Bilateral Posterior Cerebral Artery Stroke From COVID-Related Multisystem Inflammatory Syndrome in a Child

Running title: MIS-C and Bilateral PCA Stroke

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Conflicts of Interest: All authors have no conflicts of interest to report.

Keywords: Multisystem Inflammatory Syndrome in Children; COVID-19; Pediatric stroke; Posterior Cerebral Artery Stroke; Virtual Visual Field
Funding: Supported in part by an Unrestricted Grant from Research to Prevent Blindness, New York, NY, to the Department of Ophthalmology & Visual Sciences, University of Utah.
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection can cause Multisystem Inflammatory Syndrome in Children (MIS-C). MIS-C and severe SARS-CoV-2 infections have been associated with thrombotic events\(^1\) and mild to severe neurologic conditions, including strokes.\(^2\) Beslow et al. found that, 8 of 971 (0.82%) hospitalized pediatric patients with SARS-CoV-2 infection suffered from ischemic stroke.\(^3\) Multiple cases of middle cerebral artery (MCA) stroke have been published. Two cases of bilateral posterior cerebral artery (PCA) stroke in patients with MIS-C have been published. One PCA stroke case involved a 10-year-old boy in Egypt whose information is included in an international survey, but a detailed case report cannot be found.\(^3\) The second was a 2-month-old boy on extracorporeal membrane oxygenation (ECMO) - an intervention with known risk of thrombosis.\(^4,5\) To our knowledge this is the first case report of bilateral PCA stroke in a MIS-C patient not on ECMO.

A previously healthy 12-year-old girl arrived at the emergency department with fever, abdominal pain, and laboratory evidence of severe inflammation (CRP 21.5 mg/dL, ESR 44 mm/hr, fibrinogen 566 mg/dL, D-dimer 7.93 mcg FEU/mL, and ferritin 1,681 ng/mL), multisystem dysfunction (troponin 0.09 ng/mL, BNP 284 pg/mL, creatinine 0.92 mg/dL, BUN 23 mg/dL, AST 72 unit/L, ALT 97 unit/L), and SARS-CoV-2 infection (positive SARS-CoV-2 by PCR [Cepheid] and SARS-CoV-2 IgG Antibody [Abbott]). Her past medical, surgical, and family history were unremarkable. The patient acutely decompensated in the emergency department. Given concerns for an acute abdomen, exploratory laparotomy was performed, but was unremarkable, except for bilious fluid throughout her abdomen. She had less than five milliliters of blood loss. The patient
remained intubated and sedated and became hypotensive, requiring vasopressor support in the pediatric intensive care unit. Echocardiography showed mildly decreased left ventricular function. Rheumatology and infectious disease were consulted, and treatment for presumed MIS-C was started with intravenous immunoglobulin, anakinra 200 mg, intravenous methylprednisolone 40 mg twice daily, aspirin 81 mg daily, and enoxaparin 36 mg twice daily. Vasopressors were weaned on Day 3. On Day 4, the patient returned to the operating room for delayed abdominal closure and was extubated on room air. She was transitioned to oral prednisone 40 mg twice daily with down trending inflammatory markers on Day 5. Repeat echocardiography on Day 7 showed normal left ventricular function. The patient was discharged on Day 8 on aspirin 81 mg daily and prednisone 40 mg twice daily.

On Day 9, the patient’s mother offered her gummy bears from her right side; however, the patient did not notice and had to be verbally prompted to reach for the food. Later, her mother attempted to hand the patient a remote from above her head, and she did not notice. The patient had blurry vision during her initial hospitalization; however, further evaluation was not performed, as her decreased vision was thought to be related to sedation. The patient reported that she had persistent peripheral vision loss, which prompted her mother to take her back to the emergency department.

On examination in the emergency department, her visual acuity was 20/20 in both eyes. Her intraocular pressures were 23 and 20 mmHg in the right and left eyes, respectively. Pupils in light were 7 mm bilaterally and sluggishly reactive to light. She had no relative
afferent pupillary defect. She had full extraocular movements and was orthophoric.

