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CASE REPORT Open Access

Covid-19-induced cavernous sinus thrombosis in a myelodysplastic syndrome patient: case report

Asuman Orhan Varoglu[1*], Asude Aksoy[2], Emre Akbas[1] and Basak Atalay[3]

Abstract

Background Cavernous sinus thrombosis (CST) is a very rare disease and can occur as a result of pharyngitis, a face infection, sinusitis, orbital cellulitis, otitis, traumatic injury, or surgery, particularly if the patient has a thrombophilic disease. So far, no myelodysplastic syndrome (MDS) cases with CST have been recorded. We describe a case of CST induced by Covid-19 in a patient with MDS.

Case presentation A 71-year-old woman with MDS was admitted to the hospital due to headache, weakness, diplopia, and drooping of the left eyelid. Pancytopenia was found. Left cavernous sinus thrombosis and encephalitis were also confirmed by Magnetic resonance imaging (MRI). A thorax Computed Tomography (CT) revealed bilateral patchy ground-glass opacities consistent with Covid-19. The patient was treated with low molecular weight heparin and discharged with partial recovery.

Conclusions It's important to remember that CST can occur in people with Covid-19 infection, even if they have severe thrombocytopenia like MDS.

Keywords Covid-19, Corona virus, Myelodysplastic syndrome, Cavernous sinus thrombosis, Thrombocytopenia, SARS-CoV-2

Introduction

CST is an uncommon and possibly fatal condition. The cavernous sinus is where the cranial nerves flow through (CN III-VI). By disrupting these tissues, CST can induce severe headaches, retro-orbital pain, visual abnormalities, and ophthalmoplegia. The sphenoid sinus and the cavernous sinus are anatomically connected. As a result of spreading through the collateral arteries or extending straight from the lateral sinus wall, acute bacterial or invasive fungal sinusitis produces thrombosis, resulting in CST development [1]. According to the published report, coagulation function is severely decreased in SARS-CoV-2 patients compared to healthy people, and D-dimer, fibrinogen, and fibrinogen degradation products should be monitored closely, especially in severe cases [2].

Myelodysplastic syndromes (MDS) are a diverse set of marrow-failing illnesses that typically affect elderly people but can also affect children and young people on occasion. The most frequent cytopenia in myelodysplastic syndromes (MDS) is anemia. Most MDS patients will need red blood cell (RBC) transfusions throughout the duration of their illness. The best approach for RBC transfusion in this patient population, however, is not widely agreed upon, unlike many other illness categories [3].

*Correspondence:
Asuman Orhan Varoglu
asumanorhan69@gmail.com
[1] Department of Neurology, Medical School, Istanbul Medeniyet University, Egitim Street, Fahrettin Kerim Gokay Street, Kadikoy, 34722 Istanbul, Turkey
[2] Department of Internal Medicine, Health Science University, Fethi Sekin Training, and Research Hospital, Elazıg, Turkey
[3] Department of Radiology, Medical School, Istanbul Medeniyet University, Istanbul, Turkey

Many investigations have shown that individuals with Covid-19 infection experience thromboembolic events in a variety of organs, including the lungs, heart, kidneys, and central nervous system. Authors have also attempted to explain the etiology of the increased thrombotic events associated with Covid-19 infection [4, 5].

Myelodysplastic syndrome (MDS) cases with CST have not been published yet. Despite severe thrombocytopenia owing to myelodysplastic disease, we describe a female case of CST induced by Covid-19.

