Trigeminal neuralgia: differences in magnetic resonance imaging characteristics of neurovascular compression between symptomatic and asymptomatic nerves

Madoka Suzuki, DDS,a Norio Yoshino, DDS, PhD,a Masahiko Shimada, DDS, PhD,a Akemi Tetsumura, DDS, PhD,a Tomoka Matsumura, DDS, PhD,b Haruhisa Fukayama, DDS, PhD,b and Tohru Kurabayashi, DDS, PhDa

Objectives. Neurovascular compression (NVC) of the trigeminal nerve is the primary cause of trigeminal neuralgia (TN) but is known to occur in both symptomatic and asymptomatic nerves. The purposes of this study were to evaluate the relationship between the magnetic resonance imaging (MRI) findings regarding the site of NVC and the manifestation of TN symptoms.

Methods. In 147 patients with unilateral TN, the presence or absence of NVC was evaluated on MRI in both symptomatic and asymptomatic nerves. In cases with NVC, the shortest distance from the trigeminal nerve root to the responsible vessel was measured.

Results. The mean distance from the trigeminal nerve root to the site of NVC in asymptomatic nerves (3.85 \pm 2.69 mm) was significantly greater than that in symptomatic nerves (0.94 \pm 1.27 mm). When the distance was 3 mm or less, the rate of the manifestation of TN symptoms was 83.1% (103/124). On the other hand, it was only 19.6% (9/46) in cases with a distance of greater than 3 mm.

Conclusions. Whether or not NVC of the trigeminal nerve was symptomatic was closely related to the distance from the trigeminal nerve root to the responsible blood vessel. (Oral Surg Oral Med Oral Pathol Oral Radiol 2015;119:113-118)

It is widely accepted that trigeminal neuralgia (TN) is primarily caused by neurovascular compression (NVC) at the root entry zone (REZ) of the trigeminal nerve in the cerebellopontine angle cistern.1-3 Thus, microvascular decompression (MVD) is considered the most effective treatment for patients with TN.4 The diagnosis of NVC is generally made by MR angiography and MR cisternography.5 It has also been reported that NVC patterns on MRI are closely related to the region of neuralgic manifestation.5 On the other hand, NVC is also known to occur in asymptomatic nerves, that is, those contralateral to TN symptoms or those in asymptomatic subjects.6-10 Thus, the clinical significance of NVC detected on MRI has not been fully established. Clarifying the distinction between symptomatic and asymptomatic NVC would further increase the validity of MRI for the treatment planning for TN.

In asymptomatic NVC, vascular contact may be present at sites distal to the REZ of the trigeminal nerve. Thus, the likelihood of NVC causing clinical symptoms of TN is thought to be closely related to the distance from the trigeminal nerve root to the responsible blood vessel. However, to our knowledge, few studies have evaluated the relationship between this distance and the manifestation of TN.

Against this background, the purposes of this study were to analyze MRI findings regarding the location of NVC in both symptomatic and asymptomatic nerves, and to evaluate the relationship between these findings and the presence or absence of clinical symptoms of TN.

MATERIALS AND METHODS
This retrospective study was approved by our institutional review board (No.895).

Patients
The subjects were 147 consecutive patients with idiopathic TN (61 men and 86 women; age range, 21-93 years; mean age, 64.7 years) who underwent MRI at our hospital from April 2010 to November 2012. Cases with brain tumor or multiple sclerosis were excluded from the study. Recurrent cases after MVD were also excluded. All 147 patients had unilateral TN. Of those, 88 had TN on their right side and 59 on their left side. The diagnosis of TN was made according to the criteria of the International Headache Society.11

Imaging examinations
A 1.5-T superconducting system (Magnetom Vision, Siemens AG, Erlangen, Germany) with a 2.5 mT/m gradient

Statement of Clinical Relevance
Neurovascular compression (NVC) is known as the primary cause of trigeminal neuralgia. This study revealed that whether NVC is symptomatic or not is closely related to the distance from the trigeminal nerve root to the responsible blood vessel.
maximum gradient capability and a circularly polarized head coil was used to obtain all MR images.

