Case Report:

Non-aneurysmal Perimesencephalic Subarachnoid Hemorrhage in A COVID-19 Patient: Case Report and Review on Subarachnoid Hemorrhage Patterns in COVID-19

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ABSTRACT

Background and Importance: The novel SARS-CoV-2 virus has had an undeniable effect worldwide in different aspects. Although cerebrovascular diseases, especially Subarachnoid Hemorrhage (SAH), have already been reported in COVID-19 patients, little is known about various types and patterns of SAH in these patients.

Case Presantation: A 63-year-old woman was admitted to the emergency department with a headache. Her headache was severe (Hunt and Hess score, grade 2). She was diagnosed with COVID-19 by a positive nasopharyngeal swab PCR test. Her CT scan revealed a perimesencephalic hemorrhage, thick SAH without any signs of hydrocephalus or intraventricular hemorrhage.

Conclusion: Regarding the different associations of SAH with COVID-19, the perimesencephalic hemorrhage in our case is a novel type. Although not uncommon among non-infected populations, SAH occurrence in COVID-19 patients has not been reported before and needs further investigation.

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Highlights

- The novel SARS-CoV-2 virus has had an undeniable effect worldwide.
- Perimesencephalic hemorrhage is a novel type of subarachnoid hemorrhage among COVID-19 patients.

Plain Language Summary

COVID-19 virus has had a major impact on our lives today. It can affect different parts and systems of the body. In the brain, it can lead to a special type of bleeding named subarachnoid hemorrhage which can be fatal in uncontrolled cases. Understanding the exact association of the virus with the blood vessels of the brain can help us to manage such cases efficiently. In this article, we have introduced a new case of such bleeding in the brain in a patient with COVID-19 infection. We have managed our case non-surgically and fortunately, she recovered well.

1. Background and Importance

The novel SARS-CoV-2 virus has had an undeniable effect worldwide in different aspects. High numbers of daily positive cases and mortality, together with its novelty, have been a great motivation for different researchers to investigate different aspects of this novel disease. In this regard, seeking the coexistent non-respiratory symptoms in infected patients and their relation to the actual pathology is a growing field of research.

Although cerebrovascular diseases and especially Subarachnoid Hemorrhage (SAH), have already been reported in COVID-19 patients [1], little is known about types and patterns of SAH in COVID-19 patients. Hence, besides presenting a novel association between COVID-19 and SAH in a patient, we aimed to review the literature to find the patterns of SAH in COVID-19 patients.

2. Case Presentation

A 63-year-old woman was presented in the emergency department with a headache. Her headache was severe (Hunt and Hess scale, grade 2) [2], bilateral, with a new-onset, and progressive, accompanied by nausea and two episodes of vomiting. She had been admitted to another hospital for dry coughs and fever a week before and was diagnosed with COVID-19 by a positive nasopharyngeal swab Polymerase Chain Reaction (PCR) test. However, she still complained of dry cough without dyspnea.

Her past medical history was positive for diabetes and hypertension, which were under treatment with aspirin 80 mg daily, metformin 1 g daily, long- and short-acting insulins, losartan 25 mg BID, and atorvastatin 20 mg daily. She had no history of alcohol, tobacco, or other substance use. On admission, her vital signs were normal. Her blood pressure was 120/75 mm Hg. She had a normal temperature, SpO_2, and respiratory rate. Her Glasgow Coma Scale (GCS) on admission was 15. Pupils were normal in size and reactive. She had no other abnormal neurological examination.

Due to her worsening headache and nausea, she underwent a brain Computerized Tomography (CT) scan without contrast. Her CT revealed a perimesencephalic, thick SAH without any signs of hydrocephalus or intraventricular hemorrhage (Fisher grade III) [3]. No intraparenchymal hemorrhage, no midline shift, and no signs of mass were detected. She was immediately treated with an antiepileptic drug (levetiracetam), nimodipine for vasospasm prevention, and analgesics for her severe headache. She underwent a control brain CT scan 6 hours later and a brain CT angiogram to identify any vascular abnormalities. The new imaging did not show any hematoma expansion, hydrocephalus, or vascular anomaly.

According to the protocols of our center for SAH evaluation, Digital Subtraction Angiography (DSA) was performed for the patient, and no vascular abnormalities were detected. She stayed in the hospital for 10 days, and her symptoms, including headache and vomiting, improved, and she was discharged without any new symptoms. Two weeks after SAH, another DSA was performed, which was negative for any vascular abnormalities.

3. Discussion

More than a year has passed since the outbreak of COVID-19 disease caused by SARS-CoV-2. Still, there is an ambiguity about its effects on non-respiratory organs. The nervous system is not an exception, and the

association between neurological events and COVID-19 infection is unclear. One of the important coexisting events reported in COVID-19 patients is subarachnoid hemorrhage. This type of intracranial hemorrhage has gained special attention both in clinic and research due to its association with aneurysms and potential danger. Unfortunately, there is no clear review and classification of this issue in the literature. Hence, we aimed to report a novel association between SAH and COVID-19 (non-aneurysmal pure perimesencephalic SAH) and tried to identify different patterns in a review.

