Basilar Artery Atherosclerotic Plaques in Paramedian and Lacunar Pontine Infarctions
A High-Resolution MRI Study

Isabelle F. Klein, MD, PhD; Philippa C. Lavallée, MD; Mikael Mazighi, MD, PhD; Elisabeth Schouman-Claeys, MD; Julien Labreuche, BS; Pierre Amarenco, MD

Background and Purpose—Pontine infarction is most often related to basilar artery atherosclerosis when the lesion abuts on the basal surface (paramedian pontine infarction), whereas small medial pontine lesion is usually attributed to small vessel lipohyalinosis. A previous study has found that high-resolution MRI can detect basilar atherosclerotic plaques in up to 70% of patients with paramedian pontine infarction, even in patients with normal angiograms, but none has evaluated the presence of basilar artery plaque by high-resolution MRI in patients with small medial pontine lesion in the medial part of the pons.

Methods—Consecutive patients with pontine infarction underwent basilar angiography using time-of-flight and contrast-enhanced 3-dimensional MR angiography to assess the presence of basilar artery stenosis and high-resolution MRI to assess the presence of atherosclerotic plaque. Basilar artery angiogram was scored as “normal,” “irregular,” or “stenosed” ≥30% and basilar artery by high-resolution MRI was scored as “normal” or “presence of plaque.” Medial pontine infarcts were divided into paramedian pontine infarction and small medial pontine lesion groups.

Results—Forty-one patients with pontine infarction were included, 26 with paramedian pontine infarction and 15 with small medial pontine lesion. High-resolution MRI detected basilar artery atherosclerosis in 42% of patients with a pontine infarction and normal basilar angiograms. Among patients with paramedian pontine infarction, 65% had normal basilar angiograms but 77% had basilar artery atherosclerosis detected on high-resolution MRI. Among patients with small medial pontine lesion, 46% had normal basilar angiograms but 73% had basilar artery plaques detected on high-resolution MRI.

Conclusions—This study suggests that medial pontine lacunes may be due to a penetrating artery disease secondary to basilar artery atherosclerosis. High-resolution MRI could help precise stroke subtyping. (Stroke. 2010;41:1405-1409.)

Key Words: basilar artery atherosclerosis ■ HR MRI ■ pontine small deep infarction
imated stroke mechanism in SDPI. For the purpose of the study, we evaluated the prevalence of BA atherosclerosis using HR MRI in patients with PPI and SDPI.

Materials and Methods

Study Population

Between June 2005 and October 2008, 43 consecutive patients admitted to our department for acute medial pontine infarction underwent a standard protocol of investigations, including brain MRI, MR angiography (MRA), 12-lead echocardiogram, electrocardiographic telemetry, and echocardiography. In a second set of investigation within 6 months, HR MRI was performed to evaluate the prevalence of BA plaque. Patients were divided into 2 groups according to the type of medial pontine infarct: (1) SDPI when the lesion did not reach the surface of the pons; and (2) PPI when the lesion abutted on the basal surface of the pons.

Imaging Protocol

Images were performed using a 1.5-T GE scanner (TwinSpeed; GE Medical Systems) with a standard quadrature radiofrequency head coil. To examine the basilar arterial wall, multicontrast black blood sequences using T2-, proton density, and postcontrast T1-weighted images were performed. Twelve slices were acquired along the orbit sagittal plane on the following parameters: TR/TE=2500/70 (T2), 1500/15 (proton density), 900/15 (T1 postcontrast); field of view=12×12 cm²; thickness between 2 and 3 mm; 288×224 matrix; and number of excitations=5. Best voxel size was 0.4×0.5×x2 mm. Preregional saturation pulse of 80 mm thickness to saturate incoming arterial flow was used for all 3 black blood MRI sequences. To study BA lumography, white blood imaging was performed using the 3-dimensional time-of-flight sequence: TR/TE=27/6.9; field of view=24×16, thickness=1.6 mm, with 0.8 mm overlapping, matrix=320×256, number of excitations=1, and fluoroscopically triggered contrast-enhanced MRA acquired during 0.2 mL/kg intravenous injection of gadoterate meglumine (Dotarem, Guerbet, France) at a flow of 3 mL/s; TR/TE field of view=24×16, thickness=1.2 mm, with 0.8 mm overlapping, matrix=416×384, number of excitations=1. No smoothing filter was applied. A zip 512 matrix was used to enhance spatial resolution.

