“Tail Sign” Associated With Microembolic Signals

Eisuke Furui, MD; Kazuhiko Hanzawa, MD; Hajime Ohzeki, MD; Takashi Nakajima, MD; Nobuyoshi Fukuhara, MD; Masaharu Takamori, MD

Background and Purpose—Transcranial Doppler ultrasound (TCD) can detect circulating microembolic signals (MES). We focused our attention on tail signs (TS), a signal associated with MES that appeared as a small reversal signal after MES on the high time resolution spectral display. We examined MES and artifacts in an animal study to determine whether TS were specific changes associated with MES and investigated the characteristics of TS in both animal and clinical studies.

Methods—In an animal study, adult pigs with venoarterial extracorporeal membrane oxygenation and minimal anticoagulation therapy were used as a model for cerebral embolism. After performing TCD monitoring with a multigated approach, we did an offline analysis to investigate several parameters concerning MES and TS. We also examined TS in patients in a clinical study.

Results—From a total of 362 MES investigated in the animal study, 72.9% were followed by TS. We could not find any TS associated with artifacts. The time delay between TS and MES was negatively correlated with the velocity of MES. MES almost always appeared first in the proximal channel, whereas TS conversely appeared first in the distal channel. In the clinical study, we were also able to observe TS associated with MES.

Conclusions—TS may represent emboli passing down a branch vessel or twisted downstream vessel. TS are specific for MES and can be used as another criterion for MES identification. (Stroke. 1999;30:863–866.)

Key Words: cerebral embolism ■ diagnostic imaging ■ ultrasonography, Doppler

Cerebral microembolic signals (MES) were first described during carotid surgeries.1 Transcranial Doppler ultrasound (TCD) has been reported2–3 to be capable of detecting circulating cerebral MES in patients with ischemic stroke. Most common identification criteria for MES are based on the basic audiovisual characteristics of high-intensity transient signals.4 Applying this technique to clinical practice, it is not always easy to differentiate true embolic signals from artifact. Spontaneous speckling in the background signal makes differentiation even more difficult. Automated detection software including neural network5 or multigate approach6 systems have been developed recently. Although the differentiation between MES and artifact is, in principle, possible with these methods, they are all dependent on different methodological limitations. The optimal recording time of TCD monitoring remains undetermined.7 If the prevalence of MES is too low and the intensity of MES is too small throughout the entire recording time, the differentiation of MES from artifact is extremely difficult. Therefore, another useful criterion is needed. We noticed and focused on tail signs (TS), a postembolic signal associated with MES which appeared as a small reversal signal after MES on the high time-resolution spectral display (Figure 1A). We attempted to determine whether TS were characteristic of the change associated with MES in both animal and clinical studies.

Subjects and Methods
The same TCD machine (Multi-Dop X4, DWL) was used with a multigate 2-MHz probe in both animal and clinical studies. In an animal study, 2 adult pigs weighing 24 to 26 kg, treated with venoarterial extracorporeal membrane oxygenation (VA ECMO) and minimal anticoagulation therapy, were used as a model for cerebral embolism. During the experiment, the animals were anesthetized with 2.0% to 3.0% halothane and treated following Niigata University Animal Care Guidelines. Following a left thoracotomy, VA ECMO was performed by aortic and pulmonary cannulation with use of a roller pump and membrane oxygenator. Heparin was administered once before the cannulation. After the bypass was started, numerous MES were recorded, and anticoagulation therapy was added only when the frequency of MES increased excessively. A major branch of the carotid artery, which displayed flow directed toward the probe, was insonated through the left transorbital route at a depth of ≈50 mm. Two sample volumes of 5 mm were set at a distance of 5 mm. The probe was fixed with an external device. During TCD monitoring, the automatic embolic detection system in this Doppler machine was able to detect and save any relevant segments, which we reviewed later. The criteria for MES identification were as follows: (1) short duration (<100 ms), (2) unidirectional signal, (3) intensity increase at least 7 dB above the background, (4) random appearance in the cardiac cycle, and (5) sufficient time delay between the 2 channels. We performed an offline analysis of the recorded MES that met the criteria to investigate the prevalence of the TS, the time delay between TS and MES, the relative dB level, and the velocity of MES in the proximal channel. TS were counted only during carotid surgeries.1 Transcranial Doppler ultrasound (TCD) has been reported2–3 to be capable of detecting circulating cerebral MES in patients with ischemic stroke. Most common identification criteria for MES are based on the basic audiovisual characteristics of high-intensity transient signals.4 Applying this technique to clinical practice, it is not always easy to differentiate true embolic signals from artifact. Spontaneous speckling in the background signal makes differentiation even more difficult. Automated detection software including neural network5 or multigate approach6 systems have been developed recently. Although the differentiation between MES and artifact is, in principle, possible with these methods, they are all dependent on different methodological limitations. The optimal recording time of TCD monitoring remains undetermined.7 If the prevalence of MES is too low and the intensity of MES is too small throughout the entire recording time, the differentiation of MES from artifact is extremely difficult. Therefore, another useful criterion is needed. We noticed and focused on tail signs (TS), a postembolic signal associated with MES which appeared as a small reversal signal after MES on the high time-resolution spectral display (Figure 1A). We attempted to determine whether TS were characteristic of the change associated with MES in both animal and clinical studies.

