Enlargement of the middle meningeal artery on MR angiography in chronic subdural hematoma

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The middle meningeal artery (MMA) is suspected to play an important role in the development of chronic subdural hematoma (CSDH). Histological findings have shown that communicating small vessels penetrate from the MMA through the dura mater and connect to sinusoidal neovessels in an outer membrane of the CSDH. The suspected mechanism of the enlargement of the hematoma is intermittent bleeding to the hematoma cavity caused by the rupture of these neovessels. Catheter embolization of the MMA was recently reported to be effective for treating recurrent CSDH. Conversely, several studies have reported that MMAs observed with MR angiography (MRA) were enlarged in patients with meningioma, in whom the MMA was a feeding artery to the tumor, and in patients with moyamoya disease, in whom the MMA was collagen circulation to the occluded arteries. Quantitative measurement of MMA diameter with MRA in patients with migraine has also been reported. To the best of our knowledge, no previous study has elucidated alteration of the MMA in patients with CSDHs. Clarification of MMA changes associated with the development of a CSDH may lead to elucidation of the pathogenesis of CSDH and may also ameliorate treatment strategies for refractory CSDH.

The purpose of this study was to evaluate the diameters of MMAs with MRA in patients with CSDHs.

Methods

Patient Population

We retrospectively assessed consecutive patients with CSDH who were admitted to our hospital between January 2010 and November 2014. Patients whose MMAs were identified on MRA performed before surgery were included. Patients who underwent surgery for CSDH were included. Patients who underwent surgery for CSDH were

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including, but conservatively treated patients with CSDH were excluded. Each patient aged 20 years or younger was included, and outpatients who were not admitted to our hospital were also excluded. Each patient was evaluated by a neurosurgeon. Every patient’s age and sex and the laterality of their hematomas were recorded from chart review. The Institutional Review Board for Clinical Research of Tokai University Hospital approved this retrospective study.

Control Patients
For each included patient with CSDH, we selected a control patient of the same sex and age (± 3 years) from the clinical records of consecutive outpatients with an unruptured aneurysm during the same period. All the unruptured aneurysms were asymptomatic and discovered incidentally. Patients who had a history of acute subdural hematoma, CSDH, acute epidural hematoma, subarachnoid hemorrhage, dural arteriovenous malformation, major artery occlusion, brain tumor, or brain surgery were excluded.

Magnetic Resonance Angiography
Magnetic resonance imaging was performed with the aid of a 1.5-T superconductive system (Achieva, Philips), and MRA was performed using the 3D time-of-flight (TOF) method. The protocol used for MRA was gradient-echo imaging (TR 24 msec, TE 6.9 msec, flip angle 20°, FOV 18.0 × 18.0 cm, matrix size 304 × 160, and voxel size approximately 0.72 × 1.13 × 1.40 mm). The brain slab under investigation was parallel to the circle of Willis and extended from the petrous portion of the temporal bone to the distribution of the middle cerebral artery and posterior cerebral artery. After data acquisition was completed and each of the 146 sections was reconstructed, MR angiograms in different view directions were obtained by means of a maximum-intensity projection (MIP) algorithm. To interpret the MR angiograms, both the MIP and section images were reviewed.

Image Postprocessing and Diameter Calculations
All MR angiograms were transferred to a remote workstation for quantitative analysis. The diameters of the MMAs were measured on each of the MIP images. These measurements were made using SDS DICOM Viewer version 7.3.2.6. (TechMatrix Co.). Because the signal intensity of arteries on MR angiograms obtained using the TOF method depends on flow velocities, intensity variations are usually observed, even in the same artery. Therefore, it is often difficult to determine the exact rim of each artery. Therefore, we supposed that they represented the actual internal cavity of the MMA, assuming that there was nonnegligible flow in these selected pixels. The MMA was measured at its anterior branch distal to the sphenoid bone, and the maximum measured diameter was used (Fig. 1). Diameters of the MMAs were measured by a board-certificated neurosurgeon (T.S.) with more than 20 years of experience in his specialty. The reader was blinded to detailed clinical information, including the existence of the hematoma. In each patient, the maximum diameter of a CSDH was measured on MR/FLAIR image slices caudal to the lateral ventricle body.