Visual field testing using red targets showed symmetric bilateral superior hemifield
defects. She had normal color vision. Anterior segment exam was normal. Posterior
segment exam showed normal optic nerves with a cup-to-disc ratio of 0.1, normal
macula, vessels, and peripheries. Virtual visual fields (Virtual Field™ – a technology
with ongoing validation studies) were obtained at the bedside and demonstrated a
dense superior altitudinal defect and nasal step bilaterally with partial inferotemporal
defect of the right eye and inferonasal step of the left eye (see Figure 1). Visual field
defects were confirmed with Humphrey visual field. Complete neurological exam was
otherwise normal.

Given concern for bilateral PCA strokes, MRI brain with contrast and MRA of the head
and neck were obtained. The MRA of the brain showed posterior circulation arterial
ischemic strokes involving the bilateral PCA and hippocampal arteries. The imaging was
suggestive of focal cerebral arteriopathy-inflammatory subtype, involving the bilateral P1
and proximal P2 segments, likely related to SARS-CoV-2 and MIS-C (see Figure 2).

The patient was discharged home with continuation of prednisone 40 mg twice daily and
aspirin 81 mg daily with neurology and neuro-ophthalmology follow up. At follow up four
weeks later, her deficits were unchanged.

In summary, our patient is a previously healthy 12-year-old girl with recent hospital
admission for MIS-C with gastrointestinal and cardiac involvement with exploratory
laparotomy. She presented to the emergency department one day after discharge with
complaints of visual field deficits. She was found to have arterial ischemic strokes involving the bilateral PCA and hippocampal arteries thought to be secondary to SARS-CoV-2 and MIS-C. She had no other risk factors for ischemic stroke, including no evidence of thrombosis on echocardiography, hematologic conditions, arteriovenous malformation, history of genetic syndromes or metabolic disorders associated with stroke, history of cancer, trauma, inciting drugs, or vasculitis. The hemodynamic instability during her exploratory laparotomy was brief, and imaging was not typical for systemic hypotension. Hypotension would also not result in the focal arteriopathy. There were no features to suggest embolic source.

While the underlying etiology for thrombosis in SARS-CoV-2 is poorly understood, Hanff et al. propose five underlying mechanisms for hypercoagulability that could explain this patient’s outcome, including disseminated intravascular coagulation, cytokine storm, complement activation, macrophage activation syndrome and hyperferritinemia, and renin angiotensin system overactivation.1 While rare, this case highlights one of the severe, potentially vision-threatening complications of pediatric SARS-CoV-2 infection. More research is needed to evaluate the best management in pediatric SARS-CoV-2 infection and MIS-C patients.
References


Figure 1 Legend. Selected images from a virtual visual field (Virtual Field \textsuperscript{TM}) obtained at the bedside. Right eye visual field (right) showed good reliability, dense superior altitudinal defect and nasal step with an inferotemporal defect. Left eye visual field (left) showed good reliability, dense superior altitudinal defect, and inferior nasal step. Overall, she has a congruous left superior quadrantanopia and an incongruous right homonymous hemianopia.
**Figure 2 Legend.** Selected images from an MRI of the brain. Axial correlating DWI (A), ADC (B), and FLAIR (C) images demonstrate restricted diffusion within the bilateral medial occipital lobes with bright DWI signal intensity (A, arrows), and dark ADC signal intensity (B, arrows), consistent with restricted diffusion, and abnormally correlating bright T2/FLAIR signal intensity (C, arrows), consistent with ischemia most likely greater than 6 hours and less than 10 days in age. Superior to inferior collapsed view of the 3D TOF MRA sequence demonstrates focal narrowing of the bilateral PCA vessels (D, arrows) near the P2/3 junction on the left, and the P3 segment on the right.
Statement of Authorship

1. Category 1:
   a) Conception and design
      N/A
   b) Acquisition of data
   c) Analysis and interpretation of data
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2. Category 2:
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   b) Revising it for intellectual content
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3. Category 3:
   a) Final approval of the completed manuscript