Vessel Wall MRI to Differentiate Between Reversible Cerebral Vasoconstriction Syndrome and Central Nervous System Vasculitis
Preliminary Results

Daniel M. Mandell, MD; Charles C. Matouk, MD; Richard I. Farb, MD; Timo Krings, MD, PhD; Ronit Agid, MD; Karel terBrugge, MD; Robert A. Willinsky, MD; Richard H. Swartz, MD, PhD; Frank L. Silver, MD; David J. Mikulis, MD

Background and Purpose—Prospective differentiation between reversible cerebral vasoconstriction syndrome and central nervous system vasculitis can be challenging. We hypothesized that high-resolution vessel wall MRI would demonstrate arterial wall enhancement in central nervous system vasculitis but not in reversible cerebral vasoconstriction syndrome.

Methods—We identified all patients with multifocal segmental narrowing of large intracranial arteries who had high-resolution vessel wall MRI and follow-up angiography at our institute over a 4-year period and performed a detailed chart review.

Results—Three patients lacked arterial wall enhancement, and these all had reversal of arterial narrowing within 3 months. Four patients demonstrated arterial wall enhancement, and these had persistent or progressive arterial narrowing at a median follow-up of 17 months (range, 6–36 months) with final diagnoses of central nervous system vasculitis (3) and cocaine vasculopathy (1).

Conclusions—Preliminary results suggest that high-resolution contrast-enhanced vessel wall MRI may enable differentiation between reversible cerebral vasoconstriction syndrome and central nervous system vasculitis. (Stroke. 2012;43:860-862.)

Key Words: magnetic resonance imaging ■ reversible cerebral vasoconstriction syndrome ■ vasculitis ■ vasoconstriction ■ vessel wall

Proposed diagnostic criteria for “reversible cerebral vasoconstriction syndrome” (RCVS) are sudden-onset severe headache, multifocal segmental narrowing of cerebral arteries, lack of aneurysmal subarachnoid hemorrhage, near-normal cerebrospinal fluid, and spontaneous resolution of arterial narrowing within 3 months.1,2 Early discrimination between RCVS, and its principal differential, central nervous system (CNS) vasculitis, is important: RCVS is treated with observation or possibly calcium channel blockers, whereas CNS vasculitis is treated with steroids and immunosuppression.3 However, the diagnosis of RCVS is currently confirmed only in retrospect, when arterial narrowing resolves.

High-resolution vessel wall MRI is an emerging technique for characterizing intracranial arterial disease.3,4 Large artery CNS vasculitis is associated with arterial wall thickening and enhancement.4,5 RCVS is a disorder of arterial tone regulation, and the limited histopathologic data available suggest an absence of arterial wall inflammation6-7; therefore, we hypothesized that patients with RCVS would lack arterial wall enhancement. We reviewed our database of intracranial vessel wall MRI to identify all patients with multifocal segmental narrowing of large intracranial arteries and angiographic follow-up and report the findings.

Patients and Methods

Patients
We routinely perform vessel wall MRI for patients with intracranial arterial narrowing of unclear etiology. From a database of 114 patients studied between January 2006 and December 2010, we identified all patients with multifocal segmental narrowing of large intracranial arteries, vessel wall MRI performed at presentation, and angiographic follow-up. Multifocal narrowing was defined as multiple smooth concentric regions of narrowing that are long relative to the diameter of the artery, excluding the focal irregular stenoses that are typical of atherosclerosis.8 We performed a detailed chart review for each case. Institutional Review Board approval was obtained.
Vessel Wall MRI Protocol
MRI was performed using a Signa HDx 3.0-T scanner with an 8-channel head coil (GE Healthcare, Milwaukee, WI). Vessel wall protocol included a time-of-flight MR angiography of the circle of Willis, T1-weighted black blood vessel wall sequence (single inversion recovery-prepared 2-dimensional fast spin echo acquisition with field of view $/H_11021$22 $/H_11022$22 cm, acquired matrix $/H_11005$512 $/H_11003$512; slice thickness $/H_11005$2 or 3 mm; total slab thickness 2–3 cm, TR/TI/TE $/H_11005$2263/860/13 ms) before and after intravenous gadolinium (with constant scan parameters) and T2-weighted vessel wall sequences, which are not included in this Brief Report. Images were obtained through the most severely narrowed arterial segments in each patient. Each vessel wall sequence was performed in both the short and long axes of the artery of interest.