In all patients, transverse T1-weighted spin-echo images (repetition time/echo time [TR/TE] = 560/14 msec) and T2-weighted turbo spin-echo images (TR/TE, 5000/96 msec; echo train length, seven) were obtained with a field of view of 230 × 230 mm, a matrix of 256 × 256, and a section thickness of 3 mm with a 1-mm intersection gap. These images were used to rule out the diagnoses of multiple sclerosis and brain tumor.

MR angiography was performed using a 3D fast imaging with steady-state precession (3D-FISP) sequence with the following parameters: TR/TE 39/6.5 msec, 20-degree flip angle, 230 × 230-mm field of view, and 256 × 512 matrix. The other imaging parameters included a slab thickness of 60 mm with 60 sections, yielding transverse images with a section thickness of 1 mm. The acquisition slab was oriented in the transverse direction on the sagittal and coronal scout images so that both sides of the trigeminal nerve could be included in the image. After obtaining transverse images, coronal reformatted images were also obtained by using a multiplanar reconstruction (MPR) algorithm.

MR cisternography was performed using a 3D constructive interference in steady state (3D-CISS) sequence with the following parameters: TR/TE 12.25/5.9 msec, 70-degree flip angle, 230 × 230-mm field of view, and 512 × 512 matrix. The other imaging parameters included a 34-mm slab thickness with 34 sections, which yielded transverse images with section thicknesses of 1 mm. The acquisition slab was oriented in the same direction as in the 3D-FISP sequence. Coronal reformatted images were also obtained by using an MPR algorithm.

**Image analysis**

All 3D-FISP and 3D-CISS images were independently and separately evaluated for the presence or absence of NVC by two radiologists (M.S. and N.Y.) who were blinded to the clinical findings. NVC was regarded as present when no cerebrospinal fluid (CSF) was visible between the vessel and the nerve in both of transverse and coronal 3D-CISS images. 3D-FISP images were used to determine whether the responsible blood vessel was an artery or a vein. When disagreement existed about the presence or absence of NVC, a consensus was reached through discussion. In cases with NVC, the same two radiologists used a DICOM viewer (Syngo Via version: VA20A, Siemens AG, Erlangen, Germany) to independently and separately measure the shortest distance between the trigeminal nerve root and the responsible blood vessel. The details of the measurement methods are shown in Figure 1. To evaluate both intra- and interobserver agreement, they measured the distance twice, with a 1-week interval. The mean value of the four measurements (two observers, two measurements each) was adopted as the distance from the trigeminal nerve root to the responsible blood vessel in each case, and this distance was compared between symptomatic and asymptomatic nerves.

**Statistical analysis**

Statistical analysis was performed using IBM SPSS 21.0 software (New York, NY). Interobserver agreement regarding the presence or absence of NVC was evaluated by the κ-coefficient. The κ values were interpreted as follows: less than 0.40, poor agreement; 0.40-0.59, fair agreement; 0.60-0.74, good agreement; and 0.75 or more, excellent agreement. The intra- and interobserver agreements for the distance from the trigeminal nerve root to the responsible blood vessel were evaluated using the intraclass correlation coefficient (ICC). An ICC of 0.20 or less was considered to indicate slight agreement; 0.21-0.40, fair; 0.41-0.60, moderate; 0.61-0.80, substantial; and 0.81 or more, almost perfect. The Mann-Whitney U test and the chi-square test were used to compare symptomatic and asymptomatic nerves in terms of the mean value and distribution, respectively, of the distance from the trigeminal nerve root to the responsible blood vessel.

