospital with the confirmed diagnosis of the novel SARS-CoV-2.

#### Case

A 67-year-old women M.A with the history of type 2 diabetes since 2002, arterial hypertension, and obesity (BMI 32.3) underwent in-hospital COVID-19 treatment for 8 days (description below). On September 2, the 3<sup>rd</sup> day after discharge from the COVID-19 hospital (14<sup>th</sup> day from COVID-19 disease onset), the patient developed pain in the right orbital fissure, difficulty to move right eye, nasal congestion, headache, general malaise, and fever up to 38.4°C. She was tested negative for RT-PCR COVID, Influenza, and Strep. In spite of strongly recommended in-hospital treatment and future tests, the patient made a decision to continue treatment at home. On September 6, the patient admitted to the Department of Adult ENT and Maxillofacial Surgery with a fever of 38.5°C, necrotic wound of glabella region (Fig.1) and right side hard palate (Fig.1B), maxillar osteomyelitis, inflammatory infiltration in the right infraorbital region and nasolabial fold, right upper eyelid ptosis,

exophthalmos, restricted movement of the right eyeball, chronic pansinusitis. Due to progressive right side facial drooping, weakness of right hand, and blurred speech, while on ENT exam, the patient was transferred to the intensive care unit where she stayed until September 14, 2020. The treatment regimen for acute stroke, cavernous sinus thrombosis, as well as purulent-necrotic complications and comorbidities was prescribed (e.g. Enoxaparin 80mg/0.8 ml twice/day, insulin, antibacterial medication Meropenem 1g 3 times/day IV, Fluconazol 150/100 ml IV).

Rhinoscopy showed necrotic lesions in the right nasal cavity. On admission ANCA screen test was negative (0.08). CRP-latex 80 mg/L, glucose on insulin 6.0 mmol/L, Prothrombin time 15.5sec, prothrombin index 90%, International Normalized Ratio 1.23, Activated partial thromboplastin time 21.9sec, thrombin time 19.3sec, fibrinogen 750mg/dl, total cholesterol 5.4 mmol/l, Triglycerides 2.8 mmol/L, LDL-C 2.7 mmol/L, VLDL-C was 1.25 mmol/L, HDL-C 1.6 mmol/L. Otherwise, other tests were within the normal range.

The patient underwent functional endoscopic sinus surgery to remove necrotic tissue from the nasal cavity under intravenous anesthesia. Chest CT scan (September 7, 2020) showed signs of bilateral interstitial pneumonia, a picture typical for the COVID-19 disease (Fig D 1-3). On September 07, Brain and facial CT scan examination revealed e.g. right cavernous sinus thrombosis, signs of ischemic stroke of the frontal, temporal and parietal lobes on the right side in the basin of the middle cerebral artery, chronic pansinusitis, right side exophthalmos (Fig E 1-3).

The operation was performed to open an abscess in the right buccal and glabellar region. The culture shower the abundance of Staphilococcus Aureus, and Streptococcus piogenes, sensitive to Meropenem,

Meticillin, Vancomycin. The results of the treatment showed the absence of hyperemia around the necrotic wounds (Fig.1C) and the hard palate (Fig.1 B2)

Before discharge, the patient underwent MRI with angiography of cerebral vessels, which showed cavernous sinus thrombosis, occlusion of the right internal carotid artery, signs of acute ischemic stroke at the border of the basins of the right anterior and middle cerebral artery (Fig1. F-K).

Patient is stable, no fever, BP 120/80 mmHg, Pulse 76 beats per min, SpO<sub>2</sub> – 99%. There is scarring of right buccal and glabella region without inflammation. There is a mucous and bone defect 3.5 x 1.5 cm in the right half of the hard palate without hyperemia or pathologic discharge.

#### **COVID-19 disease**

The clinical manifestations of COVID-19 disease were a fever up to 39°C, loss of smell and taste, severe fatigue on August 19, 2020. Consuming over-the-counter anti-inflammatory medications, the patient went to a primary care physician only 4 days after the onset of the symptoms. Computed tomography of the chest was performed immediately, where images showed multiple patchy ground-glass opacities in bilateral areas. After being tested positive for SARS-CoV-2 infection by a real-time polymerase chain reaction (RT-PCR) in a nasopharyngeal swab sample, the patient was admitted the same day in the COVID-19 hospital on August 23. Physical exams showed normal vital signs with oxygen saturation of 95-97% while the patient was breathing ambient air. No oxygen supplements were used. Lung auscultation revealed rales. Neurological and ENT exams did not indicate any acute conditions. Ophthalmological exam indicated diabetic retinopathy. HbA<sub>1c</sub> was 8.6 with blood glucose 8-9 mmol/L (at admission), 5-6 mmol/L on