Statistical Analysis
Univariate analyses were performed by using the Wilcoxon signed-rank test and standard least-squares regression analysis for continuous variables. Numerical data are expressed as means ± SD. Any analysis resulting in a p value of less than 0.05 was considered statistically significant. The Youden index (I = sensitivity + specificity − 1) for the receiver operating characteristic curve was used to validate the optimal cutoff level of MMA diameter to allow for differentiation between CSDHs and non-CSDHs. All statistical analyses were performed with JMP 10 (SAS Institute, Inc.).

Results
Between January 2010 and November 2014, MRA was performed at admission in 57 patients with CSDHs. Because the MMAs were not identified on MR angiograms in 2 of the 57 patients with MRA, 55 patients were the subjects of this study. The mean age of the 55 patients was 72.5 ± 13.6 years; 42 (76.4%) patients were male, and 13 (23.6%) were female. Eighteen patients had a CSDH on the right side, and 13 had one on the left side; bilateral CSDHs were found in 24 patients (n = 79 MMAs). The mean diameter of the 79 MMAs on the side of the CSDHs was 1.48 ± 0.48 mm. Conversely, the mean diameter of the 31 MMAs on the non-CSDH side was 0.93 ± 0.21 mm. The mean diameter of the MMA was significantly larger on the CSDH side than on the non-CSDH side (p < 0.0001) (Figs. 1 and 2). In the 79 MMAs belonging to the CSDH side, no significant relationship was found between the diameters of the MMA and the maximum diameters of the hematomas according to our univariate regression analysis (p = 0.7294). In 24 patients with bilateral CSDHs, the mean diameter of the MMAs on the side of the larger hematoma was 1.48 ± 0.52 mm, and that on the side of
the smaller hematoma was $1.46 \pm 0.59$ mm. No significant difference in the diameters of the MMAs was found between the 2 groups ($p = 0.7878$).

**Chronological Changes in the MMA**

From 1 month to 4 years before onset of the CSDHs, 13 patients underwent MRA. The reasons for previous MRA were scrutiny for dizziness (3 patients), cerebral concussion (3), follow-up study of cerebral infarction (2), dementia (2), headache (1), black-out attack (1), and head injury (1). Five patients had bilateral CSDHs, and 8 had a unilateral CSDH. The mean diameters of these 18 MMAs on the CSDH side(s) were $0.92 \pm 0.23$ and $1.37 \pm 0.35$ mm on previous MRA and on MRA performed at admission, respectively. The diameters of the MMAs were significantly larger on the MR angiograms acquired after occurrence of the CSDHs than on the previous MR angiograms (Figs. 3 and 4). On the contrary, in 8 hemispheres on the non-CSDH side, no significant difference in the MMA diameters was found between the previous MR angiograms ($0.89 \pm 0.16$ mm) and the MR angiograms obtained after the onset of CSDH ($0.85 \pm 0.21$ mm) ($p = 0.7334$).

**Case-Control Study**

The mean age of the 55 control patients was $71.8 \pm 11.0$ years. The mean diameter of the 110 control MMAs was $1.05 \pm 0.25$ mm, and the mean diameter of the 110 MMAs in patients with CSDHs, including those on non-CSDH sides, was $1.32 \pm 0.49$ mm. The diameters of the MMAs of patients with CSDH were significantly larger than those of control MMAs ($p < 0.0001$) (Fig. 5).

**Cutoff MMA Diameter Value for the Presence of a CSDH**

The cutoff MMA diameter value for the presence of a CSDH was evaluated among 79 MMAs on the CSDH side and a combination of 31 MMAs on the non-CSDH side in patients with CSDHs and 110 MMAs in the controls. The receiver operating characteristic curve analysis revealed that a cutoff point of 1.3 mm for the MMA diameter provides the best combination of diagnostic specificity and sensitivity for whether a CSDH will exist (74.7% sensitivity, 83.7% specificity, Youden index 0.5837, area under the curve 0.82817).