Eleven studies reporting 29 cases of SAH hemorrhage in COVID-19 patients in English literature were found. All COVID-19 infections were confirmed by nasopharyngeal swab PCR or COVID-19 IgM/IgG assays. Two patients had no respiratory symptoms simultaneous with SAH diagnosis and were only diagnosed with COVID-19 after abnormal chest CT findings and subsequent PCR/IgM tests. Most cases had a close confirmed COVID-19 diagnosis (up to 4 months interval). It is important to note that only 2 patients presented with respiratory symptoms, and others had neurological signs or symptoms [4].

Demographic factors

The details of 11 patients were not evident in one study [5]; therefore, detailed demographic data could not be obtained. Table 1 depicts the details of some of these studies. Of the other 18 patients, most were female (10), and their mean age was 47.5 years (ranged 9-74).

SAH patterns

The patterns of hemorrhage can be grouped into aneurysmal and non-aneurysmal. Eight cases did not undergo any angiographic study either DSA (Digital Subtraction Angiography) or CTA (Computed Tomography Angiography), and of the other 21 cases, and of the other 21 cases, 4 were positive for aneurysms [4-6]. The non-aneurysmal types (confirmed by angiographic studies) can further be grouped into 6 subtypes:

- Cortical or hemispheric SAH
- Pseudo- or post-resuscitation SAH
- Perimesencephalic (present case)
- Sylvian cisterns
- Interhemispheric fissure
- Not defined in the article

Cortical SAH had the most case reports, of which 5 patients did not undergo any angiographic studies to rule

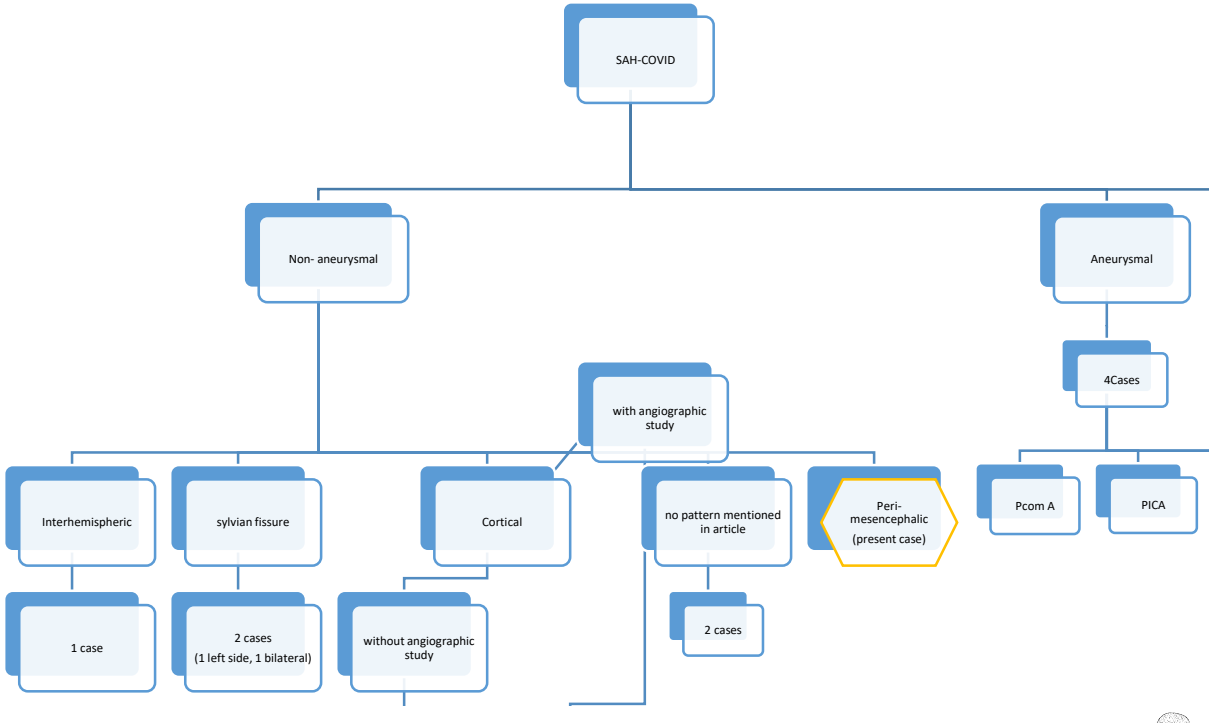

Figure 1. Different types of SAH reviewed in this study

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Table 1. Studies reporting on different cases of subarachnoid hemorrhage in detail

