Biomarkers of arteriopathy in pediatric stroke
An array of options

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Cerebral arteriopathy is an increasingly recognized cause of arterial ischemic stroke in previously healthy children. Focal cerebral arteriopathy (FCA) is a recently coined term for focal cerebral arterial stenosis with no apparent cause, and excludes children with intracranial dissection, moyamoya, sickle cell arteriopathy, postvaricella arteriopathy, vasculitis, or other specific diagnoses. Stroke recurrence in children with all types of arteriopathy is high compared to those without arteriopathy, although recurrence risk specifically associated with FCA is unclear. Given the paucity of data, there is no consensus regarding management of childhood stroke associated with FCA.

In this issue of Neurology®, Mineyko et al. present a series of 3 adolescents with acute stroke, 2 of whom have arteriopathy manifesting as irregular stenosis and dilatation of the internal carotid and middle cerebral arteries. Both patients underwent high-resolution contrast-enhanced vessel-wall imaging (VWI) showing features suggestive of inflammation. CSF showed elevated protein without a cellular response in 1 patient and was not examined in the other. A novel cytokine array quantified 65 inflammatory cytokines, chemokines, and growth factors in sera of the 2 patients with FCA and, for comparison, an adolescent with stroke of presumed cardioembolic origin. Findings from the array were interpreted as evidence of an active inflammatory arteriopathy. Both patients were treated with IV and oral steroids and 1 also received cyclophosphamide after recurrent strokes and progression of arteriopathy. Both remained free of recurrent stroke.

The findings of arterial wall enhancement and elevated cytokine markers in the 2 patients with FCA and, for comparison, an adolescent with stroke of presumed cardioembolic origin, and 1 healthy 24-year-old. Findings from the array were interpreted as evidence of an active inflammatory arteriopathy. Both patients were treated with IV and oral steroids and 1 also received cyclophosphamide after recurrent strokes and progression of arteriopathy. Both remained free of recurrent stroke.

The findings of arterial wall enhancement and elevated cytokine markers in the 2 patients with FCA are intriguing and suggest these methods may be useful to understand childhood cerebral arteriopathies better. In that sense, the results are of great interest and deserve evaluation in larger, diverse cohorts. There are a number of limitations and questions. The sensitivity and specificity of novel VWI methods and biomarker panels in determining stroke etiology are unknown. It is uncertain how the 2 patients with arteriopathy could be distinguished from childhood primary angiitis of the CNS (cPACNS). Both patients were treated with immunosuppressive regimens typically recommended for cPACNS. As the risk-benefit ratio of immune modulation in patients with FCA is not known, immunosuppression might be viewed as an aggressive treatment strategy for the patient without progressive disease. Improvement in the treated patients could be part of the natural history in this condition; in a recent series of 79 previously healthy children with stroke due to FCA, 23% normalized, 77% stabilized or partially improved, and only 6% had radiologic progression of their disease.

VWI may be used to identify vascular inflammation. Several small case series suggest VWI can distinguish atherosclerotic inflammation vs non-atherosclerotic inflammation. Wall inflammation has been seen in cPACNS with wall thickening and edema and seems to be absent in the cases presented.

These are novel, interesting findings. As the authors appropriately note, studies in large cohorts are necessary to clarify the pathophysiologic significance and utility of measuring inflammatory biomarkers in children with stroke. Further understanding of the natural history of FCA and predictors of progressive vasculopathy and recurrent stroke is urgently needed.

REFERENCES

DISCLOSURE
L. Jordan receives research support from NIH/NINDS [K23NS062110 (PI)] and served as a consultant/advisory board member for Berlin Heart. R. Ichord receives research support from NIH/NINDS and served as a consultant/advisory board member for Berlin Heart. Go to Neurology.org for full disclosures.

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