Image Interpretation
A neuroradiologist, blinded to vessel wall imaging and clinical data, graded the angiographic arterial narrowing as mild ($<50$%), moderate (50%–79%), or severe (>80%) for each study. A different neuroradiologist, blinded to angiography and clinical data, categorized vessel wall thickness as “normal” (barely perceptible) versus “thickened,” and comparing the pre- and postgadolinium mages, classified arterial wall enhancement in narrowed segments as “absent/minimal” versus “present” for each study. Categorization was qualitative based on clinical experience interpreting a wide range of intracranial vessel wall MRI examinations.

Results
Seven patients satisfied the inclusion criteria. Median age was 45 years (range, 19–69 years) and 6 of 7 patients were women. Presenting symptoms were acute headache (n=2), neurological deficit (n=2), and headache with deficit (n=3). Laboratory testing included a serum vasculitis work-up in 7 of 7 patients and cerebrospinal fluid analysis in 5 of 7 patients. High-resolution vessel wall MRI findings, patient management, angiographic follow-up, and final diagnoses are listed in the Table. Representative images are provided in Figures 1 and 2.

Discussion
We have used high-resolution contrast-enhanced vessel wall MRI to characterize the intracranial arterial wall in patients. High-resolution vessel wall MRI findings, patient management, angiographic follow-up, and final diagnoses are listed in the Table. Representative images are provided in Figures 1 and 2.

Vessel Wall MRI Protocol
MRI was performed using a Signa HDx 3.0-T scanner with an 8-channel head coil (GE Healthcare, Milwaukee, WI). Vessel wall protocol included a time-of-flight MR angiography of the circle of Willis, T1-weighted black blood vessel wall sequence (single inversion recovery-prepared 2-dimensional fast spin echo acquisition with field of view $/H_11021$22 $/H_11022$22 cm, acquired matrix $/H_11005$512 $/H_11003$512; slice thickness $/H_11005$2 or 3 mm; total slab thickness 2–3 cm, TR/TI/TE $/H_11005$2263/860/13 ms) before and after intravenous gadolinium (with constant scan parameters) and T2-weighted vessel wall sequences, which are not included in this Brief Report. Images were obtained through the most severely narrowed arterial segments in each patient. Each vessel wall sequence was performed in both the short and long axes of the artery of interest.

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Age, y</th>
<th>Sex</th>
<th>Arterial Wall Thickening</th>
<th>Arterial Wall Enhancement</th>
<th>Angiographic Degree of Narrowing</th>
<th>Management</th>
<th>Angiographic Follow-Up Length, mo</th>
<th>Outcome</th>
<th>Final Diagnosis* (Evidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>32</td>
<td>F</td>
<td>Yes</td>
<td>Absent/minimal</td>
<td>Severe</td>
<td>Calcium channel blocker and steroid</td>
<td>3</td>
<td>Resolution</td>
<td>RCVS†</td>
</tr>
<tr>
<td>2</td>
<td>56</td>
<td>F</td>
<td>Yes</td>
<td>Absent/minimal</td>
<td>Moderate</td>
<td>Calcium channel blocker</td>
<td>1</td>
<td>Resolution</td>
<td>RCVS†</td>
</tr>
<tr>
<td>3</td>
<td>45</td>
<td>F</td>
<td>Yes</td>
<td>Absent/minimal</td>
<td>Moderate</td>
<td>Calcium channel blocker and steroid</td>
<td>1.5</td>
<td>Resolution</td>
<td>Possible RCVS‡</td>
</tr>
<tr>
<td>4</td>
<td>69</td>
<td>F</td>
<td>Yes</td>
<td>Yes</td>
<td>Severe</td>
<td>Antiplatelet agent and steroid</td>
<td>24</td>
<td>Persistence</td>
<td>Giant cell arteritis (superficial temporal artery biopsy)</td>
</tr>
<tr>
<td>5</td>
<td>53</td>
<td>F</td>
<td>Yes</td>
<td>Yes</td>
<td>Severe</td>
<td>None</td>
<td>6</td>
<td>Persistence</td>
<td>CVS vasculitis (biopsy-proven sarcoidosis)</td>
</tr>
<tr>
<td>6</td>
<td>19</td>
<td>M</td>
<td>Yes</td>
<td>Yes</td>
<td>Moderate</td>
<td>Steroid and immunosuppressant</td>
<td>6</td>
<td>Persistence</td>
<td>Probable CNS vasculitis (clinical course, angiography, CSF)</td>
</tr>
<tr>
<td>7</td>
<td>19</td>
<td>F</td>
<td>Yes</td>
<td>Yes</td>
<td>Severe</td>
<td>None</td>
<td>36</td>
<td>Persistence</td>
<td>Cocaine vasculopathy (symptom onset immediately after first-time cocaine use)</td>
</tr>
</tbody>
</table>

