Successful thrombectomy in a pediatric patient with large vessel occlusion and COVID-19 related multisystem inflammatory syndrome

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Abstract
This is a case report of a child with multisystem inflammatory syndrome in children (MIS-C) complicated by an acute ischemic stroke with right M1 occlusion and large penumbra who underwent thrombectomy with TICI 3 recanalization. There were no complications and the patient had improvement in the pediatric NIHSS from 16 to 3 in the subsequent days. This is the first known report of successful mechanical thrombectomy performed in a pediatric patient with MIS-C associated with COVID-19.

Keywords
Stroke, pediatric, MIS-C, thrombectomy, COVID-19

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Introduction
Multisystem Inflammatory Syndrome in Children (MIS-C) is a rare condition in which there is a severe hyperinflammatory response associated with recent or active COVID-19 infection characterized by persistent fevers with laboratory evidence of inflammation and dysfunction of at least two organ systems. Cardiovascular and gastrointestinal involvement are most common, seen in greater than 80% of patients. Neurologic complications of MIS-C are seen less frequently, though a recent study of 1695 patients demonstrated neurologic involvement in up to 22% of cases, including twelve patients with ischemic or hemorrhagic stroke.

Mechanical thrombectomy for large vessel occlusions in pediatric patients has not yet been established as the standard of care, despite clear consensus of its benefit in adults. We present the first known case of a child with MIS-C who developed a large vessel occlusion and underwent successful mechanical thrombectomy.

Case report
A previously healthy school-age child was admitted to the pediatric intensive care unit (PICU) with MIS-C requiring vasoactive and respiratory support. Presenting symptoms included fever, abdominal pain, sore throat, myalgias, emesis and conjunctival injection with laboratory evidence of multi-organ dysfunction. He was treated with intravenous immunoglobulin (IVIG, 2 grams/kilogram as a single dose) and high-dose methylprednisolone. He was additionally placed on prophylactic enoxaparin per institutional MIS-C protocol. On the third day after admission, the child developed left hemiplegia, left facial droop, homonymous hemianopsia and dysarthria with a pediatric NIH stroke scale (PedNIHSS) of 16. Emergent imaging demonstrated an acute right lenticulostriate infarct and occlusion of the right M1 segment of the middle cerebral artery. Perfusion imaging was suggestive of a large ischemic penumbra, as shown in Figure 1. Last known well at time of imaging was six hours prior. The child was given aspirin and transferred emergently to a comprehensive stroke center for endovascular thrombectomy.

Procedure
Under general anesthesia, right femoral access was obtained with a micropuncture kit under ultrasound guidance. A 6 French Arrow-FlexTM 65-centimeter sheath (Teleflex, Morrisville, NC, USA) was placed. The right internal carotid artery was selectively catheterized with a 5 French angled glide catheter over a 0.035 inch glide-wireTM (Terumo, Somerset, NJ, USA). The shuttle was advanced over the select catheter to the distal cervical right internal carotid artery. Right internal carotid artery

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angiography was performed, which demonstrated a right M1 occlusion. A Catalyst-6™ distal access catheter was advanced co-axially with a Marksman™ (Medtronic, Dublin, Ireland) 0.027 inch microcatheter and 0.014 inch wire. The microcatheter and 0.014 inch wire were used to cross the lesion and the distal access catheter was advanced to the proximal face of the lesion. A Solitaire™ 4 × 40 mm stent retriever was deployed across the lesion. The microcatheter was removed and the stent retriever was left open for four minutes under continuous aspiration. The stent retriever was then retrieved under continuous aspiration. Control angiography after the first pass showed proximal migration of the clot to the more proximal M1 segment. The same technique was repeated for a second pass using a Solitaire™ 6 × 40 mm stent retriever. Control right internal carotid artery angiography was performed and demonstrated TICI3 revascularization as shown in Figure 2. There was no radiologic evidence of vasculitis.

**Investigations**

At time of stroke, the child had a reduced left ventricular ejection fraction of 28%. Laboratory evaluation demonstrated transaminitis, acute kidney injury, hyponatremia, elevated inflammatory markers, elevated troponin and elevated D-dimer. Blood cultures and respiratory virus panels were negative. SARS-COV-2 PCR was negative, though positive IgG was suggestive of prior infection and he had a known COVID-19 exposure several weeks prior.