insulin, C-reactive protein (CRP)-latex – 30mg/L, fibrinogen 488. Blood routine tests, liver function, renal function, myocardial enzymes, electrolyte, and serum procalcitonin, other coagulogram tests were otherwise normal. COVID-19 disease treatment included Favipiravir 200 mg tab per scheme, Enoxaparin 60mg/0.6 ml twice daily for 6 days following by 80mg/0.8 ml 8 more days, insulin, antibacterial medications (Ceftazidime 1g x 2 times/day IM, levofloxacin 500mg/100ml IV daily, 5 days) dexamethasone 8 mg/daily 4 days, fluconazol 150 mg 1 tab per day 5 days. In-hospital stay was uneventful; patient was discharged on the 8th day (August 30) with significant improvement after two negative COVID-19 RT-PCR tests.

#### **Discussion**

The patient we report in this article presented an inconsistent situation. While her respiratory COVID-19 symptoms had already improved, and she was successfully discharged from the hospital without fever and negative COVID-19 PCR tests, on the 3<sup>rd</sup> day after discharge she appeared with fever, pain in the right orbital fissure, nasal congestion, and headache. Refusing future examination and hospitalization, she was back in severe general condition with necrosis of upper palate and glabella region, maxillary osteomyelitis. The diagnosis of cavernous sinus thrombosis was confirmed on the brain and facial CT scan examination. Acute ischemic stroke symptoms were supported by CT scan findings. While in COVID-19 hospital, no acute neurological signs, oropharyngeal symptoms, infection of eyes or skin were observed. Patient denied facial trauma, nasal cannula/face mask oxygen treatment. She did not stop enoxaparin subcutaneously and aspirin orally at home after discharge from the COVID-19 hospital.

Cavernous sinus thrombosis has led to the syndrome of the upper orbital fissure, acute impairment of the blood circulation of the eye and orbit, which further leads to inflammation of the retrobulbar tissue, orbital and periorbital regions, following by acute perfusion impairment of the bone and soft tissue structures of the middle face. These changes further may cause maxillar osteomyelitis, necrosis of mucous and the hard palate, promote inflammatory processes in the paranasal sinuses. Motor and sensory functions of III, IV, V, VI pairs of cranial nerves may be affected<sup>7</sup>.

### **Ethical approval**

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Patients informed consent. Written informed consent was obtained from the patient, her husband, and children for publication of this case report and accompanying images.

### **Declaration of interests**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Legend Figure -1



Figure A



Figure C



Figure B1



Figure B2

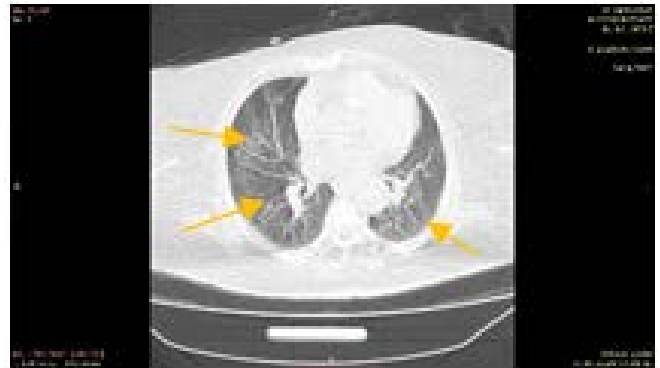


Figure D1



Figure D2

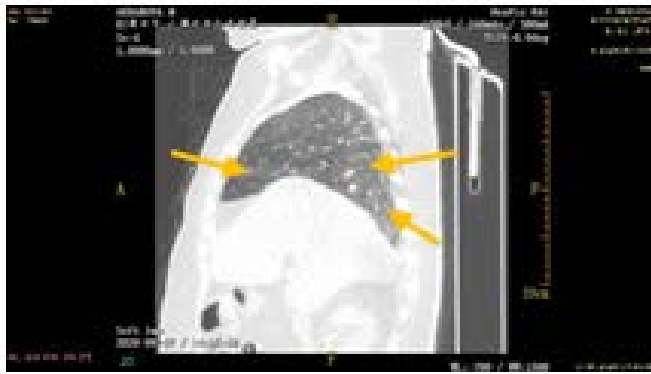


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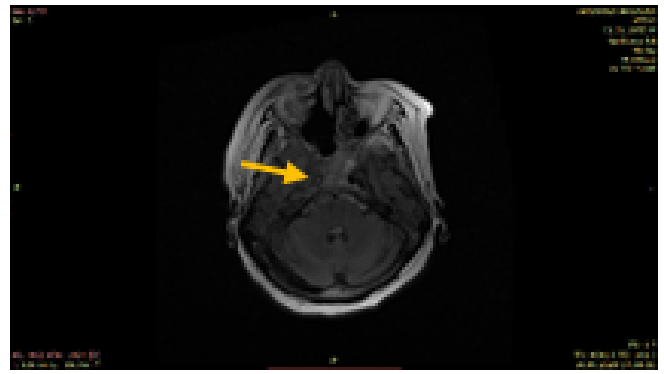


