De novo hemorrhagic sporadic cavernous malformation appearance after COVID-19 respiratory infection: illustrative case

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BACKGROUND Little is known about whether coronavirus disease 2019 (COVID-19) influences cavernous malformation (CM) formation or hemorrhage risk.

OBSERVATIONS The authors present the case of a 31-year-old patient who developed a hemorrhagic, de novo CM in the setting of a developmental venous anomaly within 3 months of COVID-19 respiratory disease. The authors speculate that COVID-19 disease stimulated formation of the CM through TLR4 inflammatory pathways and subsequently led to the hemorrhagic presentation because of hypercoagulability related to the disease.

LESSONS This case raises the possibility that COVID-19 may be a risk factor for de novo development of CMs in predisposed patients.

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KEYWORDS cavernous malformation; cavernous angioma; COVID-19; inflammation

Very little has been published regarding the influence of coronavirus disease 19 (COVID-19) on cavernous malformation (CM) formation and hemorrhage. A recent, small study suggests a possible increased risk of CM hemorrhage in patients who develop COVID-19.1 To date, there have been no reported cases of de novo CM formation in the setting of COVID-19.

Illustrative Case

In the summer of 2020, our patient, a 31-year-old female, developed mild galactorrhea and was subsequently found to have mildly elevated prolactin level. A brain MRI with dedicated pituitary sequences showed no pituitary abnormality and was otherwise unremarkable with exception of a right temporal developmental venous anomaly (DVA) without an associated CM (Fig. 1 upper).

In late March 2021, the patient contracted COVID-19 and experienced symptoms of headache, extreme lethargy, and shortness of breath. After the acute illness, she has continued to experience chronic, residual symptoms, including fatigue, shortness of breath, and intermittent dizziness.

In early June 2021, the patient awoke with symptoms of tachycardia, visual illusions, depersonalization, and emotional lability that progressed over the course of 1 day. At this time, she visited a local emergency department and was diagnosed with a panic attack after a negative cardiac workup without neurological investigation. Over the course of the next 4 weeks, symptoms persisted, and certain shapes and patterns remained distorted, “like a funhouse.” Due to persistent symptoms, she again sought medical attention and was diagnosed with a migraine. The patient ultimately sought care for the third time. At that time, the patient finally received head imaging. Noncontrast computed tomography of the head demonstrated a 12-mm intraparenchymal hemorrhage of the right temporal lobe. Subsequent magnetic resonance imaging (MRI) of the brain showed the characteristic appearance of a sporadic hemorrhagic CM with associated DVA and surrounding edema (Fig. 1 lower). She underwent 36-hour prolonged encephalogram monitoring without evidence of epileptiform discharges.

Following discharge, the patient continued to have fluctuating severe anxiety and depersonalization requiring multiple trials of psychiatric medications. Ultimately, her symptoms improved with Paxil and Seroquel. By the fall of 2021, symptoms of depersonalization and visual distortions had nearly resolved.

ABBREVIATIONS CM = cavernous malformation; COVID-19 = coronavirus disease 2019; DVA = developmental venous anomaly; MRI = magnetic resonance imaging.

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fl thought to play a role in the inflammatory syndrome coronavirus 2 can bind to TLR4 receptors and are It is known that the spike glycoprotein of the severe acute respiratory system may have triggered the TLR4 pathway, resulting in lesion formation. According to the appearance of a CM. The acute inflammatory response may have triggered the TLR4 pathway, resulting in lesion formation. It is known that the spike glycoprotein of the severe acute respiratory syndrome coronavirus 2 can bind to TLR4 receptors and are thought to play a role in the inflammation associated with the disease. In addition, because COVID-19 is associated with venous thrombotic events, it is plausible that the patient in question may have developed thrombosis of one of the radicles of the DVA, resulting in outflow resistance and poor CM drainage with resultant increased pressure in the fragile cavernous endothelial walls resulting in rupture. A recent report has also raised this possibility in patients with COVID-19.

The MRI scan performed in the summer of 2020 was dedicated to the pituitary gland and did not contain susceptibility weighted images. It is possible that she may have had a very tiny, Zabramski type 4 CM present, but this does not take away the fact that the aggressive behavior of her lesion occurred after the COVID-19 respiratory disease.

In conclusion, we believe this case raises questions about the possibility that de novo formation of a CM adjacent to a preexisting DVA may be triggered shortly (within a few weeks and not years) after a significant inflammatory response and, in particular, COVID-19. Further studies may elucidate whether there are specific precautions patients with DVA may take to reduce the risk.

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