Data Analysis

A descriptive analysis of HR MRI and MRA images was performed independently by 2 experienced readers (I.F.K. and P.C.L.) in the 2 groups of medial pontine infarction. Readers were blinded to clinical and etiologic data. Discrepancies between the 2 readers were solved by a visual consensus. Patients with obscured lumen or outer boundary of the artery on HR MRI were excluded from the study. HR MRI data were analyzed before MRA lumograms.

The presence of a BA plaque was assessed using HR T2, proton density, and T1 postcontrast arterial wall sections. For each patient, we assessed the presence of a BA plaque and postgadolinium wall contrast enhancement. Plaque was defined as a focal wall thickening identified on HR T2 and proton density sections compared with beneath or above BA wall slices. Wall abnormalities were scored as: (1) presence of plaque: when a wall thickening was observed with or without gadolinium enhancement; (2) presence of gadolinium enhancement without plaque: when the BA wall appeared thin but was enhanced after gadolinium infusion; and (3) normal artery wall defined as a thin wall without contrast enhancement. Finally, when HR MRI displayed a BA plaque, the degree of stenosis was eyeball-measured in a cross-sectional section on HR MRI sequences.

BA lumography was analyzed on 3-dimensional time-of-flight TOF MRA and contrast-enhanced MRA using source images and 3-dimensional reconstructed views for the presence of lumen stenosis. Stenoses were classified in 3 stages: (1) normal: when the lumen was regular; (2) irregular: when the outer boundaries of BA were not strictly parallel but without significant lumen reduction; and (3) stenotic: when we observed a lumen with a significant stenosis ≥30%.9

### Table 1. Demographics and Vascular Risk Factors of Patients With Pontine Infarction

<table>
<thead>
<tr>
<th></th>
<th>PPI (n=26)</th>
<th>SDPI (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>66 (42–86)</td>
<td>67 (34–80)</td>
</tr>
<tr>
<td>Male gender, % (no.)</td>
<td>84.6 (22)</td>
<td>80.0 (12)</td>
</tr>
<tr>
<td>Hypertension, % (no.)</td>
<td>88.0 (23)</td>
<td>86.7 (13)</td>
</tr>
<tr>
<td>Dyslipidemia, % (no.)</td>
<td>69.2 (18)</td>
<td>53.3 (8)</td>
</tr>
<tr>
<td>Current smokers, % (no.)</td>
<td>30.8 (8)</td>
<td>20.0 (3)</td>
</tr>
<tr>
<td>Diabetes, % (no.)</td>
<td>34.6 (9)</td>
<td>26.7 (4)</td>
</tr>
</tbody>
</table>

All P values for between-group comparisons >0.30.

Comparison of patients’ characteristics between the 2 medial pontine infarction groups were performed by using Fisher exact test for proportions and Mann-Whitney U test for continuous variables.

Results

Demographic and the main clinical characteristics of the 2 medial pontine infarction groups are summarized in Table 1.

Among the 43 patients with pontine infarction, 26 had PPI and 15 had SDPI. Because of poor-quality HR MRI images, 2 patients were excluded from the analysis.

Table 2 gives the prevalence of BA atherosclerosis on time-of-flight MRA and HR MRI.

### Table 2. Distribution of BA Atherosclerosis According to Imaging Modality (MRA Versus HR-MRI) Among Patients With PPI

<table>
<thead>
<tr>
<th></th>
<th>HR-MRI</th>
<th>MRA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Irregular</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Stenosis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td>16</td>
</tr>
</tbody>
</table>

Gd (+)/Plaque (-) indicates gadolinium enhancement of the vessel wall without plaque; Plaque (+), presence of atherosclerotic plaque on HR MRI.