**RESULTS**

The interobserver agreement for the presence or absence of NVC was excellent (κ = 0.8534). For the measured distance from the trigeminal nerve root to the
Table I. The presence or absence of neurovascular compression (NVC) in symptomatic and asymptomatic nerves

<table>
<thead>
<tr>
<th>Number of cases (%)</th>
<th>Symptomatic nerves</th>
<th>Asymptomatic nerves</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVC (+)</td>
<td>112 (76.2)</td>
<td>58 (39.5)</td>
</tr>
<tr>
<td>NVC (-)</td>
<td>35 (23.8)</td>
<td>89 (60.5)</td>
</tr>
<tr>
<td>Total</td>
<td>147 (100)</td>
<td>147 (100)</td>
</tr>
</tbody>
</table>

Table II. The responsible blood vessels in the cases with neurovascular compression

<table>
<thead>
<tr>
<th>Responsible blood vessel</th>
<th>Symptomatic nerves</th>
<th>Asymptomatic nerves</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCA</td>
<td>65 (58.0)</td>
<td>28 (48.3)</td>
</tr>
<tr>
<td>Vein</td>
<td>25 (22.3)</td>
<td>27 (46.6)</td>
</tr>
<tr>
<td>AICA</td>
<td>10 (8.9)</td>
<td>2 (3.4)</td>
</tr>
<tr>
<td>BA</td>
<td>5 (4.5)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>PICA</td>
<td>3 (2.7)</td>
<td></td>
</tr>
<tr>
<td>VA</td>
<td>1 (0.9)</td>
<td></td>
</tr>
<tr>
<td>SCA and vein</td>
<td>1 (0.9)</td>
<td></td>
</tr>
<tr>
<td>SCA and AICA</td>
<td>1 (0.9)</td>
<td></td>
</tr>
<tr>
<td>BA and vein</td>
<td>1 (0.9)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>112 (100)</td>
<td>58 (100)</td>
</tr>
</tbody>
</table>

AICA, anterior inferior cerebellar artery; BA, basilar artery; PICA, posterior inferior cerebellar artery; SCA, superior cerebellar artery; VA, vertebral artery.

As shown in Table I, the frequencies of NVC of symptomatic and asymptomatic trigeminal nerves were 76.2% (112/147) and 39.5% (58/147), respectively. Forty-five patients (30.6%) had NVC of both symptomatic and asymptomatic nerves, 67 (45.6%) of only symptomatic nerves, and 13 (8.8%) of only asymptomatic nerves. In the remaining 22 patients (15.0%), NVC was not observed with either nerve. The responsible blood vessels in the cases with NVC are shown in Table II. In both symptomatic and asymptomatic nerves, the most common blood vessel was the superior cerebellar artery, followed by the vein. The arterial NVC was significantly more frequent in symptomatic nerves (77.7%; 87/112) than in asymptomatic nerves (53.4%; 31/58) (P < .002, chi-square test).

The mean value of the distance from the trigeminal nerve root to the responsible blood vessel in the cases with NVC was 0.94 ± 1.27 mm for symptomatic nerves (112 cases), and 3.85 ± 2.69 mm for asymptomatic nerves (58 cases). The latter was significantly larger than the former (P < .0001). The distribution of the distances for both symptomatic and asymptomatic nerves is shown in Table III. When the distance was 3 mm or less, symptomatic nerves were more common than asymptomatic nerves. On the other hand, when it was greater than 3 mm, this relationship was not found. Specifically, the rate of TN occurrence was 83.1% in cases with a distance of 3 mm or less (103/124), compared with 19.6% in cases with a distance greater than 3 mm (9/46). The latter was significantly lower than the former (P < .0001). In particular, in 22 cases with a distance greater than 5 mm, all cases but one were asymptomatic.

MR images of a representative case are shown in Figures 2 and 3.

