Eccentric Narrowing and Enhancement of Symptomatic Middle Cerebral Artery Stenoses in Patients With Recent Ischemic Stroke

Mervyn D. I. Vergouwen, MD, PhD; Frank L. Silver, MD, FRCP; Daniel M. Mandell, MD; David J. Mikulis, MD, FRCP; Richard H. Swartz, MD, PhD, FRCP

**Objective:** To characterize the vessel wall imaging findings and enhancement patterns in the middle cerebral artery of patients with presumed atherosclerotic disease and recent infarction in the territory of the affected artery.

**Design:** Case series.

**Setting:** University hospital.

**Patients:** We included patients with (1) 2 or more risk factors for atherosclerotic disease; (2) middle cerebral artery stenosis shown on computed tomography, magnetic resonance, or conventional angiography; and (3) recent infarction in the territory of the affected artery.

**Intervention:** 3-T contrast-enhanced high-resolution magnetic resonance imaging.

**Results:** Eight patients were identified: 6 had an eccentric M1 stenosis, 1 had an eccentric proximal M2 stenosis, and 1 had a distal M2 stenosis with inconclusive eccentricity. Enhancement of the lesion was observed in all patients who underwent scanning within 5 months of the index event. Four intracranial atherosclerotic plaques were found in asymptomatic vessels (1 contralateral middle cerebral artery and 3 other intracranial arteries), and none of these had enhancement.

**Conclusion:** Patients with presumed intracranial atherosclerosis of the middle cerebral arteries have eccentric plaques that enhance after the administration of contrast medium when imaging is performed within weeks to months of a cerebral infarct within the arterial territory.

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**Recent Studies**\(^1\)\(^2\) have shown that 3-T high-resolution magnetic resonance imaging (HR-MRI) can be used to study the wall of intracranial arteries. Early experience with wall imaging suggests that intracranial atherosclerosis is associated with eccentric, usually irregular wall thickening similar to extracranial atherosclerosis.\(^1\)\(^2\) It remains unknown whether HR-MRI can discriminate between active and stable plaques in patients with presumed intracranial atherosclerotic disease. Therefore, the aim of this case series was to further describe the wall imaging findings of the middle cerebral arteries (MCAs) of patients with presumed atherosclerotic intracranial disease who had developed a recent ischemic stroke in the territory of their stenosis.

**Methods**

**Patients**

We reviewed the medical records of patients admitted to our institution (Toronto Western Hospital, a designated stroke center) who underwent 3-T MRI vessel wall imaging. These files contained data on 107 patients from February 1, 2006, through January 5, 2010, including 37 previously reported patients.\(^1\) Inclusion criteria for the present study were (1) 2 or more risk factors for atherosclerotic disease; (2) MCA stenosis shown on computed tomography, magnetic resonance, or conventional angiography; (3) cerebral infarction in the territory of the affected MCA; and (4) use of 3-T contrast-enhanced HR-MRI. Exclusion criteria were (1) complete MCA occlusion; (2) vasculitis; (3) Moy-a-Moya disease; (4) poor image quality secondary to motion artifacts; and (5) previously reported in the literature. We scored the following stroke risk factors in each patient: age, sex, hypertension, diabetes mellitus, dyslipidemia (defined as current use of lipid-lowering drugs or low-density lipoprotein cholesterol >96.5 mg/dL [to convert to millimoles per liter, multiply by 0.0259]), coronary artery disease, previous stroke or transient ischemic attack, (paroxysmal) atrial fibrillation or flutter, and cigarette smoking. Results of hypercoagulable and vasculitis workup were retrieved from electronic patient records. Information on the presence of atherosclerosis in the carotid and vertebral arteries was...
IMAGING PROTOCOL AND ANALYSIS