Case report

For the past five days, a 71-year-old female patient with MDS has been admitted to our outpatient clinic with headaches, weakness, diplopia, and drooping of the left eyelid. The patient said that for around 10 days, she had complained of having a fever, cough, cold, and weakness. The patient's neurological examination revealed that the left eye had a limitation of downward, upward, and outward gazing, as well as ptosis and proptosis. The patient was taken to the hospital with abnormalities in the third and sixth cranial nerves and a preliminary diagnosis of CST. MDS, hyperlipidemia, hypothyroidism, and hypertension were all present in the patient. The first results of the patient's Covid-19 PCR test at the emergency room was negative. The patient had been diagnosed with MDS for three to four years and was receiving erythrocyte replacement every 3 weeks for MDS. Pancytopenia was discovered during the patient's laboratory evaluation. The Blood analysis results are summarized in Table 1. Fat-suppressed Orbita MRI shows left-sided extraconal phlegmon displacement of the medial rectus muscle and frontal dural enhancement. It was compatible with ethmoid and sphenoid sinusitis, and pachymeningeal contrast enhancement was identified in the left frontal area of the MRI (Fig. 1a–c). The lumbar puncture results are summarized in Table 2. There was no growth in the cerebrospinal fluid (CSF) culture and no growth in the mycobacteria culture. CSF tested negative for polymerase chain reaction (PCR) of cytomegalovirus, mycobacteria, herpes simplex virus 1–2, and meningitis panel. The lumbar puncture revealed mononuclear leukocytosis and an increase in protein, which was consistent with encephalitis. Galactomannan and 1,3-D-Glucan levels in serum were also negative. To rule out mucor infection, a sphenoid bone aspiration was conducted. The macroscopic inspection of the aspiration material revealed no Hyphae structure, and the pathology result was described as incompatible with Mucor infection. Blood cultures and tracheal aspirate cultures yielded no causal agent. The left superior ophthalmic vein and cavernous sinus were enlarged, and a temporal dural enhancement was discovered during the patient's follow-up, indicating CST (Fig. 2a, b). D-Dimer was 0.55 mg/L (0.55 mg/L), and fibrinogen was 545 mg/dl (200–400 mg/dl). For the treatment of CST, low molecular weight heparin at the appropriate dose after consulting hematology, and ampicillin-sulbactam treatments were started after

Table 1 Blood analysis

Platelets (100–400 uL)	White blood cell (4000–10000 uL)	Hemoglobin (13–17 g/dl)	D-dimer (< 0,55 mg/L)	C-reactive protein (0–5 mg/L)	Glucose (74–106 mg/dl)	INR (0.8–1,25)	PTT (25,6–33,6)	PT (11,5–15,5)	LDL (0–130 mg/dl)	TSH (0,54–4,31 µlU/ml)
34 10×3	3.5 10×3	6.6	0,55	63.85	102	1.37	63	17.7	79	2.42

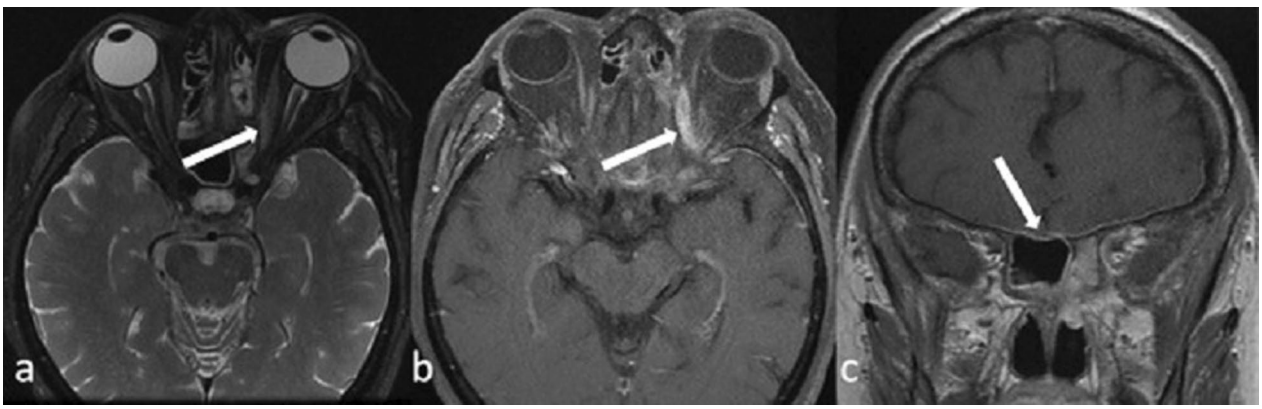

Fig. 1 **a** T2 weighted (W), **b** postcontrast T1W axial, and **c** postcontrast T1W sagittal images. Left-sided extraconal phlegmon and the displacement medial rectus muscle, frontal dural enhancement (White arrow). Ethmoid and sphenoid sinusitis

Table 2 Cerebrospinal fluid analysis

Protein (150–450 mg/L)	Glucose (40–70) mg/dl	Na (135–150 mmol/L)	K (2,7–3,9 mmol/L)	Cl (700–750 mg/dl)	White blood cell $\times 10^3/\mu L$	Mononuclear cells µL	Polynuclear cells µL	CSF/plasma glucose ratio
1009	49.9	137	2.58	112,8	157	77	80	49.9/102 = 0,49