Patients With PPI

On source and MIP angiograms, among 26 patients with PPI, 17 (65%) had normal basilar lumography, 5 (19%) had irregular lumen, and 4 (16%) displayed basilar stenosis (Table 2). Among the 17 patients without BA stenosis on MRA, HR MRI found a BA plaque in 7 cases, including gadolinium enhancement in 5 of 7 cases. In the cross-sectional area on HR MRI sequences, the stenosis was evaluated to 10% in 1 patient, 20% in 5 patients, and 40% in the remaining patient. We observed a gadolinium enhancement without plaque in 6 of 17 patients. In only 4 patients, the arterial wall appeared normal on HR MRI. All patients with irregular lumen on MRA had plaque on HR MRI. The plaque was enhanced after gadolinium infusion in 4 of 5 cases. In the cross-sectional area, the degree of stenosis was 20% in 1 patient, 30% in 2 patients, 40% in 1 patient, and 50% in the last patient.

Similarly, in all patients with BA stenosis on MRA, HR MRI confirmed the presence of plaque. All lesions were enhanced. The degree of stenosis estimated by HR MRI and MRA was comparable.
Patients With SDPI

In patients with SDPI, BA MRA was normal in 7 of 15 patients (47%), whereas 5 of 15 (33%) had an irregular lumen and 3 (20%) a stenosis (Table 3).

Three of 7 patients with normal BA luminography had a plaque identified by HR MRI; 2 of 3 were enhanced after gadolinium injection. On HR MRI, BA stenosis, measured in the cross-sectional area, was graded as 10% in 2 patients and as 30% in the other patient. The other 4 patients had a normal wall on HR MRI without contrast enhancement.

Among the 5 patients with irregular lumen on MRA, HR MRI confirmed the presence of plaque, all of them contrast-enhanced. In the cross-sectional area, BA stenosis was graded as 10% in 1 patient, 20% in 1 patient, 30% in 1 patient, and 50% in the remaining 2 patients.

All patients with BA stenosis on MRA had a plaque on HR MRI. Two of 3 were gadolinium-enhanced. MRA and HR MRI were concordant for quantification of stenosis.

Examples of HR MRI in patients with SDPI and PPI are illustrated respectively in Figure 2 and Figure 1.

Discussion

HR MRI detected BA atherosclerosis in 42% of patients with pontine infarction and normal BA MRA. Among patients with PPI, HR MRI detected a plaque in 61.5% of patients, whereas only 35% had BA lumen narrowing on conventional time-of-flight MRA. These results replicated those previously reported in our previous pilot study, confirming that PPI could be mostly caused by penetrating branch artery disease related to BA atherosclerosis, a mechanism identified in 1971 by Fischer and Caplan in an autopsy study. Interestingly, a similar pattern was found in suspected patients with SDPI. In this population, a BA plaque was detected in 73% of SDPI cases, whereas lumen narrowing of BA was found in 54% of patients. These results suggest that large vessel branch atherosclerotic disease could also be a prevalent mechanism in SDPI usually attributed to occlusion of the penetrating branch in its intraparenchymatous course (so-called “small vessel disease”).

Neuropathological studies by Ferrand and Marie in the beginning of the 20th century and by Fisher 60 years later have described pontine SDPI as an ischemic lesion <15 mm in diameter principally in the basis pontis and have noted that these infarctions were frequently associated with abnormal thickening of the penetrating arteries with segmental arterial disorganization, lipohyalinosis, and fibrinoid degeneration of the media, a unique pattern different from atherosclerosis. However, with the development of neuroimaging such as CT and MRI, large artery atherosclerosis (eg, BA stenosis) or cardiac thrombus have been identified as rare causes of pontine SDPI. In our study, we showed that basilar atherosclerotic plaque could be in fact much more frequent in SDPI than previously thought. Our results were different from Fisher’s pathological observation. He found small vessel disease in 6 of 7 autopsy cases. However, this discrepancy could have different explanations. First, Fisher’s study was conducted in the 1960s when uncontrolled hypertension (the main cause of small vessel disease) was very common. Second, autopsy cases were not consecutive, and it is possible that they have been chosen because the whole brains were highly suggestive of multilacunar state. In contrast, we have conducted a systematic study of consecutive cases limiting this selection bias.