Figure F

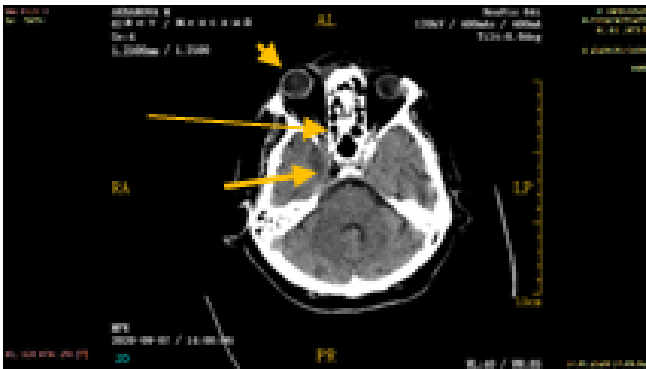


Figure E1

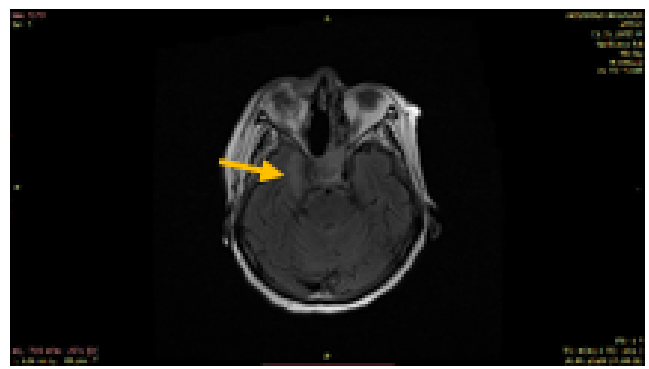


Figure G

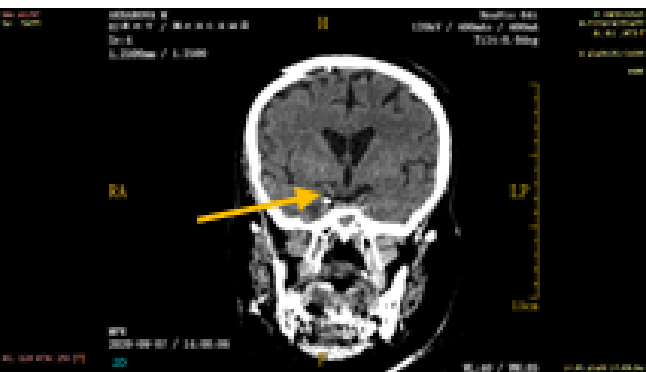


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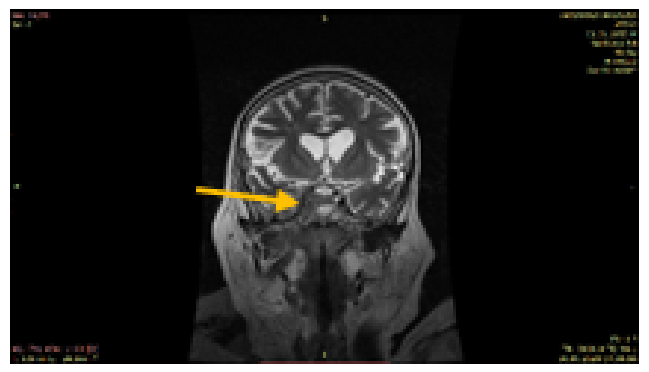