Information on at least 1 method of conventional luminal imaging (magnetic resonance, computed tomography, or digital subtraction angiography) was available for all patients to confirm the presence of an MCA stenosis. Scanning was performed with a 3-T MRI system (HDX platform; GE Healthcare, Milwaukee, Wisconsin) using an 8-channel head coil. All sequences applied were standard, approved, vendor-supplied pulse sequences. No experimental sequences were applied. The vessel wall imaging protocol consisted of a minimum of 7 sequences on 3-T MRI: (1) axial and coronal T2-weighted images; (2) precontrast axial and coronal T1 fluid-attenuated inversion recovery images; (3) postcontrast axial and coronal T1 fluid-attenuated inversion recovery images; and (4) time-of-flight magnetic resonance angiography. Sagittal images were added if needed. All sequences were monitored for appropriate targeting of the vessel of interest and to ensure that the orientation was successful to capture the affected artery at the site of stenosis in at least 2 planes of section. Imaging analysis was performed using a radiology information system picture archiving and communication system. Vessel wall images were scored by visual inspection for location of MCA stenosis, pattern of stenosis (eccentricity), and enhancement of the vessel wall. Eccentric enhancement was defined as either clearly limited to 1 side of the vessel wall or, when circumferential enhancement was noted, the thinnest part of the wall enhancement was estimated to be less than 50% of the thickest enhancing wall component. The presence of enhancement was assessed qualitatively by an experienced observer (D.J.M.) through comparison of the T1 images before and after gadolinium administration. Intracerebral arteries other than the affected MCA were scored for the presence of stenosis.

RESULTS

We identified 8 previously unreported patients (Table 1, Table 2, and Figure 1). Mean age was 67 years (range, 50-76 years), and 3 patients were male. Median time of vessel wall imaging after the index event was 5.5 days (range, 1 day to 5 months). Nine MCA stenoses were identified (1 patient had bilateral stenoses). In 6 patients, the MCA stenosis involved the M1 segment (for example, Figure 2) in combination with cerebral infarction within this territory. All M1 stenoses had eccentric morphology. Two patients had an M2 branch stenosis without involvement of the M1 segment: 1 patient had a distal M2 stenosis with inconclusive eccentricity and possibly a filling defect, and 1 patient had bilateral M2 stenoses. In the latter patient, the symptomatic MCA had a proximal eccentric M2 stenosis. All patients with infarcts within the MCA territory who underwent scanning within 5 months of the index event had enhancement of their stenotic plaques. The patient who had bilateral MCA stenoses had enhancement only of the plaque on the side of the recent infarction and not on the asymptomatic contralateral side. Three patients had atherosclerotic changes in other intracranial arteries without enhancement, and 3 patients had atherosclerotic changes in the extracranial cervical arteries.

COMMENT

Our data suggest that patients with presumed intracranial atherosclerosis of the MCAs have eccentric plaques that enhance after the administration of contrast medium when imaging is performed within weeks to months of a cerebral infarct within the arterial territory. We speculate that plaque enhancement may represent an unstable plaque and unstable plaques may be more likely to lead to cerebral infarction.

In our case series, the patient who underwent scanning 5 months after stroke still had enhancement of the affected MCA. In previous case series,1 enhancement was not shown when scans were performed more than 2 months after stroke. It could be that the patient with plaque enhancement after 5 months had a plaque that was still unstable or again unstable. Fortunately, this patient did not have recurrence of stroke symptoms at the time of the scan. Studies are needed to determine whether

