

# May Covid-19 cause intracerebral hemorrhage in patients with cavernous malformation?

## Covid-19, kavernöz malformasyonlu hastalarda intraserebral kanama'ya neden olabilir mi?

Ali Şahin<sup>1</sup>, Şükrü Oral<sup>1</sup>, Esmâ Eren<sup>2</sup>

<sup>1</sup> Kayseri City Education and Research Hospital, Department of Neurosurgery, Kayseri, Turkey

<sup>2</sup> Kayseri City Education and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, Kayseri, Turkey

ORCID ID of the author(s)

AS: 0000-0001-7231-2394

ŞO: 0000-0003-4328-0690

EE: 0000-0002-2712-9694

### Abstract

Coronavirus disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, has become a global health threat. COVID-19 often involves the respiratory tract, however, it is also associated with several neurological conditions (seizures, convulsions, changes in consciousness, encephalitis, cerebral hemorrhage, and cerebral thrombosis). Cavernous malformations (CMs) are vascular lesions that occur in the central nervous system and the body. Symptomatic CMs most manifest through headaches, seizures, hemorrhage, or focal neurological deficits. The co-occurrence of COVID-19 and cavernous hemangioma hemorrhage has not been reported in the literature. The association between COVID-19 and intracerebral hemorrhage remains controversial. However, a relationship with COVID-19 infection in patients with intracerebral hemorrhage should always be considered during this pandemic. The case of a 37-year-old female patient is reported here. The patient presented to the emergency room with a headache that persisted for 2 days along with cavernous hemangioma hemorrhage and tested positive for COVID-19.

**Keywords:** COVID-19, Hemangioma, Cavernous

### Öz

SARS-CoV-2 virüsünün neden olduğu Coronavirus hastalığı 2019 (COVID-19), küresel bir sağlık tehdidi haline geldi. COVID-19 genellikle solunum yolunu tutar; bununla birlikte çeşitli nörolojik durumlara (nöbetler, konvülsiyonlar, bilinç değişiklikleri, ensefalit, serebral hemoraji ve serebral tromboz) ilişkili olduğu da bulunmuştur. Kavernöz malformasyonlar (KM), merkezi sinir sisteminde ve vücutta meydana gelen vasküler lezyonlardır. Semptomatik KM'ler en yaygın olarak baş ağrısı, nöbetler, kanama veya fokal nörolojik defisitlerle kendini gösterir. Literatürde COVID-19 ile kavernöz hemanjiyom kanamasının birlikte görülmesi bildirilmemiştir. COVID-19 ile intraserebral hemoraji arasındaki ilişki tartışmalıdır. Bununla birlikte, intraserebral hemorajili hastalarda COVID-19 enfeksiyonu ile bir ilişki bu pandemi sırasında her zaman dikkate alınmalıdır. 37 yaşında bir kadın hastanın vakası burada bildirilmektedir. Hasta kavernöz hemanjiyom kanaması ile birlikte 2 gün süren baş ağrısı ile acil servise başvurdu ve ayrıca COVID-19 testi pozitif çıktı.

**Anahtar kelimeler:** COVID-19, Hemanjiom, Kavernöz

## Introduction

Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2 virus, was first described in Wuhan, China in December 2019 and has become a global health threat. Most patients with COVID-19 manifest respiratory tract symptoms; however, extrapulmonary manifestations have also been reported. Fever, cough, myalgia, weakness, shortness of breath, headache, nausea, vomiting, diarrhea, and anosmia are common symptoms [1]. Patients may develop pneumonia, acute respiratory distress syndrome and multiorgan failure in severe cases.

COVID-19 has been associated with several neurological pathologies (seizures, convulsions, changes in consciousness, encephalitis, intracerebral hemorrhage [ICH] and cerebral thrombosis) [2].

Cavernous malformations (CMs) are vascular lesions in the central nervous system (CNS) and the body. CMs are also referred to as cavernomas, cavernous angiomas or cavernous hemangiomas. Their prevalence ranges from 0.4% to 0.6% [3]. They can be observed anywhere in the CNS. They usually are not symptomatic. Symptomatic CMs are most often manifested by headaches, seizures, hemorrhage, or focal neurological deficit [4].