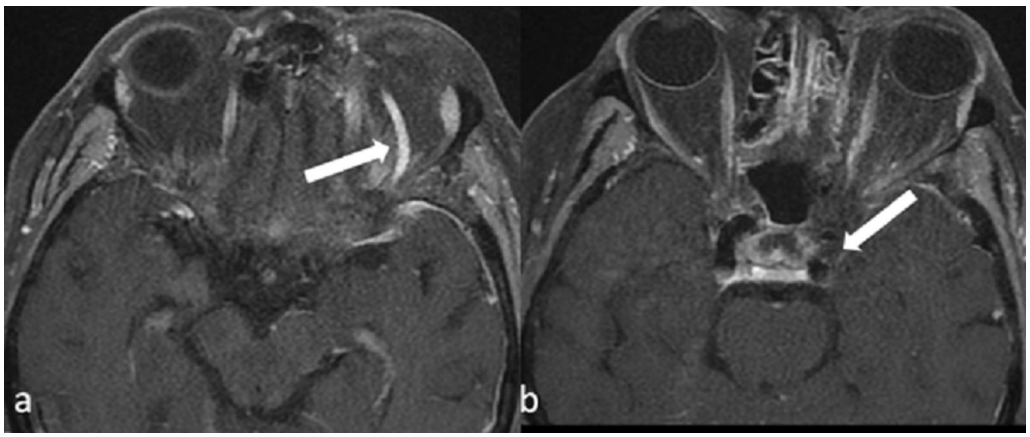

Fig. 2 **a** This case of orbital cellulitis spreading from a pansinusitis shows cavernous sinus thrombosis in follow-up, **b** axial T1W postcontrast images. The left superior ophthalmic vein is enlarging, cavernous sinus thrombosis, and temporal dural enhancement

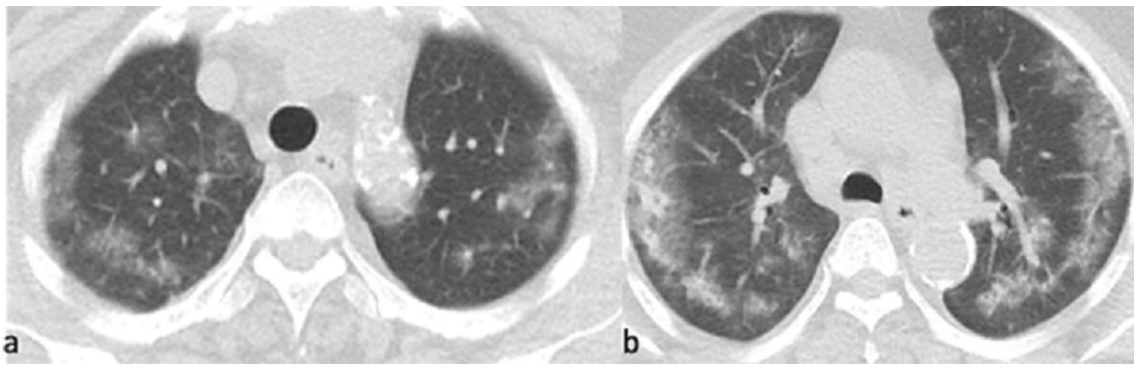

Fig. 3 Axial chest tomography images, **a**, **b** bilateral patchy ground glasses opacities

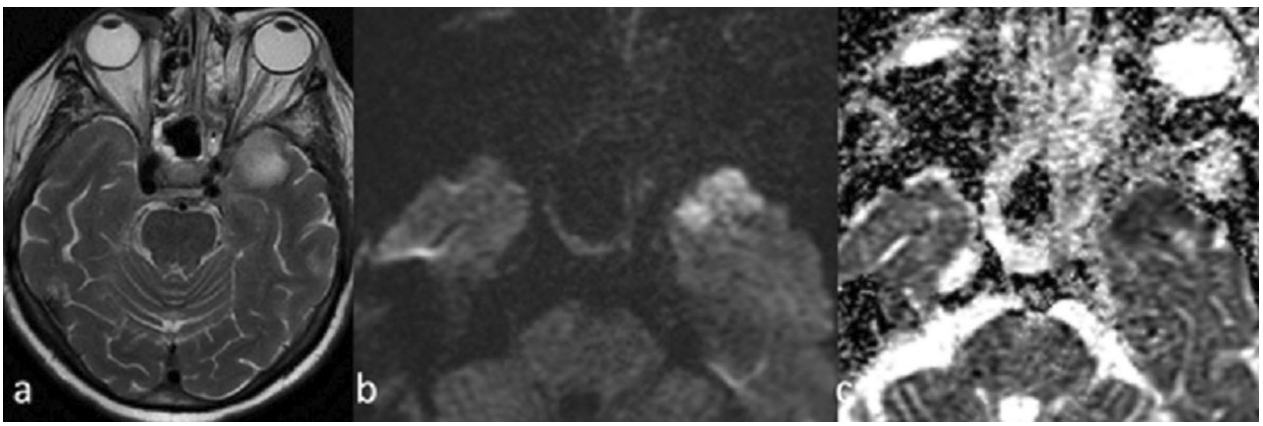

Fig. 4 **a** Axial T2W, **b**, **c** apparent diffusion coefficient images T2W hyperintense lesion shows diffusion restriction in the left temporal lobe. Findings of proptosis in the left orbit