**Discussion**

**Enlargement of the MMA in Development of a CSDH**

In this study, the mean diameter of the MMAs on the CSDH side was significantly larger than that on the non-CSDH side in patients with CSDHs. The mean diameter of the MMAs in patients with CSDHs was significantly larger than that in the controls. Compared with the MMAs on previous MR angiograms, the MMAs on MR angiograms obtained at the onset of CSDH were significantly larger in diameter. Therefore, the ipsilateral MMA to a CSDH became enlarged with the development of a CSDH. To the best of our knowledge, no previous studies have reported enlargement of the MMA after development of a CSDH. Tanaka et al. reported superselective angiography findings of the MMA in 4 patients with a CSDH. Enlargement of the MMAs in patients with a CSDH relative to those in a control was shown in their study, which is compatible with our study results, although the diameters of the MMAs were not evaluated objectively.
Mechanisms of MMA Enlargement in a CSDH

After mild trauma causes a tear of the arachnoid membrane, CSF leaks into the subdural space. Such fluid collection mixed with a blood cell component persists for a certain period, which causes inflammatory changes in the dura mater and can form a neomembrane on the inner side of the dura. Histopathological findings have shown that the membranes of the hematoma cavity have a 2-layered structure. In the inner layer, sinusoidal neovessels and inflammatory cells such as macrophages and polymorphonuclear leukocytes are found.11,16 The mechanism of the enlargement of the hematoma cavity is considered to be intermittent bleeding to the hematoma cavity caused by the rupture of these neovessels.11 A histological study of vascular structure between the dura and the outer membrane in a CSDH revealed that a lot of communicating small vessels penetrate through the dura and connect to the MMA.16 Superselective angiography of the MMA in patients with CSDHs showed cotton wool–like staining of the peripheral end of the MMA, which is speculated to be communicating vessels of the outer membrane of the hematoma.17 Computed tomography obtained immediately after embolization of the MMA for treatment of a recurrent CSDH showed a marked high-density area, which is consistent with extravasation of contrast material into the subdural space.9 This finding also indicates communication between the hematoma cavity and the MMA. Several cases of effective embolization to prevent the recurrence of refractory CSDHs were reported recently.5,8–10,17 which also suggests that embolization of the MMA can intercept the blood supply to the outer membrane of the CSDH and stop hematoma enlargement. The MMA might play an important role in the development of a CSDH. We speculate that an increase of blood supply to a CSDH through the MMA results in enlargement of the MMA. The retrospective nature of this study cannot lead us to conclude a role of MMA enlargement in the development of CSDHs. A prospective study to evaluate the relationship of MMA diameter to the development and improvement of CSDHs is necessary to clarify the role of MMA enlargement.

Relationship Between MMA Diameter and Size of a CSDH

No significant relationship was found between the diameters of the MMA and the maximum diameters of the hematomas, according to our univariate regression analysis among the patients with CSDHs. In patients with bilateral CSDHs, the mean diameter of the MMAs on the side of the larger hematoma was not significantly larger than that of those on the side of the smaller hematoma. This finding suggests that the MMA might become enlarged during an early development period of a CSDH, and afterward, its diameter might become stable. The volume of a CSDH may depend on absorption of the hematoma rather than blood supply to the hematoma through the MMA.

Clinical Implications

The efficacy of intraarterial embolization of the MMAs for treatment of recurrent CSDHs has been reported in several cases.5,8–10,17 Information about the MMA on MRA performed before intervention may be useful for developing a strategy for embolizing the MMA. During bur-hole drainage surgery, direct coagulation or embolization of the MMA through a bur hole might facilitate shrinkage of the hematoma. A future prospective study to evaluate the effect of MMA occlusion via an intraarterial route or at the time of drainage surgery on the recurrence rate of CSDHs is expected to determine the clinical utility of information about MMA enlargement in CSDHs.
Limitations
Several studies have reported measuring the MMA in patients with migraine. Because the signal intensity of arteries on MR angiograms obtained by using the TOF method depends on the flow velocities and flow directions, measurement of an MMA diameter on MR angiograms could not reflect the exact diameter of the MMA. To obtain consistent results in the study, signal intensities of the pixels were measured semiautomatically to determine the diameter of the MMAs.

In our case-control study, patients with unruptured aneurysms found incidentally were selected as controls. Their MMAs might not have represented exactly the MMAs of healthy subjects, but patients with various diseases that affect MMA diameter were excluded from the controls.

Conclusions
In patients with CSDHs, the MMA on the side of the CSDH became enlarged with the development of the CSDH. No relationship was found between the diameter of the MMA and the size of the CSDH. Information about CSDHs might not have represented exactly the MMAs of healthy subjects, but patients with various diseases that affect MMA diameter were excluded from the controls.

References

Disclosure
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

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