CASE REPORT

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Cavernous Sinus Thrombosis Due to Mucormycosis After COVID-19 Pneumonia

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ABSTRACT Coronavirus disease 2019 (COVID-19) could be complicated by venous or arterial stroke. However, to the best of our knowledge, there is a limited number of cases reported to develop cavernous sinus thrombosis (CST) after COVID-19. Herein, we present a 61-year-old diabetic male with persistent pain in his right forehead and periorbital region after COVID-19 pneumonia and diagnosed with CST after developing diplopia and periorbital ecchymosis. Magnetic resonance imaging revealed right maxillary sinusitis, inflammatory changes extending through the medial wall of the orbit and medial rectus muscle. CST was diagnosed. The mucormycosis was diagnosed by examining the extracted material with surgical thrombectomy. Appropriate surgical intervention, anticoagulant, and antifungal treatment yielded in a significant improvement in pain and orbital movements. In conclusion, in the presence of prothrombotic risk factors, like uncontrolled diabetes or recent COVID-19 infection, the physicians should consider the probability of CST in the differential diagnosis of persistent periorbital headache.

Keywords: Coronavirus; COVID-19; cavernous sinus thrombosis; mucormycosis

Novel coronavirus disease 2019 (COVID-19) is revealed to cause hypercoagulation, and systemic infection might complicate the patients with venous or arterial strokes by triggering systemic inflammation, endothelialitis, and thrombosis.[1-5] Poorly controlled diabetes was also associated with increased inflammation, hypercoagulation, low SaO2, and increased mortality in patients with COVID-19 infection.[6] The rate of cerebrovascular stroke is reported between 1.5% and 6% in COVID-19 infection, more in hospitalized patients older than 40 years of age.[2,3] However, to the best of our knowledge, there are a few case reports experiencing cavernous sinus thrombosis (CST) after COVID-19 infection up to date.[7,8]

CASE REPORT

A 61-year-old diabetic male was admitted with a resistant headache in his right forehead and periorbital region, and diplopia. In his past medical history, there was a history of hypertension and Type 2 diabetes mellitus (DM) for 10 years, and coronary bypass surgery 5 years ago. He had been using rivaroxaban (20 mg/day) during the last 10 months for the primary prevention of cardiac embolism as he has atrial fibrillation and heart failure. He had also used insulin therapy for Type 2 DM (insulin glargine 30 unit once in a day, s.c.). In addition, he was hospitalized and treated for COVID-19 pneumonia in our hospital for 10 days about 2 months ago.

Approximately 2 weeks after the discharge from our hospital, a frontal headache developed slowly and gradually increased. Within the last 2 days, a severe throbbing pain, including his right forehead and the periorbital region, was developed. His pain did not relieve with oral paracetamol (1,500 mg/day) and acemetacin (120 mg/day). The day after the onset of

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this headache, tearing, swelling, and redness on his right eyelid were also developed. He was admitted to the emergency room (ER) of another hospital. His headache did not relieved with parenteral analgesics, including intramuscular diclofenac and intravenous paracetamol. He was transferred to our ER. Cranial computed tomography and diffusion magnetic resonance imaging (MRI) did not reveal any abnormal findings. In laboratory examinations; glucose: 120 mg/dL, urea: 238 mg/dL, creatinine: 1.94 mg/dL, and Na: 123 mg/dL. Our internal diseases department consulted him for acute renal failure, and the relevant department hospitalized him to the primary intensive care unit. Although the urea and sodium levels were ameliorated with hydration, his periorbital pain was not relieved with parenteral analgesics (diclophenac sodium 75 mg twice in a day, i.m.) in clinical follow-up. His visual acuity was preserved in the ophthalmologic examination (0.4-0.6); however, diplopia was detected due to limitations in right globe movements and periorbital ecchymosis in right side. An ophthalmologist recommended neurology department consultation.

During our examination, direct and indirect light reflexes were slightly diminished, bilaterally. The movements of the right glob were painful and restricted almost completely in inward gaze, prominently in lateral gaze, and partially in upward gaze. Exophthalmos was also observed in his right eye.

Although the headache could be seen in many patients with COVID-19 infection, we excluded the diagnosis of COVID-19 related headache in our patient as there was a 3 weeks-interval between the diagnosis of COVID-19 and initiation of headache, and as he had a unilateral periorbital headache with restricted orbital movements and congestive findings which are commonly seen in locally invasive masses, suppurative infections, and CST.

Contrast-enhanced brain and orbital MRI was performed on the same day. It revealed a hyperintense material fulfilling the right maxillary sinus and inflammatory changes showing gadolinium enhancement in the mucosa of the sinus wall extending through the medial wall of the orbit and the right medial rectus muscle. In addition, contrast enhancement in periorbital soft tissues possibly secondary to infection was detected (Figure 1).

As his symptoms did not regress despite anticoagulant (enoxaparine 6,000 IU twice in a day s.c.), anti-inflammatory (diclophenac sodium 75 mg twice in a day, i.m. and oxymetazoline hydrochloride 0.05% twice in a day, intranasal), antibiotic [ceftriaxone 2 g/day intravenous (i.v.) and vancomycine 2 g/day i.v.] and antifungal (amphotericin B 70 mg/day i.v.) treatments, he was operated on for CST by our otolaryngology department. Mucormycosis was diagnosed with the examination of extracted thrombectomy material. Amphotericin B was sustained in a dosage of 50 mg per day.