Here, the case of a 37-year-old female patient is reported. The patient presented to the emergency room with a persistent headache for 2 days and had a hemorrhage of the cavernous hemangioma and tested positive for COVID-19.

Corresponding author / Sorumlu yazar:  
Ali Şahin  
Address / Adres: Kayseri Şehir Eğitim ve  
Araştırma Hastanesi, Nöroşirurji Kliniği, Kayseri,  
Türkiye  
E-mail: dralishn@gmail.com

Informed Consent: The authors stated that the written consent was obtained from the patient presented with images in the study.

Hasta Onamı: Yazarlar çalışmada görüntüleri ile sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.

Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Published: 10/28/2020  
Yayın Tarihi: 28.10.2020

Copyright © 2020 The Author(s)  
Published by JOSAM

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-NoDerivatives License 4.0 (CC BY-NC-ND 4.0) where it is permissible to download, share, remix, transform, and build upon the work provided it is properly cited. The work cannot be used commercially without permission from the journal.



## Case presentation

A 37-year-old female patient presented to the emergency room with a severe headache that persisted for 2 days. The results of neurological examination were normal. She had no history of trauma and no additional diseases. She had no history of use of anti-aggregates or anticoagulants. Her blood pressure was 120/80 mm Hg. C-reactive protein was 9 mg/L, and D-dimer was 480  $\mu\text{g/L}$ . Liver function test results were normal. No hematological abnormalities such as thrombocytopenia or hemorrhagic diathesis were found. As a large number of patients with COVID-19 report headache as a key symptom, a throat swab was taken from the patient. Real-time polymerase chain reaction (PCR) test was performed with the throat swab sample, which confirmed COVID-19. Ground-glass opacity was seen in the lower left lobe of the lung that could be consistent with COVID-19 on computed tomography (CT) of the thorax (Figure 1). On the brain CT performed to exclude neurological pathologies, an ICH sized  $1 \times 1 \text{ cm}^2$  was seen in the right frontal region (Figure 2a) and the hemorrhage in the right frontal region was consistent with a cavernous hemangioma in the magnetic resonance imaging (Figure 2b, 2c). The patient's general condition was good, and her neurological examination was normal. Therefore, she was not considered for any surgical intervention and admitted to the pandemic ward. Treatment was initiated for COVID-19. However, she did not need treatment in the intensive care during her hospitalization. The patient's follow-up PCR on the fifth day was positive. Follow-up CT performed on the 10<sup>th</sup> day revealed that the bleeding was resorbed. The patient's condition improved, and she was discharged after 11 days of hospitalization with an advice to isolate herself at home to prevent the spread of infection among family members.

Written informed consent was obtained from the patient for this case report.

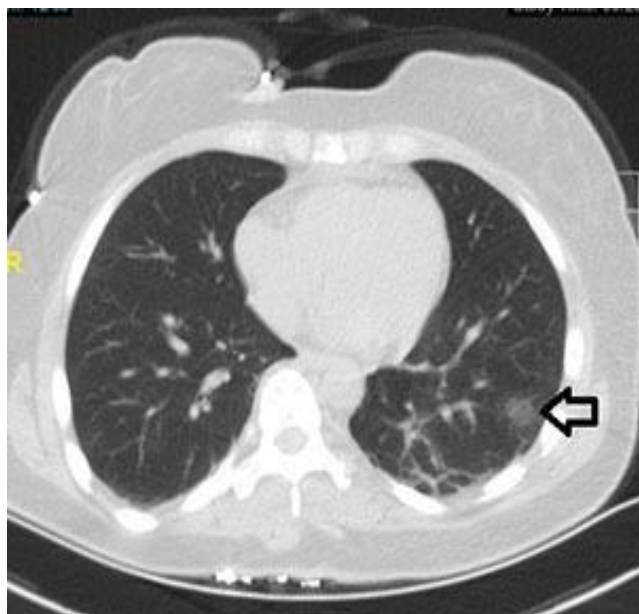


Figure 1: Axial non-contrast-enhanced thoracic computed tomography image in the parenchyma window shows area of infiltration with ground-glass density at the lower lobe of the left lung.