Transesophageal echocardiogram and extremity ultrasounds were negative for thrombus. Cardiac MRI demonstrated no evidence of myocarditis. Thrombophilia workup including beta-2 glycoprotein antibodies, rapid plasma reagin, lupus anticoagulant, factor V Leiden mutation, protein C, protein S and factor II prothrombin variant were negative aside from a mildly low protein S, which was suspected to be consumptive in nature and normalized on repeat testing.
Outcome and follow-up

The patient was taken back to the PICU for post-thrombectomy care and treatment of other comorbidities. Cardiac function normalized two days following stroke. Follow-up imaging 48 h after thrombectomy showed stable size of the known infarction and four small areas of micro-infarction in right cortical white matter. The child was transferred to the inpatient rehabilitation ward on post stroke day seven, where he completed two weeks of intensive therapy. At time of discharge, he was walking independently and had a PedNIHSS of 1 for mild left arm weakness. He continued to take daily aspirin at a dose of 4.7 milligrams/kilogram of body weight.

At two month follow-up in the pediatric stroke clinic, he reported a full return to school without any cognitive or physical limitations. The child continued to get weekly physical therapy for mild left-sided weakness and exam demonstrated a stable PedNIHSS of 1 for left arm weakness.

Discussion

Stroke associated with MIS-C has been described in two other papers, including a recent article with two children developing large vessel occlusion. However, those cases did not meet criteria for thrombectomy. This is the first description of a child with MIS-C and ischemic stroke due to large vessel occlusion who underwent mechanical thrombectomy. The etiology of stroke in this case is suspected to be multifactorial due to significant cardiac dysfunction and hypercoagulable state due to IVIG and inflammatory nature of MIS-C. Thrombosis is an established adverse effect of IVIG administration and while considered rare in the pediatric population, it is an important risk to be aware of when caring for children with MIS-C as recommended treatment, particularly with high daily doses such as that administered in this case.

Safe and effective use of thrombectomy in pediatric stroke has been described with increasing frequency, though is not considered standard of care and equipment has not been optimized for pediatric patients.

In conclusion, this case raises the possibility that acute ischemic stroke secondary to a large vessel occlusion, though rare, may occur in cases of MIS-C. We presented a case of a pediatric patient with MIS-C and cardiac dysfunction who underwent mechanical thrombectomy without complication. Our case demonstrates the potential for success in performing a safe and efficacious thrombectomy for carefully selected pediatric patients. This is increasingly important in light of the COVID-19 pandemic and threat of MIS-C associated strokes in pediatric patients. Further study may help clarify selection criteria for pediatric patients who would benefit the most from mechanical thrombectomy.

Declaration of conflicting interests

All authors confirm there are no conflicts of interest to disclose. Institutional IRB approval is not required for a case report. The patient and family did provide informed written consent for the case to be published.

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References

1. Feldstein LR, Rose EB, Horwitz SM, et al. Multisystem inflammatory syndrome in U.S. Children and adolescents. *N Engl J Med* 2020; 383: 334–346. Available from: http://dx.doi.org/10.1056/NEJMoa2021680
2. LaRovere KL, Riggs BJ, Poussaint TY, et al. Neurologic involvement in children and adolescents hospitalized in the United States for COVID-19 or multisystem inflammatory syndrome. *JAMA Neurol* 2021; 78: 536–547. Available from: https://pubmed.ncbi.nlm.nih.gov/33666649/ (accessed 23 November 2021).
3. Guo Y, Tian X, Wang X, et al. Adverse effects of immunoglobulin therapy. *Front Immunol* 2018; 9: 1299. Available from: http://dx.doi.org/10.3389/fimmu.2018.01299
4. Chang J, Bulwa Z, Brett H, et al. Acute large vessel ischemic stroke in patients with COVID-19-related multisystem inflammatory syndrome. *Pediatr Neurol* 2022; 126: 104–107. Available from: https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC8464033/
5. Sporns PB, Kemmling A, Hanning U, et al. Thrombectomy in childhood stroke. *J Am Heart Assoc* 2019; 8: e011335. Available from: https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC6474928/
6. Ravindra VM, Alexander M, Taussky P, et al. Endovascular thrombectomy for pediatric acute ischemic stroke: a multi-institutional experience of technical and clinical outcomes. *Neurosurgery* 2020; 88: 46–54. Available from: https://pubmed.ncbi.nlm.nih.gov/32761237/