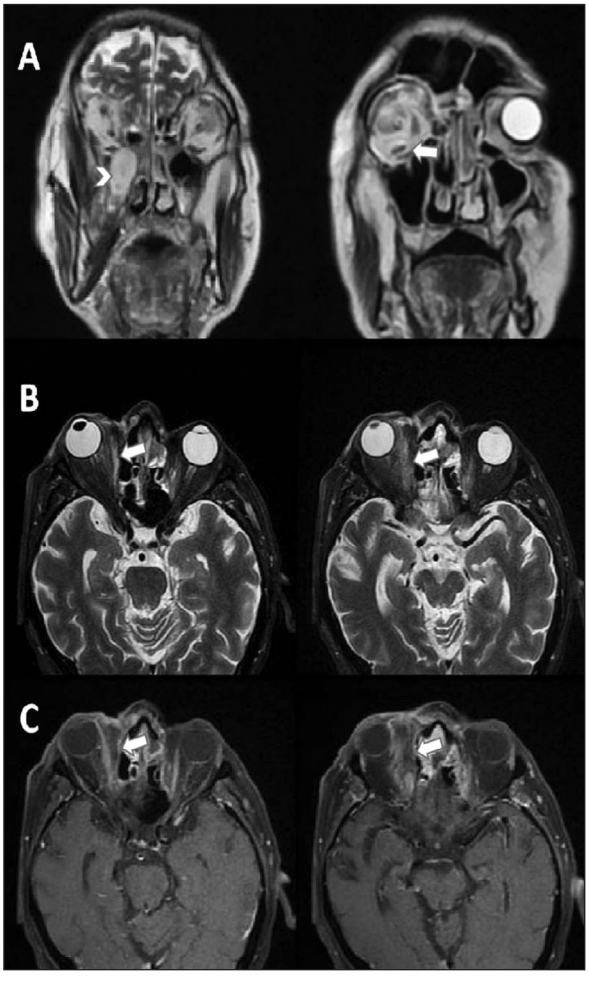

FIGURE 1: (A) Coronal T2-weighted sequences, **(B)** axial T2-weighted sequences, **(C)** contrast enhanced T1-weighted sequences of MRI revealing an hyperintense material fulfilling the right maxillary sinus (arrowhead), and inflammatory changes showing gadolinium enhancement in the mucosa of the sinus wall extending through the medial wall of the orbit and the right medial rectus muscle (arrows).
MRI: Magnetic resonance imaging.

He reported a significant improvement in his headache within the next few days in postoperative follow-ups. Partial improvement in eye movements was detected. There was a droopy eyelid, and no additional deficit was observed on his neurological examination.

Informed consent was obtained from the patient for participation of his clinical and radiological information in this report.

DISCUSSION

Headache is a common complaint in patients with viral infections. COVID-19 related headache was reported in 20-70% of the patients.[9-12] Bilateral headache, duration over 72 hours, analgesic resistance, fever, dehydration, previous primary headache, and having male gender were reported to be independent variables in differentiating the patients having headache associated with COVID-19 from ones not associated with COVID-19.[9,10] Various red flags like prior medical history, systemic symptoms, neurologic symptoms, fever, cough, and abnormal laboratory results including elevated C-reactive protein were reported to be present in most of the COVID-19 patients having a headache.[11] However, there was no reported universal red flag indicating the patient has a COVID-19 related headache. Although most of those clinical characteristics of headache associated with COVID-19 infection were present in our patient, we excluded it as there was a three weeks-interval between the diagnosis of COVID-19 and initiation of headache, and he had a unilateral headache with restricted orbital movements with congestion findings.

CST is among the rare causes of unilateral periorbital pain. Numbness, diplopia, vision loss due to cranial nerve impairments, eyelid edema, congestion, chemosis, and exophthalmos due to impaired venous drainage could also be commonly seen in these patients.[13] Pupils may be dilated, and papillary edema and retinal hemorrhages can be observed during fundus examination. Vision loss can progress to total blindness. Depending on the underlying infection; hyperemia, mucosal edema, fever, tachycardia, and neck stiffness could be accompanied.

Viral infections themselves could cause venous thromboembolism, including CST.[14] However, there is a limited number of case reports regarding the CST in COVID-19 patients up-to-date.[7,8] Recently, Khacha and colleagues reported a 55-year-old COVID-19 patient with no significant past medical history hospitalized for shortness of breath, fever, and the signs of dehydration.[7] He experienced acute frontal headache with diplopia, left exophthalmia with total ophthalmoplegia, and dilated pupil due to CST. He was treated with heparin infusion with curative dosages, and his headache and exophthalmia were reported to be started to fade away 1 week after the onset of the treatment. In another report, Aljanabi and colleagues presented a 52-year-old man experiencing bilateral CST who recovered uneventfully from mild COVID-19 infection 3 months ago.[8] He was not known to have chronic illnesses, but there was a history of teeth extraction 7 days before admission, involving the left and right upper 1st molars. He had progressive facial swelling, reduced vision, diplopia, and high-grade fever without any respiratory symptoms. There were bilateral orbital proptosis, chemosis, and restricted orbital movements at all gazes upon examination. There was no light perception in the left eye with a fixed and dilated pupil. The right side pupil was noted to have a sluggish reaction to light. He had elevated leukocytes (30,000 cubic millimeters) with predominantly neutrophilia and a high CRP level (above 300 mg/L). His glucose level was reported to be normal initially but deranged subsequently secondary to severe sepsis. Against the aggressive treatment with high dose triple antibiotics, high dose of heparin, and steroids, his condition deteriorated within 72 hours, and he died.

In conclusion, the presence of prothrombotic factors, like uncontrolled diabetes, dehydration, and recent severe COVID-19 infection should be evaluated as red flag signs for secondary causes in case of a resistant headache. Physicians should consider the probability of CST in the differential diagnosis of persistent unilateral periorbital pain. An early diagnosis with prompt medical interventions and surgery, if needed, could prevent possible mortality and morbidity.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

This study is entirely author's own work and no other author contribution.

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