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## Association of Pediatric COVID-19 and Subarachnoid Hemorrhage

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**Abstract**

We read with great interest an article from Li colleagues describing “The Neuroinvasive Potential of SARS-CoV2 May Play a Role in the Respiratory Failure of COVID-19 Patients”. Here we describe subarachnoid hemorrhage (SAH) as a severe neurological manifestation associated with pediatric COVID-19.

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Dear Editor:

We read with great interest an article from Li and colleagues<sup>1</sup> describing “The Neuroinvasive Potential of SARS-CoV2 May Play a Role in the Respiratory Failure of COVID-19 Patients”. Here we describe subarachnoid hemorrhage (SAH) as a severe neurological manifestation associated with pediatric COVID-19.

A 9-year-old boy was hospitalized and intubated with cardiopulmonary arrest and low Glasgow Coma Scale (GCS) and COVID-19 symptoms, including respiratory insufficiency, fever, nausea, abdominal pain, headache, anorexia and fatigue. He had no past medical history and close contact with a person who tested positive for COVID-19. Reverse transcription-polymerase chain reaction (RT-PCR) from nasopharyngeal swab specimens confirmed positive COVID-19. Laboratory testing Table 1 revealed development of nonoliguric renal failure due to a 4-fold increase in creatinine. Patient's blood type was A+. He received IV dopamine for low blood

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pressure and fresh frozen plasma (FFP) in addition to Meropenem, Vancomycin, Azithromycin, Oseltamivir, levofloxacin, Lopinavir/Ritonavir and Hydroxychloroquine. Two times chest computed tomography (CT) scan Figure 1 performed; 1) on the first day of hospitalization exhibited consolidation at posterior basal segments of both lungs with air bronchogram sign, 2) on the second day revealed consolidation with progression of air bronchogram and a mild right side pleural effusion occurred.

Due to fixed and dilated pupils (FDPs) on the second day, brain CT scan Figure 1f performed that uncovered hyperdensity at basal cisterns, interhemispheric and bilateral Sylvian fissures in favor of SAH, and reduction of white matter density in favor of brain edema. World Federation of Neurologic Surgeons (WFNS) grading scale for SAH was 5. Timely follow-up chest CT along with RT-PCR confirmed COVID-19 pneumonia in which pediatric pulmonary damage and hypoxemia affected multi-organ systems owing to the involvement of the lung parenchyma. Finally, he died after 2 days of hospitalization. Furthermore, there were no lesions in anatomical pathways of cerebral arteries in favor of cerebral aneurysm and no suspected parenchymal lesions observed for arteriovenous malformation (AVM). We speculate that infection as a miscellaneous cause of SAH taken place based on previous data that showed infection triggers SAH<sup>2</sup>.

## **Discussion**

Pediatric COVID-19 appeared with mild symptoms<sup>3</sup> with severe complications of COVID-19 less frequent than adults<sup>4</sup>. However, the clinical course and complications

related to the COVID-19 in children are still unclear. One of the reasons is that parents show immense fear to take the children to the hospital during the coronavirus crisis.

Striking evidence exhibited that COVID-19 impacts multi-organ system in adults, including the central nervous system (CNS) and cerebrovascular events (CVEs) including intracranial hemorrhage, has been published in association with this infection<sup>5</sup>. While infections have been described in relation to SAH little is known for the pediatric COVID-19 infection<sup>2</sup>. Severe COVID-19 may cause neurologic manifestations because the virus has the potential to enter the CNS through hematogenous spread or retrograde neuronal route<sup>6</sup>. The expression of angiotensin-converting enzyme 2 (ACE2) as the SARS-CoV-2 main receptor in the brain may promote virus entry<sup>7</sup>. The direct route of neuroinvasion has not been established for SARS-CoV-2 so far but the virus or its particles were present in brain autopsy samples<sup>8</sup>. Aside from direct CNS infection, consequences of peripheral infection such as hyperinflammation and cytokine storm, endothelial injury, coagulopathy, and unopposed Ang II activation due to ACE2 reduction leading to vasoconstriction and hypertension are possible mechanisms for CVEs<sup>9</sup>. An increase in leukocyte count and elevated C-reactive protein (CRP) in the presented case might be interpreted as activation of the immune system and inflammation that can be associated with both COVID-19 and SAH. CRP is an inflammatory marker that has revealed to be associated with the severity of COVID-19<sup>10</sup>. A recent report of SAH in a SARS-COV-2 infected adult patient linked the event with abnormal coagulation or cytokine storm<sup>11</sup>.

Moreover, ABO blood type might have a prognostic role in the severity of COVID-19. There is a positive association between ACE activity and the GATC haplotype of the ABO gene which is prevalent in non-O blood group. Thus, patients with blood type O might have protection against severe COVID-19<sup>12</sup>. However, patients with blood group type A, as the patient described in this report, might be more predisposed to severe infection.

Overall, we describe a pediatric COVID-19 case associated with nonoliguric renal injury and SAH. Presented case of pediatric COVID-19 developed SAH while he had no underlying neurological disease highlighting that children are at risk of severe complications of COVID -19 and immediate medical care is required.

#### **Disclosure statement**

The authors declare no competing interests.