However, we cannot be sure that the observed BA plaque on HR MRI was not an incidental finding rather than the culprit lesion. Actually, in his anatomic report of 114 patients with lacunar stroke, Fisher noted that apart from the small vessel disease, 64% of the patients had severe intracranial atherosclerosis. However, the reverse is also true, and because Fisher did not report a systematic analysis of the pathology of pontine microscopic-sized arteries, we cannot be sure that SDPIs he observed were, in fact, due to basilar branch disease rather than to small vessel disease. Moreover,
We did not have a control population without pontine infarction to estimate the prevalence of BA plaque on HR MRI. We found that 15% of our patients with normal or irregular BA on MRA sequences had a stenosis ≥40% when measured on HR MRI in cross-sectional area. Underestimation of BA stenosis on luminography sequences suggests a BA arterial remodeling at the early stage of atherosclerosis development, a mechanism previously described by Glagov in coronary arteries and reported in previous studies on middle cerebral arteries and BA.

Until now, because no test was available in vivo to identify branch artery disease or small vessel disease, diagnosis was made by exclusion. Because HR MRI visualizes the BA wall and not only luminography, this imaging modality should enable direct in vivo diagnosis of atheromatous branch disease. Hence, HR MRI could help stroke phenotype characterization as recently proposed in the new stroke subtype classification (Atherosclerosis, Small vessel disease, Cardiac source, Other cause [ASCO]). In case of SDPI, atheromatous branch disease detected by HR MRI should be considered as an alternative stroke mechanism if other findings suggestive of small vessel disease such as lacunar infarcts, microbleeds, leukoaraiosis, dilated perivascular spaces, and intracranial dolichoectasia are not identified.

Our study has several limitations. Although identifying a BA plaque is highly suggestive of a causative mechanism for the infarction, we cannot formally exclude another etiology. In our series, several patients had a coexisting cause of stroke. Among patients with PPI with a BA plaque, 7 had also a vertebral stenosis. In the SDPI group, 1 patient had an atrial fibrillation and 1 had a vertebral stenosis. We did not investigate healthy control subjects. When examining HR MRI of the vessel wall, the readers were not blind for the pontine stroke subtype, which might have influenced data analysis. However, BA plaques were considered as present when clearly identified on HR MRI sequences. Technically, spatial resolution of HR MRI is still limited. We used a 1.5-T MRI, although it has recently been reported that 3 T better identifies BA plaques. However, we used 1.5 T in the first publications of HR MRI in intracranial atherosclerotic disease. In the present series, we possibly underestimated the prevalence of BA plaques in both PPI and SDPI, but we believe that this does not alter the direction of our conclusions. Moreover, the use of contrast agent may likely enhance detection of wall lesions. Increasing the magnetic field will probably help discriminate them more accurately. In vivo comprehension of intracranial HR MRI wall lesions and plaque components is inherently challenged by the lack of histological correlations. However, consistent with our data, a previous postmortem study showed that moderate middle cerebral artery stenosis might be responsible for parent artery stroke. Knowledge from carotid plaques studies should improve our understanding. However, intracranial vessel wall lesions may behave in various ways because of different sizes of vessels, arterial wall composition, and tissue environment. In our study, most wall lesions were enhanced. This may reflect active inflammation or neoangiogenesis as described for carotid plaques or thrombus enhancement at the origin of perforating arteries. It does not seem to be always related to thrombus enhancement at the acute phase because many patients had HR MRI several months after the acute event.

In conclusion, although larger cohorts with follow-up and reproducibility studies are needed, this study strongly suggests that atherosclerotic branch disease is frequent in medial pontine infarction even in patients with medial pontine lacunar infarct. Using in vivo imaging modalities such as HR MRI will help study further on intracranial arterial diseases and comprehension of stroke mechanisms.

Disclosures

None.

References

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