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Patient No./Sex/Age, y</th>
<th>HTN</th>
<th>DM</th>
<th>Hyperlipidemia</th>
<th>Smoking Status</th>
<th>Afib or Flutter</th>
<th>CAD</th>
<th>Prior Stroke or TIA</th>
<th>Hypercoagulation/ Vasculitis Screening</th>
<th>Other Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/76</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>NP</td>
<td>No</td>
</tr>
<tr>
<td>2/F/66</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Current</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>APL-AB negative</td>
<td>No</td>
</tr>
<tr>
<td>3/F/60</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>ESR, 30 mm/h</td>
<td>No</td>
</tr>
<tr>
<td>4/M/75</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>NP</td>
<td>No</td>
</tr>
<tr>
<td>5/M/66</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Current</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>APL-AB negative</td>
<td>Alcohol abuse</td>
</tr>
<tr>
<td>6/F/74</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Former</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>ESR, 24 mm/h; normal homocytomegaly, protein C activity, protein S free antigen, APL-AB, anti-dsDNA</td>
<td>Hypertrophic CMP</td>
</tr>
<tr>
<td>7/F/60</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Unknown</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Sickle cell screen results negative</td>
<td>No</td>
</tr>
<tr>
<td>8/M/69</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Former</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Family history of stroke and CAD</td>
<td>No</td>
</tr>
</tbody>
</table>

Abbreviations: Afib, (paroxysmal) atrial fibrillation; anti-dsDNA, anti-double-stranded DNA; APL-AB, antiphospholipid antibodies; CAD, coronary artery disease; CMP, cardiomyopathy; DM, diabetes mellitus; ESR, erythrocyte sedimentation rate; HTN, hypertension; NP, not performed; TIA, transient ischemic attack.
Table 2. Results of Vessel Wall Imaging Studies in 8 Patients With MCA Stenoses

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Vessel Wall Imaging Findings in Affected MCA (Time of Scanning After Index Event)</th>
<th>Infarct Location</th>
<th>Other Atherosclerotic Vascular Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Severe stenosis of proximal R M1 with eccentric enhancement (1 d)</td>
<td>tPA administered acutely, minimal infarction</td>
<td>Both carotids and R VA</td>
</tr>
<tr>
<td>2</td>
<td>Severe L M2 branch stenosis with enhancement, inconclusive eccentricity (2 d)</td>
<td>L insular cortex</td>
<td>R VA and VA</td>
</tr>
<tr>
<td>3</td>
<td>Severe stenosis of distal L M1 with eccentric wall thickening and enhancement (3 d)</td>
<td>L internal capsule lacune</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>Severe stenosis in R M1 segment with a small amount of eccentric enhancement (2 mo)</td>
<td>R parietal cortical wedge-shaped infarct</td>
<td>All major arteries of circle of Willis</td>
</tr>
<tr>
<td>5</td>
<td>Severe stenosis of L proximal superior M2 branch, with irregular wall enhancement, uncertain eccentricity (5 d)</td>
<td>L frontal cortical and subcortical embolic infarcts</td>
<td>Contralateral superior M2/M3 junction, both carotids, both VAs</td>
</tr>
<tr>
<td>6</td>
<td>Severe stenosis of R MCA bifurcation involving the distal M1 and proximal M2 segments, with eccentric wall thickening and enhancement (6 d)</td>
<td>R frontal cortical and subcortical embolic infarcts</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>Severe stenosis of distal L M1, with eccentric wall thickening and enhancement (8 d)</td>
<td>L frontal subcortical infarcts</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>Severe stenosis of proximal L M1, with eccentric wall thickening (5 mo)</td>
<td>Small L lacunar infarct</td>
<td>All major arteries of circle of Willis</td>
</tr>
</tbody>
</table>

Abbreviations: ICA, internal carotid artery; L, left; MCA, middle cerebral artery; R, right; tPA, tissue plasminogen activator; VA, vertebral artery.