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when unequivocal reversal signals were recognized after MES on the high time resolution spectral display in both channels. To calculate these parameters, MES and TS were defined as the point of Doppler frequency shift at the maximum amplitude. In addition, 100 episodes of artifact were produced by lightly tapping skin around the probe before the cannulation. We could not determine the beginnings of MES and TS on the raw Doppler time displays unless both of them were clear. The time delays of both MES and TS between 2 channels were calculated on the raw Doppler time displays when possible. In a clinical study, we analyzed patients with a mechanical prosthetic cardiac valve or ischemic stroke and performed TCD monitoring from 1 middle cerebral artery for more than 30 minutes using the universal technique. Informed consent was obtained from all patients before the study. The sample volumes setting and the MES identification criteria were same as in the animal study. We performed an offline analysis of the recorded MES to investigate the prevalence of the TS. For statistical analysis, the nonparametric Mann-Whitney \( U \) test was used to compare different groups. Significance was declared at the \( P<0.05 \) level.

Results

In the animal study, from a total of 362 MES investigated, 264 (72.9%) of MES were followed by TS. The mean±SD time delay between MES and TS was 52.7±18.5 ms in the proximal channel. The mean±SD relative dB level of MES was higher with TS (35.7±9.9 dB) than without TS (30.9±7.1 dB; \( P<0.0001 \)). The mean±SD velocity of MES was higher with TS (26.4±8.6 cm/s) than without TS (14.5±6.7 cm/s; \( P<0.0001 \)). The time delay between MES and TS in the proximal channel was negatively correlated with the velocity of MES (\( r=-0.478 \), \( n=264 \), \( P<0.0001 \); Figure 2). We could not find any TS associated with the artifacts. We could clearly measure the beginnings of 44 sets of MES and TS in both channels. The time delay ranged from 1.2 to 38.6 ms (mean±SD, 11.6±9.1) and that of TS from -9.0 to 1.1 ms (mean±SD, -2.18±1.9 ms). These results mean that MES always appeared sequentially in the 2 channels, first in the proximal one, then in the distal; and that TS almost always appeared first in the distal then in the proximal channel (Figure 1B). Judging from the spectral data, the intensity of TS was always lower than that of the corresponding MES (Figure 1B).
In the clinical study, we were also able to observe TS associated with MES (Figure 1A). Among a total of 160 MES investigated, 16 (10.0%) were followed by TS; 6 of the patients (42.9%) presented with TS (Table). TS in the clinical study also had the same characteristics as in the animal experiment: (1) TS appeared first in the distal channel, then in the proximal one and (2) the intensity of TS was lower than that of the corresponding MES.

To confirm that TS were not artifacts specific to this Doppler machine, we examined TS in the animal and clinical studies with another Doppler machine (TC 2020, Nicolet/EME). We were also able to record TS associated with MES using that machine (Figure 1C).

**Discussion**

The purpose of this study was to evaluate the implication of TS. Under the strict identification criteria for MES, we were able to observe TS associated with MES in both animal and clinical studies. TS were never seen after artifacts. We recorded TS using 2 different Doppler machines. These results indicate that TS are highly specific for MES.

What accounts for TS? TS tended to follow larger and faster MES, so the turbulence flow after the embolus may be one explanation for TS. If an embolus becomes larger and flows faster, the turbulence flow after the embolus may become larger and easier to detect. However, our results with the multigate approach do not support this hypothesis. If this were true, TS might have appeared sequentially in both channels, first in the proximal then in the distal one, just as MES did. The main points of our results are summarized as follows: (1) the intensity of TS was lower than that of the corresponding MES, (2) TS appeared as a reversal signal first in the distal channel and then in the proximal one, and (3) the time delay between MES and TS negatively correlated with the velocity of MES. According to these points, TS seem to have been recorded farther away from the core of the sample volume than MES were. TS may be estimated to represent emboli passing down a branch vessel or twisted downstream vessel, which has a direction of flow away from the probe (Figure 3). Some pairs of MES and TS, recorded only in the proximal channel (Figure 4), may represent emboli that pass down branch vessels before they are detected in the distal channel. The presence of these pairs supports the hypothesis that TS represent emboli passing down a branch vessel or twisted downstream vessel. The time delay between MES and TS depended on the velocity of MES. The faster the MES flowed, the earlier the TS appeared with a shorter time delay. The detection of TS is highly dependent on the spatial arrangement of the vessels and the sample volumes. The smaller size of a pig’s brain may explain the higher prevalence of TS in the animal study than in the clinical study. Not the prevalence but the presence of TS has important implications for clinical practice.