consulting otolaryngology. Since blood O2 saturation was 34.5 mmHg (83–100 mmHg) during the follow-up, a thorax CT was conducted on the patient, and broad ground glass images were compatible with Covid-19 (Fig. 3a, b). The repeated Covid-19 PCR test was positive on the first day of admission to the hospital. Due to her clinic, laboratory data, and lung tomography, the patient was diagnosed with Covid-19. In the follow-up, the patient developed clouded consciousness and restricted cooperation. CST, which occurred following pansinusitis caused by Covid-19, was found in the patient with MDS. Combined liposomal amphotericin b, meropenem, and trimethoprim-sulfamethoxazole treatments were started for opportunistic infections. Despite therapy, the patient's condition worsened, and complete vision loss in the left eye resulted. A few days later, the patient experienced cerebral ischemia in the left arteria cerebri media region. The left temporal lobe had a diffusion limitation (Fig. 4a–c). After approximately 2–3 months, the patient was discharged with partial recovery.

Discussion

The severe acute respiratory syndrome is caused by a novel coronavirus (SARS-CoV-2). The authors claimed that endothelial problems are likely due to cytokines produced during the inflammatory response. It can trigger a systemic inflammatory response, which is referred to in the literature as a "storm of cytokines." The balance between procoagulant and anticoagulant processes was disrupted during this storm. They increase the development of coagulation by increasing procoagulant and antifibrinolytic activity such as the Von Willebrand factor resulting from the dysfunction of endothelial cells [4, 5].

Some authors asserted that circulating megakaryocytes (MKs) were to blame for the development of thrombosis in patients with immune thrombocytopenia (ITP), both those who were getting therapy and those who were not [6]. MKs can be stimulated to generate platelets by inflammatory cytokines such as interleukins [6]. According to Rapkiewicz, the same process also causes microthrombular formation in patients with Covid-19 [7]. A strong association was identified between the load of MKs in lung biopsies and fibrin microthrombus in a postmortem investigation of 22 individuals who died from major burns [8].

Platelet production is triggered by circulating MKs. MKs cells are physiologically most predominant in the lung bed. In addition, Megakaryocytes in the frontal cortex, basal ganglia, hippocampus, pons, midbrain, and thalamus were all found to have a more or less random distribution in people with Covid-19, influenza, non-communicable diseases, and control groups [9]. Also, as an independent factor, older age, splenectomy, and inflammatory disease syndrome all contribute to the development of thrombosis [6]. In patients with Covid-19 cerebral hemorrhages may occur due to dysregulated coagulation system and cerebral thrombosis may also develop as a result of megakaryocytes in the brain [10].

Myelodysplastic syndromes (MDS) are a diverse set of marrow-failing illnesses that typically affect elderly people but can also affect children and young people on occasion. The most frequent cytopenia in myelodysplastic syndromes (MDS) is anemia. Most MDS patients will need red blood cell (RBC) transfusions throughout the duration of their illness. The best approach for RBC transfusion in this patient population, however, is not widely agreed upon, unlike many other illness categories [3]. Our patient was receiving erythrocyte replacement every 3 weeks for MDS.

Even though thrombocytopenia can be noticed during the illness, we were unable to locate any research indicating that in the Covid-19 prognosis, it is an independent predictor. Being older than 55 years, several the existence of comorbidities, hypoxia, specific computed CT results suggestive of significant involvement of the lung, a wide range of abnormal laboratory test results, and end-organ failure symptoms are all related to higher disease severity and/or death [10]. Based on lab tests, Covid-19 infection in its early stages, and a rise in the concentrations of D-dimer and fibrinogen are connected to a bad prognosis. A three-to-four-fold rise in D-dimer levels is associated with a bad prognosis [4]. Our patient was a 71-year-old woman with comorbidities, elevated fibrinogen levels, hypoxia, and CT evidence of diffuse lung involvement. Even though our patient had significant thrombocytopenia owing to MDS, Covid-19 caused CST, which led to a cerebral infarction a few days later. Despite the existence of such serious findings, the present patient was hospitalized for 3 months and was discharged with partial recovery.