Figure 1. T1–fluid-attenuated inversion recovery (FLAIR) postcontrast vessel wall imaging findings in all patients. A, Patient 1, with right middle cerebral artery (MCA) syndrome, showing eccentric right MCA enhancement on coronal (top) and axial (bottom) images. B, Patient 2, with left MCA insular cortex stroke, showing left MCA enhancement on coronal (top) and axial (bottom) images. C, Patient 3, with left internal capsule lacune, showing left MCA enhancement on coronal (top) and axial (bottom) images. D, Patient 4, with right parietal cortex wedge-shaped infarct, showing right MCA enhancement on coronal (top) and axial (bottom) images. E, Patient 5, with multiple left frontal cortical and subcortical embolic acute infarcts, showing left MCA enhancement on coronal (top) and axial (bottom) images. F, Patient 6, with multiple right frontal cortical and subcortical embolic acute infarcts, showing right MCA enhancement on coronal (top) and axial (bottom) images. G, Patient 7, with a left frontal subcortical infarct, showing left MCA enhancement on coronal (top) and sagittal (bottom) images. H, Patient 8, with a small left MCA subcortical infarct, showing left MCA enhancement on coronal (top) and sagittal (bottom) images. Arrows indicate MCA enhancement.
plaque enhancement is associated with an increased risk of future stroke.

One important limitation of the study is that histopathologic confirmation of plaque instability was not possible because all patients survived their stroke. However, a large body of indirect evidence supports the hypothesis that eccentric gadolinium enhancement represents unstable atherosclerotic plaques. First, our results are in line with results of earlier studies that investigated plaque instability shown on HR-MRI in patients with extracranial atherosclerotic disease. Carotid endarterectomy studies suggest that a large lipid core with a thin overlying fibrous cap are features of plaque vulnerability. Rupture of the thin fibrous cap exposes the thrombogenic lipid core of the atheroma to flowing blood, with subsequent thrombus formation and ischemic stroke. A histologic correlation study in patients with a carotid artery stenosis showed that gadolinium enhancement corresponded to fibrocellular tissue, including the fibrous cap. Eccentric vessel wall enhancement has been shown on histopathologic testing to be related to unstable atherosclerotic plaques in patients with femoral and abdominal aortic artery plaques. Autopsy studies of intracranial atherosclerotic disease have shown that MCA atherosclerosis is associated with an ischemic stroke in the corresponding territory and that the degree of MCA stenosis; percentage of the plaques containing more than 40% lipid area; and prevalence of intraplaque hemorrhage, neovascularature, and thrombus are higher in plaque associated with infarction.

Other common causes of intracranial vessel wall abnormalities were unlikely in our group of patients. Dissections typically show a false lumen and bright wall components on non−contrast-enhanced T1 MRI imaging as a result of methemoglobin representing intramural hematoma. This was not observed in our patients. Furthermore, vasculitis was an unlikely cause, since patients with vasculitis typically show circumferential concentric wall thickening with diffuse gadolinium enhancement of the inflamed wall, and vasculitis was an exclusion criterion for this case series.

In conclusion, our data suggest that an eccentric MCA stenosis is related to atherosclerotic disease and that enhancement may represent unstable plaque. These findings are similar to those described in patients with extracranial atherosclerotic plaques, where the presence of...
contrast enhancement has been correlated with plaque inflammation and instability. Serial imaging in patients with plaque enhancement is being planned to determine the duration of enhancement after a stroke. Prospective studies are needed in patients with symptomatic and asymptomatic MCA stenosis to investigate the vessel wall imaging characteristics that best predict an increased risk of stroke.

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Correspondence: Richard H. Swartz, MD, PhD, FRCPC, Division of Neurology, Department of Medicine, Sunnybrook Health Sciences Centre, University of Toronto, 2075 Bayview Ave, Room A442, Toronto, ON M4N 3M5, Canada (rick.swartz@sunnybrook.ca).

Author Contributions: The corresponding author had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy the data analysis. Study concept and design: Vergouwen, Mandell, Mikulis, and Swartz. Acquisition of data: Vergouwen, Mandell, Mikulis, and Swartz. Analysis and interpretation of data: Vergouwen, Silver, Mikulis, and Swartz. Drafting of the manuscript: Vergouwen, Silver, Mikulis, and Swartz. Critical revision of the manuscript for important intellectual content: Vergouwen, Mandell, Mikulis, and Swartz. Obtained funding: Silver. Administrative, technical, and material support: Mandell and Mikulis. Study supervision: Mandell, Mikulis, and Swartz.

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REFERENCES


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