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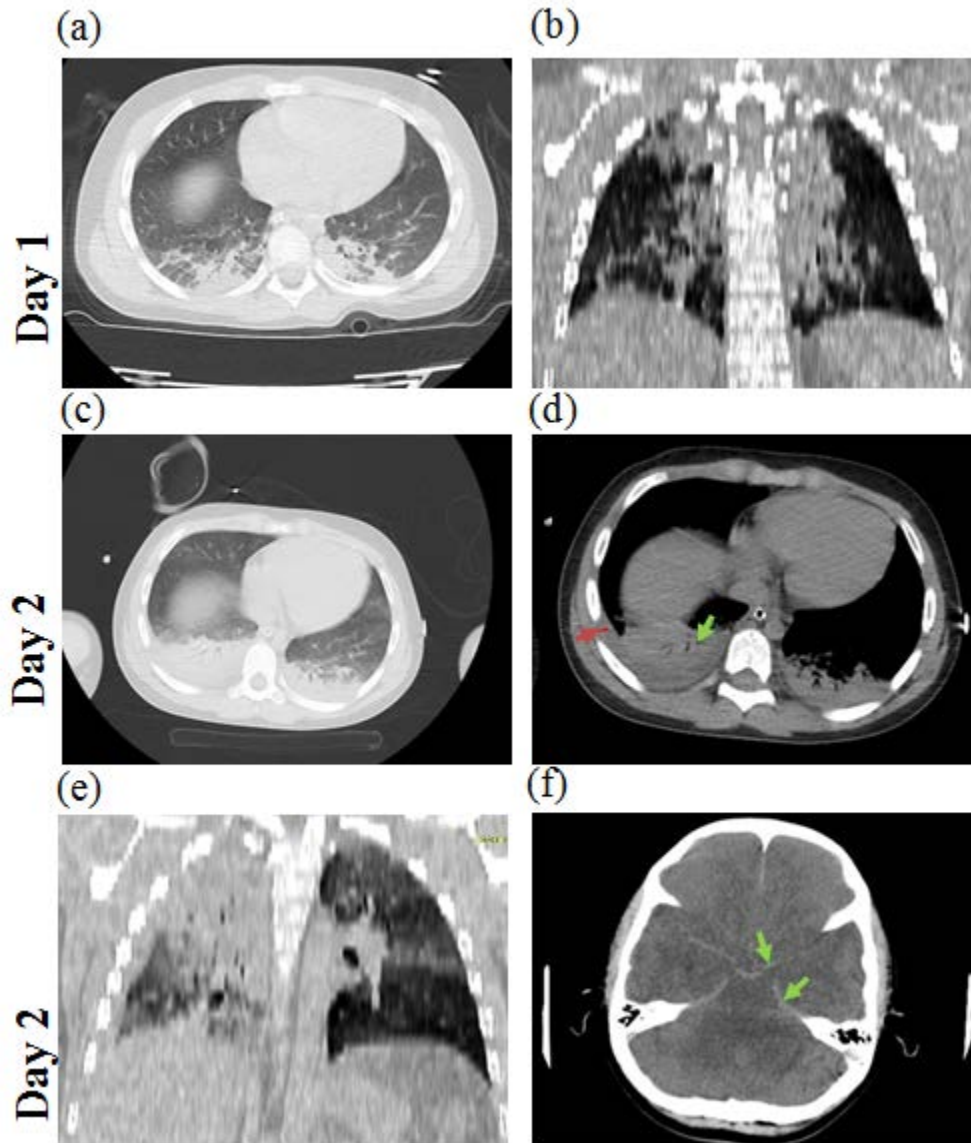
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Table1: Clinical Laboratory Results

Measure	Day1	Day1	Day2
pH	6.7*	6.86	6.82
PCO <sub>2</sub> , mmHg	31*	152	163
PO <sub>2</sub> , mmHg	37*	81	146

HCO <sub>3</sub> , mEq/L	4.4*	27.5	26
BE, mmol/L	-28	-10	-11
Urea, mg/dL	20	-	100
Creatinine, mg/dL	0.5	-	2
White blood cell count, x 10 <sup>3</sup> /μL	5.3	-	9.3
	(N:70%, L: 25%)		
Platelet count, x 10 <sup>3</sup> /μl	133	-	174
Mean Corpuscular Volume, FL	87	-	82
Hemoglobin, g/dL	18.5	-	19
Blood Sugar, mg/dL	244	-	-
C-reactive Protein	+2	-	-
Urine blood	0	0	0
Urine RBC	0	0	0
Hemoglobin A1c %	5	-	-

\*Based On Venous Blood Gase (VBG) Analysis



**Figure 1.** A 9-year-old boy presenting with cardiopulmonary arrest, fever, nausea, abdominal pain, headache, anorexia, and fatigue. Day 1; (a), Axial computed tomographic (CT) scan in parenchymal view showing consolidation at both posterior basal segments with air bronchogram sign. (b), Coronal reconstructed CT image in parenchymal view showing consolidation in both lungs. Day 2; (c), Axial CT scan in parenchymal view showing consolidation at both posterior basal segments with air



bronchogram sign which has been progressed in comparison to day 1. (d), Axial CT scan in mediastinal view showing consolidation with air bronchogram sign (green arrow). Also a mild pleural effusion at the right side (red arrow). (e), Coronal reconstructed CT image in parenchymal view showing consolidation in both lungs more prominent at right hemithorax. (f), Axial CT scan of brain showing hyperdensity at basal cisterns, interhemispheric and bilateral sylvian fissures in favor of subarachnoid hemorrhage (SAH), without intraventricular hemorrhage and hydrocephalus (green arrow). Decreased density of white matter in favor of brain edema.