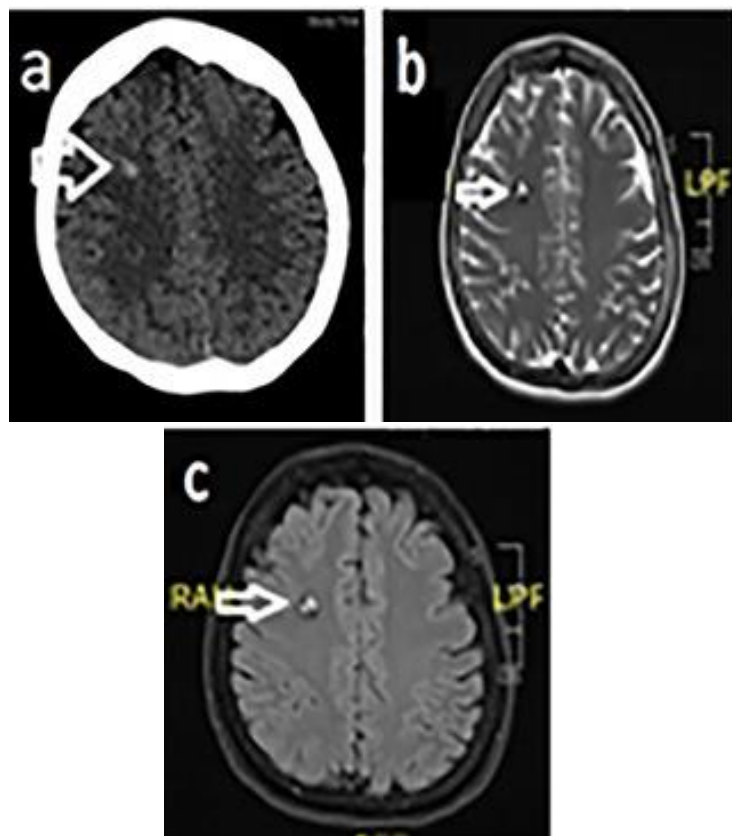


Figure 2: (a) CT brain showing hemorrhage in the right frontal region. T2 axial (b) and FLAIR axial (c) section of MRI brain showing hemorrhage related with cavernous hemangioma in the right frontal lobe.

## Discussion

COVID-19 has affected individuals worldwide. However, individuals also have to cope with financial and social disturbances during this period [5]. Its clinical manifestations vary; it can be asymptomatic, mild or severe.

Respiratory involvement is very common in patients with COVID 19, and patients often present with typical symptoms such as fever, cough, weakness and diarrhoea [1]. Some patients may exhibit neurological symptoms only, without the typical symptoms of COVID-19. Dizziness and headache are the most common neurological symptoms [2]. Our patient had severe headaches with no other additional symptoms.

Our patient was young, aged 37 years. As morbidity and mortality increase with advanced age in COVID-19, our case was found to be interesting in this regard [6].

Cavernous haemangiomas are usually located in the supratentorial region. The rate of occurrence of haemorrhage varies between 2.6% and 3.1% annually [3]. CM was supratentorial and located in the right frontal region in our patient.

Lobar ICH occurs in 15%–30% of conventional cases and is predominantly associated with an underlying vascular anomaly [7]. Cavernous haemangiomas, which are among vascular malformations, comprise enlarged blood vessels that do not have smooth muscle cells or elastic fibres in their walls and are covered only by a single layer of epithelium, and there is no normal neural tissue between these vessels. Therefore, it is considered that they can easily bleed [4]. There may also be lobar haemorrhages in COVID-19, and anterior circulation and frontal lobe may be affected [8]. The haemorrhage occurred in

the right frontal lobe, and a concomitant cavernous malformation was observed in our patient.