Figure H

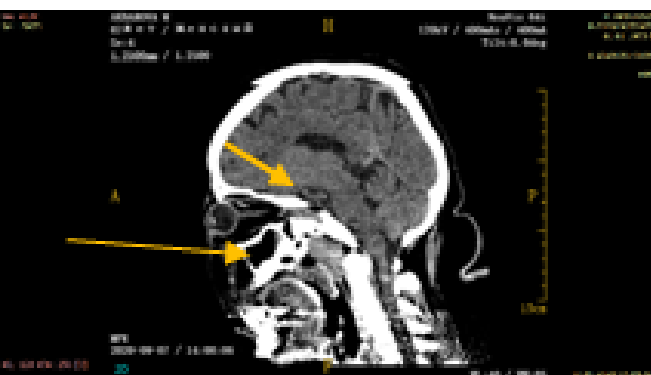


Figure E3

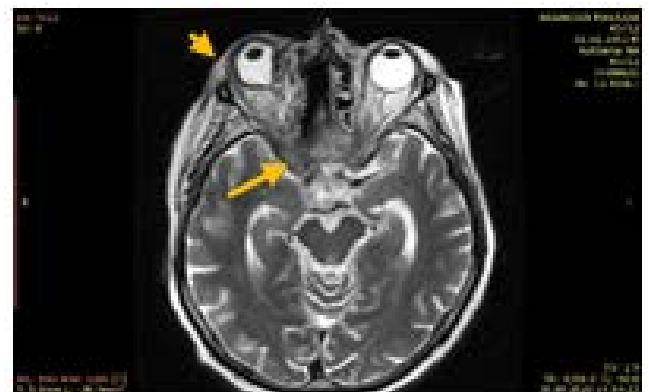


Figure I

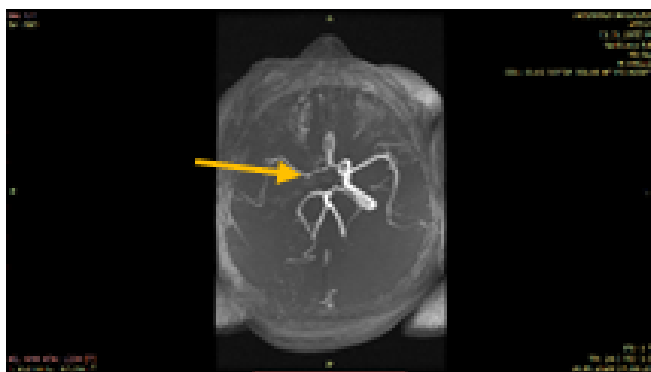


Figure J

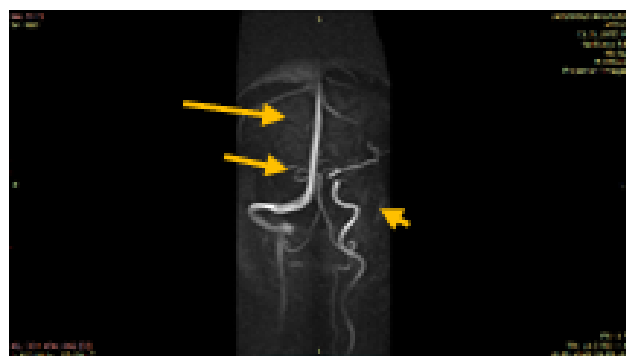


Figure K

**Figure 1.** **A)** Patient after functional endoscopic sinus surgery (arrowhead). Necrotic wound 0.8x2.5 cm of the glabella and right nasal dorsum (arrow). Inflammatory infiltration in the right infraorbital region and nasolabial fold, right upper eyelid ptosis. Patient after functional endoscopic sinus surgery to remove necrotic tissue from the nasal cavity. **B)** **B1.** Necrotic wound 2.0x5.0 cm of the right side of the hard palate covered with a fibrous film (arrow). The bottom of the necrotic wound is the hard palate bone. The mucous membrane around the necrosis is hyperemic. **B2.** After treatment: the absence of hyperemia around the necrotic wound the hard palate region (arrow). **C)** After treatment: no purulent discharge in the glabella and the right buccal region. **D)** **Chest CT scan D1.** axial, **D2** coronal, **D3** sagittal planes showed multiple patchy ground-glass opacities in bilateral areas, mainly in the central regions with a density of -510 to -520 HU. The vascular pattern

was enhanced, the intensity decreases from the center to the periphery. The density of the parenchyma in the remaining sections in the periphery was 880 HU, in the center 845 HU. **E)** **Brain and facial CT scan E1** axial, **E2** coronal, **E3** sagittal planes revealed **right cavernous sinus thrombosis** and enlargement (arrow), old pontine infarcts, right eye ptosis and orbital and periorbital swelling, gray discoloration with air-fluid content of ethmoid, sphenoid, maxillary, and frontal sinuses (thin arrow). In the projection of the right upper jaw, there were thick-walled cavities with the air bubbles content. There were hypodense foci +13 +16 HU of an irregular shape with a 10-20 mm diameter in the periventricular parts of the frontal, temporal and parietal lobes on the right side in the basin of the middle cerebral artery. Exophthalmos on the right (arrowhead). **F-I)** **Brain MRI without contrast. F, G, I)** Axial plane, thrombosis of the cavernous sinus (arrow). **H)** Coronal projection, cavernous sinus thrombosis (arrow). Infiltration of the right orbit, right exophthalmos (arrowhead). **J-K)** **Brain MRI with Angiography of cerebral vessels T1-SE sag, T2-SE cor-tra, T2-FLAIR tra, DWI, MRA, MRV: 5 mm.** Signs of acute ischemic stroke at the border of the basins of the right anterior and middle cerebral artery **J)** axial plane showed occlusion of right internal carotid artery (arrow). **K)** Cavernous sinus obstruction (arrow), hypoplasia of transversal and sigmoid sinus (arrowhead).