F indicates female; M, male; CVS, cerebrovascular; CNS, central nervous system; CSF, cerebrospinal fluid.
*In none of the cases were the clinical or imaging features suggestive of other causes of intracranial arterial stenosis such as dissection or fibromuscular dysplasia.
†Fulfilled the proposed diagnostic criteria for reversible cerebral vasoconstriction syndrome.‡Transient arterial narrowing that did not fulfill all diagnostic criteria for reversible cerebral vasoconstriction syndrome due to a cerebrospinal fluid leukocytosis.

Figure 1. Reversible cerebral vasoconstriction syndrome. Axial T1-weighted vessel wall MRI pre- (A) and post- (B) gadolinium at presentation demonstrate arterial wall thickening (arrows) but absent/minimal arterial wall enhancement. Note the slice positioning is different for the right and left middle cerebral artery images. MR angiography at presentation (C) shows segmental narrowing of the anterior, middle (arrow), and posterior cerebral arteries bilaterally. Three-month follow-up angiogram (D) shows resolution of arterial narrowing.

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patients with multifocal segmental narrowing of large intracranial arteries.

In patients with RCVS, vessel wall MRI demonstrated arterial wall thickening and a lack of arterial wall enhancement. This is consistent with the pathology of transient vasoconstriction. In vasospastic arteries, smooth muscle cells shorten in length with increased overlap among cells resulting in nearly a 500% increase in wall thickness for a 60% luminal narrowing.9 Lack of arterial wall enhancement is concordant with the limited histopathologic data in RCVS showing an absence of arterial wall inflammation.6,7 The 1 patient with transient arterial narrowing who did not fulfill all diagnostic criteria for RCVS was taking a selective serotonin reuptake inhibitor, a known risk factor for RCVS. Vessel wall MRI findings in this patient were identical to those of the patients who satisfied all criteria for RCVS.

In patients with persistent arterial narrowing, diagnoses were CNS vasculitis (N=3) or cocaine vasculopathy (N=1), and vessel wall MRI demonstrated circumferential arterial wall thickening and enhancement. Like RCVS, cocaine vasculopathy is characterized by vasoconstriction, but unlike RCVS, cocaine vasculopathy demonstrates arterial wall inflammation on histopathologic evaluation.11 Two of the patients with persistent arterial narrowing were included in previous studies4,11 of vessel wall MRI.

This preliminary study is limited by the small sample size. Although we used the existing diagnostic criteria for RCVS, it is possible that some cases truly represent variants of “vasculitis” with early resolution of arterial narrowing. Also, patients in this study received differing treatments, potentially affecting vessel wall enhancement and clinical course. Of the 2 patients who received steroids before vessel wall imaging, 1 had a final diagnosis of RCVS and the other CNS vasculitis.

Conclusions
Our preliminary results raise the possibility of using high-resolution contrast-enhanced vessel wall MRI to differentiate between vasoconstriction and CNS vasculitis.

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D.M.M. gratefully acknowledges support from the American Society of Neuroradiology Foundation, Scholar Award in Neuroradiology Research.

Disclosures
None.

References
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1 Division of Neuroradiology, Toronto Western Hospital and University of Toronto, Toronto, Canada; and 2 Divisions of Neurology at Sunnybrook Health Sciences Centre and 3 Toronto Western Hospital, Toronto, Canada.

Background and Objective: Differentiation between reversible cerebral vasoconstriction syndrome (RVCS) and central nervous system vasculitis is challenging. High-resolution vessel wall MRI has shown arterial wall enhancement in vasculitis, whereas arterial wall enhancement is not seen in RVCS.

Method: In 4 years, all patients with high-resolution vessel wall MRI examinations and follow-up angiography with multifocal segmental narrowing in the intracranial main arteries were identified, and their detailed medical records were reviewed.

Result: In 3 cases, arterial wall enhancement was not seen, and arterial narrowing improved within 3 months. In 4 cases, arterial wall enhancement was seen, with persistent or progressive arterial narrowing noted on 17-month follow-up angiography. The final diagnoses were vasculitis (3 cases) and cocaine vasculopathy (1 case).

Conclusion: Preliminary results suggest that high-resolution vessel wall MRI may distinguish between reversible cerebral vasoconstriction syndrome and vasculitis.

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