# A Multidisciplinary Approach to the Management of Recurrent Ischemic Strokes due to Moyamoya Vasculopathy

Fazila Aseem, MD, MPH, Sonia A. Varghese, MD, MPH, MBA, Nathan S. Quig, MD, Gregory Chamberlin, MD, Aliese Sarkissian, MD, Eveline Y. Wu, MD, Casey Olm-Shipman, MD, MS

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

## Introduction

Moyamoya syndrome (MMS) is a progressive steno-occlusive vasculopathy at terminal portions of the bilateral internal carotid arteries and their proximal branches with prominent collateral artery formation.[1,2] It can cause irreversible damage to the cerebral hemodynamics, causing both ischemic and hemorrhagic strokes. MMS is associated with radiation, NF1, SSD, Asian heritage, hyperthyroidism and renal-artery stenosis and hemangiomas.[1] Primary vasculitis of the central nervous system, on the other hand, is a rare and diagnostically challenging form of vasculitis limited to the brain and/or spinal cord. Primary central nervous system vasculitis can mimic MMS.[3] We report a multidisciplinary approach to management of a pediatric patient with recurrent ischemic strokes due to MMS secondary to an inflammatory vasculopathy.

## Case Report

- An 11-year-old previously healthy male presented with acute onset of persistent right-sided weakness in the setting of similar but intermittent symptoms during the preceding 3 weeks.
- Initial exam: Normal mental status, decreased strength and sensation in the right upper and lower extremities.
- Laboratory studies: Elevated ESR/CRP and heterozygosity for Factor V Leiden. Serum, CSF, and genetic workup otherwise unremarkable.
- Patient met the clinical and imaging diagnostic criteria for primary angiitis of the central nervous system (PACNS).
- Medical management: He received high-dose methylprednisolone, mycophenolate and later cyclophosphamide in setting of recurrent symptoms. He was also switched from aspirin to enoxaparin, and continued on corticosteroid taper.
- Multidisciplinary discussion: An inflammatory process was the likely trigger for the Moyamoya syndrome (Figure 2). Recurrent strokes are due to Moyamoya syndrome.
- Surgical management: Neurosurgery agreed to surgical evaluation given low risk of hemorrhage in the setting of having been treated for PACNS. Patient underwent bilateral external/internal carotid bypass surgeries.
- No new or recurrent neurological deficits reported post surgeries.

## Imaging

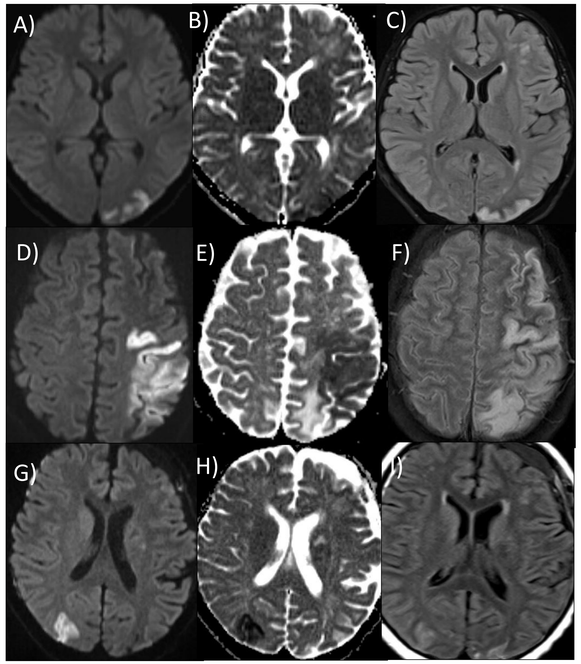


**Figure 1**: Repeat MRIs of brain showed acute ischemic strokes or extension of the prior strokes.

July, 2020
A) Diffuse restriction with B) ADC correlate and C) FLAIR hyperintensity in the left parietal lobe.

August, 2020
D) Diffuse restriction with E) ADC correlate and F) FLAIR hyperintensity in the left fronto-parietal lobe.

September, 2020
G) Diffuse restriction with H) ADC correlate and I) FLAIR hyperintensity in the right parietal lobe.