No.	Authors [Ref.]	No. of SAH cases	Age, y	Sex	PMH	SAH pattern	Additional CT Findings	Aneurysm	Res PCR	CSF PCR	Presenting Symptoms	Respiratory Symptoms	Outcome
1	Al Saiegh et al. [4]	1	31	M	Neg	Posterior fossa	Fourth ventricle. IVH	Dissecting PICA a.	+	-	LOC	+	Dischraged
2	Cezar-junior et al. [5]	4	36	F	-	Basal cisterns	IVH + hydrocephalus	ICA a.	+	N/A	Headache, cough, fever	+	Discharged
			53	M	N/A	Basal cisterns + left Sylvian fissure	-	-	+	N/A	Headache	+	Discharged
			61	F	N/A	Bilateral Sylvian	Hydrocephalus	N/A	+	N/A	Cough fever myalgia	+	Deceased
			71	F	N/A	Interhemispheric	-	-	+	N/A	Headache+ hemiparesis	+	Discharged
3	Craen et al. [10]	1	66	F	HTN, HLP, DM	Pseudo-SAH	Severe edema	-	+	N/A	Cardiac arrest	+	Deceased
4	de Castillo et al. [7]	1	64	M	HTN, Smoker	Unilateral Cortical SAH	Occipital and thalamus infarction	N/A	+	-	Hemiparesis dysarthria	-	Discharged
5	Nawabi et al. [11]	11	Not detailed for SAH patients	Not mentioned for SAH patients	Not mentioned for SAH patients	9/11 cortical 4/11 bilateral	1 case with ICH 1 case with SDH	0/11	+	N/A	Not detailed for SAH patients, but most presented with resp. symp.	Not detailed for SAH patients	mRS 4-6
6	Rustemi et al. [12]	1	68	F	Known PcomA	Perimesencephalic	-	PcomA a.	+	N/A	Sudden headache + fever	-	Discharged
7	Basirjafari et al. [13]	1	9	M	-	Pseudo-SAH	Severe edema	N/A	+	N/A	Cardiac arrest	+	Deceased

PMH: Past Medical History, SAH: Subarachnoid Hemorrhage, PICA: Posterior Inferior Cerebellar Artery, ICA: Internal Carotid Artery, IVH: Intraventricular Hemorrhage, ICH: Intracranial Hemorrhage, SDH: Subdural Hemorrhage, HTN: Hypertension, DM: Diabetes Mellitus, HLP: Hyperlipidemia, Pcom A: Posterior communicating Artery

out aneurysmal pathologies. Some were monocortical and some bicortical.

Among these types, the postcardiac arrest and resuscitation types have been seen long before COVID-19 infection. This distinct entity called "pseudo-SAH" is a false-positive finding on CT due to the difference between the profound edematous brain parenchyma and the surrounding vasculature in the basal cisterns and the falx cerebri, thus appearing as SAH. Therefore, this specific type of SAH does not seem to directly link to the pathogenesis of COVID-19 infection.

Cerebrospinal Fluid (CSF) analysis

CSF analysis detail in our patient contained Glucose,117 mg/dl; protein, 13 mg/dl; LDH (Lactate Dehydrogenase), 3059 U/L; RBC (Red Blood Cell), 50000 micL, WBC (White Blood Cell), 1 micL.

As mentioned in some studies, direct CNS invasion is a probable cause for cerebrovascular symptoms, and CSF PCR could play a role in testing this hypothesis. Unfortunately, except for two studies conducted by Al Saiegh et al. and de Castillo et al. [4, 7], in other cases, CSF was not analyzed for the SARS-CoV2 virus. Our negative CSF PCR for this patient is in harmony with these two studies but contradicts the study by Moriguchi et al. [8]. Further investigation can help us understand the association between COVID and SAH.

According to negative CSF PCR examination in our patient, SAH in this patient could be due to inflammatory mechanisms that are mediated with the infection, and primary involvement by the virus may not be the main cause. Microvascular and vascular endothelial dysfunction may also occur in COVID-19 infection. Several SAH cases in severe COVID-19 patients had been reported in the literature; one of the possible mechanisms for these severe cases is lung injury and enhanced activation of the sympathetic nerve system [9]. Figure 1 shows different patterns of SAH which have been reported previously in COVID patients [14-16].

5. Conclusion

Regarding the different associations of SAH with COVID-19, the perimesencephalic hemorrhage in our case is a novel type. Although not uncommon among non-infected populations, its occurrence in COVID-19 patients has not been reported before and needs further investigation.

Ethical Considerations

Compliance with ethical guidelines

We obtained written informed consent from the patient.

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This report was self-funded.

Authors' contributions

Study conception and design and data collection: Mohammad Kazem Sar Poolaki; Data analysis and interpretation: Arad Iranmehr; Critically revising the article: Mohammad Ali Bitaraf; Reviewing submitted version of manuscript: Soheil Naderi; Drafting the article and approving the final version of the manuscript: Mohamad Namvar.

Conflict of interest

The authors declared no conflict of interest.

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