The association between COVID-19 and ICH is controversial. However, it is established that the virus can directly reach the CNS through the olfactory receptors of the cranial nerve I in the nasal cavity cell membrane and cause neurological problems in patients [9,10].

Some publications support the association of COVID-19 with ICH and indicate possible mechanisms. Sharifi-Razavi et al. [9] and Md Noh et al. [11] reported that COVID-19 acts through angiotensin-converting enzyme (ACE) II receptors, filling ACE II receptors and may reduce the expression of ACE II and increase the risk of cerebral haemorrhage owing to high blood pressure. Levi et al. [12] reported that the risk of cerebral haemorrhage, elevated D-dimer and coagulopathy may increase secondary to prolonged prothrombin time in patients with COVID-19. Bengler et al. [8] reported that COVID-19-mediated ICH was caused by endothelial damage and indicated that both direct and indirect endothelial toxicity and renin-angiotensin system disruption were possible mechanisms.

### Conclusion

Although headache is a common symptom in patients with COVID-19, our case is interesting because she also had haemorrhage of cavernous haemangioma. To our knowledge, the co-occurrence of COVID-19 and cavernous haemangioma haemorrhage has not been reported in the literature. The relationship between COVID-19 and ICH remains controversial. To date, the evidence obtained shows a fairly low prevalence of cerebral haemorrhage in infected patients. However, a relationship with COVID-19 infection should always be considered in patients presenting with ICH during this pandemic.

### References

1. Sahin AR, Erdogan A, Agaoglu PM, Dineri Y, Cakirci AY, Senel ME, et al. 2019 novel coronavirus (COVID-19) outbreak: a review of the current literature. *EJMO*. 2020;4:1-7. doi: 10.14744/ejmo.2020.12220.
2. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol*. 2020;77(6):683-90. doi: 10.1001/jamaneurol.2020.1127.
3. Moriarity JL, Clatterbuck RE, Rigamonti D. The natural history of cavernous malformations. *Neurosurg Clin*. 1999;10(3):411-7. doi: 10.1016/S1042-3680(18)30175-X.
4. Smith ER, Scott RM. Cavernous malformations. *Neurosurg Clin North Am*. 2010;21(3):483-90. doi: 10.1016/j.nec.2010.03.003.
5. Demir ÜF. The effect of COVID-19 pandemic on sleeping status. *J Surg Med*. 2020;4(5):334-9.
6. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054-62. doi: 10.1016/S0140-6736(20)30566-3.
7. Aguilar MI, Brott TG. Update in intracerebral hemorrhage. *Neurohospitalist*. 2011;1(3):148-59. doi: 10.1177/1941875211409050.
8. Bengler M, Williams O, Siddiqui J, Sztrihai L. Intracerebral haemorrhage (ICH) and COVID-19: Clinical characteristics from a case series. *Brain Behav Immunity*. 2020;88:940-4. doi: 10.1016/j.bbi.2020.06.005
9. Sharifi-Razavi A, Karimi N, Rouhani N. COVID-19 and intracerebral haemorrhage: causative or coincidental? *New Microbes New Infect*. 2020; 35: 100669. doi: 10.1016/j.nmni.2020.100669
10. Bohmwald K, Galvez N, Rios M, Kalergis AM. Neurologic alterations due to respiratory virus infections. *Front Cell Neurosci*. 2018;12:386. doi: 10.3389/fncel.2018.00386
11. Md Noh MSF. COVID-19 and Cerebral Hemorrhage: Proposed Mechanisms, *J Neuroradiol*. 2020 Jun 1. doi: 10.1016/j.neurad.2020.05.007 (Epub ahead of print)
12. Levi M, Thachil J, Iba T, Levy JH. Coagulation abnormalities and thrombosis in patients with COVID-19. *Lancet Haematol*. 2020;7(6):e438-40. doi: 10.1016/S2352-3026(20)30145-9

This paper has been checked for language accuracy by JOSAM editors.

The National Library of Medicine (NLM) citation style guide has been used in this paper.