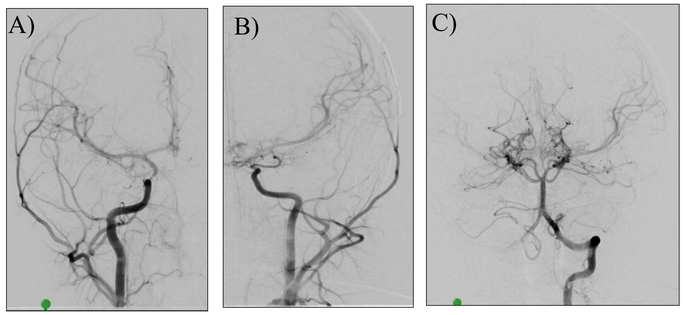


**Figure 2**: Repeat angiogram showed Moyamoya-appearing blood vessel anatomy with A) & B) progression of the bilateral internal carotid artery stenosis, and prominent formation of collateral arteries and C) posterior circulation.

## Histopathology

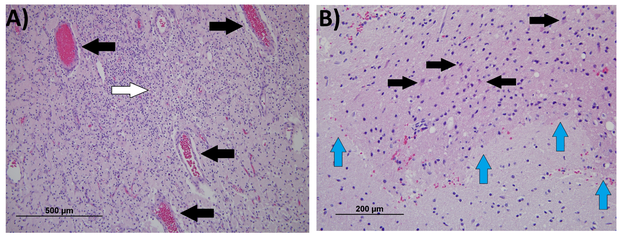


**Figure 3:** A) A biopsy collected from patient's left frontal lobe demonstrates regions of chronic infarction within the cortex. The infarcted tissue exhibits numerous foamy macrophages (white arrow) and prominent dilated, congested blood vessels (black arrows). The vessels do not demonstrate evidence of thrombosis, vasculitis, or intimal thickening. (H&E stain, 100x).
**B)** The periphery of the infarcted tissue demonstrates a well-defined border with viable tissue (blue arrows) and gliotic tissue with many reactive astrocytes (black arrows). (H&E stain, 200x).

## Conclusion

The diagnosis and management of recurrent strokes among pediatric patients is challenging. Inflammatory and infectious etiologies and Moyamoya variants should be considered in the differential of pediatric patients with ischemic strokes. Biopsy can be diagnostic in the setting of mimics. However, histological changes can be patchy and may be obscured after immunosuppressive treatment, as with this patient. Additionally, vascular changes with large vessels, such with Moyamoya, typical cannot be seen in the smaller cortical/leptomeningeal vessels present in the biopsy. Since early diagnosis predicts long-term outcomes, multidisciplinary reassessment of the diagnosis is paramount.[4] Medical therapy alone does not halt disease progression; symptomatic progression is 2.5% with intervention and 66% without intervention.[5,6] Therefore, early surgical evaluation should be pursued in moderate-severe cases as cerebral revascularization can mitigate perfusion deficits and minimize the burden of recurrent strokes.

**References**

1. R. Michael Scott, and Edward R. Smith. Moyamoya Disease and Moyamoya Syndrome. N Engl J Med 2009; 360:1226-1237
2. Li J, Jin M, Sun X, Li J, Liu Y, Xi Y, Wang Q, Zhao W, Huang Y. Imaging of Moyamoya Disease and Moyamoya Syndrome: Current Status. J Comput Assist Tomogr. 2019;43(2):257-263.
3. Kraemer M, Berlit P. Primary central nervous system vasculitis and moyamoya disease: similarities and differences. J Neurol. 2010;257(5):816-9.
4. Kuroda S, Ishikawa T, Houkin K, Nanba R, Hokari M, Iwasaki Y. Incidence and clinical features of disease progression in adult moyamoya disease. Stroke. 2005;36(10):2148-53.
5. Scott RM, Smith JL, Robertson RL, Madsen JR, Soriano SG, Rockoff MA. Long-term outcome in children with moyamoya syndrome after cranial revascularization by pial synangiosis. J Neurosurg. 2004;100(2 Suppl Pediatrics):142-9.
6. Fung LW, Thompson D, Ganesan V. Revascularisation surgery for paediatric moyamoya: a review of the literature. Childs Nerv Syst. 2005;21(5):358-64.

**Funding**: This research is not supported by any grant or funding. Authors have no conflict of interest.