We could find only one report\(^8\) dealing with postembolic signals. We thought that this sign was not unique to our study, because we found postembolic signals resembling TS in the TCD manufacturer’s brochure or a literature concerning emboli detection.\(^9\) Ries and colleagues\(^8\) reported that specific changes in Doppler spectral patterns could be identified after all embolic signals caused by solid particles in a phantom model by use of

### TS and MES Observed in Patients in Clinical Study

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age/Sex</th>
<th>Potential Embolic Source</th>
<th>Treatment</th>
<th>MES, n</th>
<th>TS, n</th>
<th>Recording Time, min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>53/F</td>
<td>MVR</td>
<td>AC</td>
<td>9</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>67/M</td>
<td>MVR</td>
<td>AC</td>
<td>2</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>68/M</td>
<td>MVR</td>
<td>AC</td>
<td>1</td>
<td>0</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>72/M</td>
<td>MVR</td>
<td>AC</td>
<td>10</td>
<td>0</td>
<td>30</td>
</tr>
<tr>
<td>5</td>
<td>37/M</td>
<td>AVR</td>
<td>AC</td>
<td>96</td>
<td>11</td>
<td>60</td>
</tr>
<tr>
<td>6</td>
<td>68/M</td>
<td>AVR</td>
<td>AC</td>
<td>8</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>7</td>
<td>61/M</td>
<td>CS</td>
<td>None</td>
<td>10</td>
<td>0</td>
<td>30</td>
</tr>
<tr>
<td>8</td>
<td>74/F</td>
<td>CS</td>
<td>AP</td>
<td>2</td>
<td>0</td>
<td>30</td>
</tr>
<tr>
<td>9</td>
<td>58/M</td>
<td>PFO</td>
<td>AP</td>
<td>5</td>
<td>0</td>
<td>10(^*)</td>
</tr>
<tr>
<td>10</td>
<td>62/M</td>
<td>PFO</td>
<td>None</td>
<td>5</td>
<td>1</td>
<td>10(^*)</td>
</tr>
<tr>
<td>11</td>
<td>67/M</td>
<td>AoA</td>
<td>AP</td>
<td>4</td>
<td>0</td>
<td>40</td>
</tr>
<tr>
<td>12</td>
<td>77/F</td>
<td>IE</td>
<td>None</td>
<td>2</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>13</td>
<td>53/M</td>
<td>ND</td>
<td>AP</td>
<td>4</td>
<td>0</td>
<td>30</td>
</tr>
<tr>
<td>14</td>
<td>73/M</td>
<td>ND</td>
<td>AP</td>
<td>2</td>
<td>0</td>
<td>60</td>
</tr>
</tbody>
</table>

MVR indicates mitral valve replacement; AVR, aortic valve replacement; CS, carotid stenosis; AoA, aortic atheroma; PFO, patent foramen ovale; IE, infective endocarditis; ND, not determined; AP, antiplatelet therapy; and AC, anticoagulant therapy.

\(^*\)MES were recorded during the contrast medium injection.
Tail Sign and Microembolic Signals

a high-resolution analysis of Doppler raw data. These postemembolic spectral patterns were always characterized by a Doppler frequency shift decreasing in time and resembling the Greek letter lambda. According to them, in 60% of all signs the velocity of the signal finally passed zero to a reverse flow direction, like TS. They assume that lambda signs can be explained by Doppler reflection phenomena caused by postemembolic flow disturbances or by technical factors concerning beam geometry. Lambda signs and TS have some similarities on the spectral display. However, we suppose that the origin of lambda signs is basically different from that of TS for the following reasons: (1) lambda signs were recorded in a phantom model using a straight polyethylene tube without branch or twisted segments, contrasting with our study, and (2) lambda signs could not be found in cases of embolism by small air bubbles, whereas TS were recorded associated with MES from a patient with a patent foramen ovale during the contrast medium injection.

We conclude that the TS are characteristic of the changes in Doppler spectra associated with MES and that the presence of TS can be a useful criterion for MES identification.

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Editorial Comment

Using a pig model, with some data from humans, the authors have tried to create an ultrasonographic finding that could have specificity for microembolic signals (MES) that can be separated from artifacts. Two pigs were studied, using a model comparable to open-heart surgery, and the authors found tail signs (TS) that they associated with MES but not with artifacts. Definitions play a large role in the findings in this study, as does the generous choice of signals 7 dB from background as a reliable finding. For many investigators, values for “MES” must be >10–11 dB to be considered less likely to be artifacts.

Whether artifact or not, the attempt here provides another target for validation by future investigators, possibly leading us closer to a reliable definition of particulate matter embolism.

Ultrasonographers continue to be unclear on what constitutes the material(s) that make up the MES found in a variety of settings, which span the gamut from harmless microcavitations generated by artificial valves at one end to particulate matter emboli from the heart and great vessels at the other. That some MES are associated with high-grade stenoses of brain–brain vessels is well established, but that the MES are harbingers of potentially serious brain-bound emboli is not. Experiences vary widely as to whether any of a number of treatments, from platelet antiaggregants to anticoagulation, alter the frequencies of MES, although most centers fail to document the MES after successful endarterectomy (or, in some cases, angioplasty and stenting) of brain-bound vessels. But what, exactly, is the range of materials is still not clear. Animal models seem a good source for such studies.
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