DISCUSSION

TN is characterized by unilateral electric shock—like pain that occurs along one or more sensory divisions of the trigeminal nerve.11,13-15 It is widely accepted that TN is primarily caused by NVC at the REZ of the trigeminal nerve.1-3 The REZ is the transition zone between the central and peripheral nervous systems, where focal demyelination of trigeminal nerve fibers is likely to occur due to continuous compression by overlying blood vessels. Such focal demyelination causes a “short circuit” of the action current in the demyelinated axons, leading to severe pain caused by excited pain fibers with abnormal discharges.1-3 Janetta first reported that MVD, which eliminates the vascular compression of the trigeminal nerve, could lead to the relief of TN symptoms.1 At present, MVD is the treatment of choice for patients with TN because it has proven to be effective and has a high rate of long-term success.4

NVC is generally diagnosed by MR angiography using Fast Low Angle Shot (FLASH), FISP, or SPoiled Gradient Recalled (SPGR) sequences and MR cisternography using CISS or Fast Imaging Employing Steady-state Acquisition (FIESTA) sequences.5-16 In our institution, we routinely use 3D-CISS and 3D-FISP. CISS images can clearly depict both arteries and veins as low-signal-intensity structures, similar to the trigeminal nerve, whereas FISP images depict only arteries. Thus, by combining these two sequences, we can determine whether the responsible vessel is an artery or a vein.5
The diagnostic criteria for NVC on MRI vary among researchers. In some studies, the presence of NVC has been defined by the lack of CSF intervention between the nerve and the vessel. In our study, we diagnosed NVC when there was no apparent CSF between the two structures on both transverse and coronal consecutive MR images, and theorized that such diagnostic criteria would be useful in reducing false-positive NVC identification. Using this approach, we found NVC in 76.2% (112/147) of symptomatic nerves. This frequency was considered consistent with those in previous studies, which ranged from 71% to 93%.

For symptomatic nerves without NVC on MR images, the causes of TN might include arachnoid adhesions at the REZ, nerve atrophy, and neuralgia after herpes virus infection. In addition, it is possible that our study included only a few cases with false-negative NVC results on MRI.

As mentioned above, NVC at the REZ is the primary cause of TN. However, it is well known that MR images reveal NVC of not only symptomatic nerves but also of asymptomatic nerves. Tash et al. reported that NVC was found in 46% (79/170) of the trigeminal nerves in asymptomatic subjects. Similarly, NVC of the nerves contralateral to TN symptoms was identified by Anderson et al. and Erbay et al. in 71% (34/78) and 25% (10/40) of cases, respectively. Similarly, in our study, NVC was found in 39.5% (58/147) of asymptomatic nerves, defined as those contralateral to clinical symptoms. Thus, the clinical significance of NVC detected on MRI has not been fully established. Against this background, we aimed to distinguish symptomatic and asymptomatic NVC on MRI.

Some studies have evaluated the relationship between the severity of NVC and the presence or absence of clinical symptoms of TN. Lorenzoni et al. reported that nerve dislocation or distortion by the vessel was observed in 32% of cases on the symptomatic side, whereas there was always simple contact on the asymptomatic side. Anderson et al. classified the severity of NVC into three grades—simple, moderate, or severe—and reported that symptomatic nerves were more likely to be associated with more severe compression. Similar results have also been

Fig. 2. Magnetic resonance (MR) images in a 76-year-old man with right trigeminal neuralgia. (A) 3D-CISS transverse image. (B) 3D-CISS coronal image. (C) 3D-FISP transverse image. (D) 3D-FISP coronal image. MR images revealed neurovascular compression on the symptomatic nerve (right side, arrows). The distance from the nerve root to the responsible blood vessel measured on the transverse image (A) was 0 mm. Both the trigeminal nerve and the blood vessel (artery) show low signal intensity on 3D-CISS images (A, B). On the other hand, on 3D-FISP images (C, D), the vessel shows high signal whereas the nerve shows intermediate signal intensity.
reported by other researchers.\textsuperscript{9,22} According to these studies, it seems that consistent nerve dislocation or distortion by the offending vessel affects the manifestation of TN.