Rare incidences of vaccine-induced immunological thrombocytopenia and cerebral venous sinus thrombosis have been reported [11]. Only cerebral thrombosis in patients with ITP who have severe thrombocytopenia has been documented in the literature, but no instance of CST owing to Covid-19 in a patient with MDS has been published. In this situation, we believe that, even though our patient already has thrombocytopenia owing to MDS illness, cerebral venous infarction and cerebral infarction developed due to elevated interleukins caused by Covid-19 stimulation megakaryocyte development in the brain.

Conclusion

It is vital to remember that CST may occur as a result of interleukins produced as a result of Covid-19 in individuals with thrombocytopenia caused by MDS.

Abbreviations

CST	Cavernous sinus thrombosis
MDS	Myelodysplastic syndrome
CSF	Cerebrospinal fluid
Plt	Platelet
WBC	White blood cell
Hgb	Hemoglobin
MN	Mononuclear cells
PN	Polynuclear cells
PCR	Polymerase chain reaction
MKs	Megakaryocytes
ITP	Immune thrombocytopenia
CT	Computed Tomography
MRI	Magnetic resonance imaging

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Author contributions

Each author has made substantial contributions to the conception and design of the work; AOV was a major contributor to writing the manuscript and reviewed the literature, BA analyzed and interpreted the patient data regarding the radiological investigations, AA collected and analyzed the data, and EA reviewed the literature. All authors read and approved the final manuscript.

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Availability of data and materials

Data sharing is not applicable to this article as no data sets were generated or analyzed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Competing interests

The authors declare that they have no competing interests.

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References

1. Weerasinghe D, Lueck CJ. Septic cavernous sinus thrombosis: case report and review of the literature. Neuroophthalmology. 2016;40(6):263–76. https://doi.org/10.1080/01658107.2016.1230138.
2. Wang W, Sun Q, Bao Y, Liang M, Meng Q, Chen H, et al. Analysis of risk factors for thromboembolic events in 88 patients with COVID-19 pneumonia in Wuhan, China: a retrospective descriptive report. Med Sci Monit. 2021;27:e929708. https://doi.org/10.12659/MSM.929708.
3. Hughes CFM, Gallipoli P, Agarwal R. Design, implementation and clinical utility of next generation sequencing in myeloid malignancies: acute myeloid leukaemia and myelodysplastic syndrome. Pathology. 2021;53(3):328–38. https://doi.org/10.1016/j.pathol.2021.01.005.
4. Páramo JA. Inflammatory response in relation to COVID-19 and other prothrombotic phenotypes. Reumatol Clin (Engl Ed). 2022;18(1):1–4. https://doi.org/10.1016/j.reumae.2020.06.007.
5. Goshua G, Pine AB, Meizlish ML, Chang CH, Zhang H, Bahel P, et al. Endotheliopathy in COVID-19-associated coagulopathy: evidence from a single-centre, cross-sectional study. Lancet Haematol. 2020;7(8):e575–82. https://doi.org/10.1016/S2352-3026(20)30216-7.
6. Rodeghiero F. Is ITP a thrombophilic disorder? Am J Hematol. 2016;91(1):39–45. https://doi.org/10.1002/ajh.24234.
7. Rapkiewicz AV, Mai X, Carsons SE, Pittaluga S, Kleiner DE, Berger JS, et al. Megakaryocytes and platelet-fibrin thrombi characterize multiorgan thrombosis at autopsy in COVID-19: a case series. EClinical Med. 2020;24:100434. https://doi.org/10.1016/j.eclinm.2020.100434.
8. Wells S, Sissons M, Hasleton PS. Quantitation of pulmonary megakaryocytes and fibrin thrombi in patients dying from burns. Histopathology. 1984;8(3):517–27. https://doi.org/10.1111/j.1365-2559.1984.tb02361.x.
9. McMullen P, Smith H, Pytel P. Entrapped megakaryocytes in the microvasculature of brain tissues are not specific to COVID-19 but can be seen across a spectrum of acute lung injuries. J Neuropathol Exp Neurol. 2021;17:048. https://doi.org/10.1093/jnen/nlab048.
10. Gallo Marin B, Aghagoli G, Lavine K, Yang L, Siff EJ, Chiang SS, et al. Predictors of COVID-19 severity: a literature review. Rev Med Virol. 2021;31(1):1–10. https://doi.org/10.1002/rmv.2146.
11. Finsterer J, Zarrouk S. Post-SARS-CoV-2 vaccination venous sinus thrombosis: a literature review of 308 cases. Egypt J Neurol Psychiatr Neurosurg. 2021;57(1):179. https://doi.org/10.1186/s41983-021-00431-z.

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