Few studies, however, have evaluated the relationship between the site of NVC and the presence or absence of clinical symptoms. To our knowledge, the only study to have done thus far is that by Miller et al.\textsuperscript{9} They defined three sites of NVC—proximal, middle, and distal—and reported that NVC at the proximal site was significantly more frequent in symptomatic nerves than in asymptomatic nerves. However, they did not clearly define the range of the proximal site. Lorenzoni et al.\textsuperscript{18} evaluated the distance between NVC and the brain stem surface in symptomatic nerves and found that it was less than 3 mm in 39 cases and 3 mm or more in 42 cases. However, they did not compare the distance between symptomatic and asymptomatic nerves. Thus, the relationship between the site of NVC and the presence or absence of clinical symptoms has not been fully examined.

In this study, we measured the distance from the trigeminal nerve root to the site of NVC, comparing symptomatic and asymptomatic nerves. As shown in Table II, the mean distance in the asymptomatic nerves (3.85 ± 2.69 mm) was significantly greater than that in the symptomatic nerves (0.94 ± 1.27 mm). Further, whereas NVC at a distance of 3 mm or less was associated with a high frequency of symptoms, the rate of symptomatic NVC significantly decreased with distances greater than 3 mm. In particular, in 22 cases with distances greater than 5 mm, all cases but one were asymptomatic. Thus, our study revealed that the frequency of clinical symptoms of TN was closely related to the site of NVC of the trigeminal nerve, that is, the distance from the trigeminal nerve root to the responsible blood vessel. Specifically, in most of the cases in which this distance was large, NVC caused no clinical symptoms of TN, presumably because it occurred at sites distal to the REZ of the trigeminal nerve. The true extent of the REZ cannot be defined on MRI. However, according to our results, it was considered that the

Fig. 3. Magnetic resonance (MR) images in a 76-year-old man with right trigeminal neuralgia (the same patient as in Figure 2). (A) 3D-CISS transverse image. (B) 3D-CISS coronal image. (C) 3D-FISP transverse image. (D) 3D-FISP coronal image. MR images revealed neurovascular compression on the asymptomatic nerve (left side, arrows). The distance from the nerve root to the responsible blood vessel measured on the transverse image (A) was 5.2 mm. Both the trigeminal nerve and the blood vessel (artery) show low signal intensity on 3D-CISS images (A, B). On the other hand, on 3D-FISP images (C, D), the vessel shows high signal, whereas the nerve shows intermediate signal intensity.
length from the trigeminal nerve root to the distal end of the REZ was usually 3 mm or less, and in only few cases was it greater than 5 mm. At least two anatomic studies have investigated the extent of the REZ. De Ridder et al.23 dissected five cadavers and reported that the average length from the trigeminal nerve root to the distal end of the REZ was 2.6 mm. Guclu et al.24 reported that the average length in six cadavers was 4.19 mm. Although there may be individual differences in the extent of the REZ, we consider that our results are largely compatible with those of these anatomic studies.

There are two main limitations to our study. First, the presence or absence of NVC was evaluated with MRI alone and was not confirmed with surgery. Although MRI findings are known to be highly consistent with intraoperative findings,5 it is possible that a few cases were misclassified with regard to the presence or absence of NVC. Second, the patients included in our study all had unilateral TN symptoms, and we compared MRI findings on the symptomatic side with those on the asymptomatic side. Further research will be necessary to confirm whether the nerves in asymptomatic subjects show MRI findings similar to those of nerves contralateral to TN symptoms.

CONCLUSIONS

The present study revealed that whether or not NVC of the trigeminal nerve caused TN was closely related to the site where NVC occurred, that is, to the distance from the trigeminal nerve root to the responsible blood vessel. The manifestation of TN decreased significantly with distances greater than 3 mm and was rarely observed when it was greater than 5 mm.

REFERENCES