Lateral and Medial Medullary Infarction
A Comparative Analysis of 214 Patients

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Background and Purpose—No large-scale study has ever compared the clinical and radiological features of lateral medullary infarction (LMI) and medial medullary infarction (MMI). The aim of this study was to investigate them through the use of cooperatively collected cases.

Methods—Medical information on all patients from 1996 to 2000 with medullary infarction (MI) proven by brain MR images at 35 stroke centers in the Tohoku district, Japan, was collected, and their clinical and radiological features were analyzed.

Results—A total of 214 cases of MI were registered. They included 167 cases (78%) of LMI, 41 (19%) of MMI, and 6 (3%) of LMI plus MMI. The mean age of onset and the male-to-female ratio were 60.7 years and 2.7:1 in LMI and 65.0 years and 3.6:1 in MMI, respectively. The middle medulla was most frequently affected in LMI, and the upper medulla was most frequently affected in MMI. Dissection of the vertebral artery was observed in 29% of LMI and 21% of MMI. Prognosis, assessed by the Barthel Index, was favorable in both LMI and MMI. Diabetes mellitus was more frequently associated with MMI than with LMI.

Conclusions—The present study surveyed a large number of MI cases and revealed that (1) the mean age of onset of MMI is higher than that of LMI, (2) the dissection of the vertebral artery is an important cause not only of LMI but also of MMI, and (3) diabetes mellitus is frequently associated with MMI. (Stroke. 2004;35:694-699.)

Key Words: cerebral infarction • diabetes mellitus • dissection • magnetic resonance imaging • medulla oblongata • vertebral artery

Before the era of MRI, a definite diagnosis of medullary infarction (MI), especially medial medullary infarction (MMI), could only be achieved by autopsy studies.1–3 For this reason, only a limited number of cases could be examined. Since the advent of MRI, the clinical diagnosis of MI has been made possible, and several clinical studies of MI are available.4–18 However, clinical information of MI, especially MMI, is insufficient. For example, although Kim and Choi-Kwon18 reported that MMI constituted 25% of all MI, other researchers believed that MMI is rare.15–17 With regard to vascular changes causing MI, the dissection of the vertebral artery (VA) is observed in a considerable number of patients with lateral medullary infarction (LMI).19–21 However, it is still controversial whether the VA dissection plays an important role in the etiology of MMI.14–17 It is also of importance to know whether there is a difference in the age of onset and the risk factors between LMI and MMI. To elucidate these issues, we compared the clinical and radiological findings between LMI and MMI from 214 patients with MI.

Subjects and Methods
The Tohoku district, which is located in northern Honshu island (the main island), Japan, consists of 6 prefectures and has a population of 9,817,589 according to the 2000 population census data of Japan. All cases of MI with the onset during the period from January 1996 to December 2000 were registered from board-certified neurosurgeons/neurologists at 35 major stroke centers in the Tohoku district, which belong to the Study Group of the Association of Cerebrovascular Disease in Tohoku. All MIs proven by MRI (0.5, 1.0, or 1.5 T) were enrolled in this study. The upper (rostral), middle, and lower (caudal) portions of the medulla oblongata were defined according to Bassetti et al.22 MR angiography (MRA)/conventional angiography were also performed in 129 (60%) of 214 patients with MI. According to the criteria reported19–21 the images of “double lumen,” “intimal flap,” and “pearl and string sign” on brain MRI, MRA, or a conventional angiogram were accepted as the presence of vascular dissection. The topographical patterns of MIs were determined with the use of the schemes by Vuilleumir et al20 and Bassetti et al:22 small midlateral, dorsolateral, inferolateral, large inferodorsolateral, dorsal, hemimedullary, paramedian, bilateral paramedian, and unilateral pyramidal. Neurological features were analyzed according to the topographical patterns. Also examined was the presence of the ipsilateral cerebellar hemispheric infarctions and vascular pathology on the MR images.
The following risk factors were assessed to determine the association with the infarction: age, sex, hypertension, hypercholesterolemia, diabetes mellitus, arrhythmia, and ischemic heart disease. Hypertension was defined as a history of antihypertensive medication use, a systolic blood pressure \( \geq 140 \text{ mm Hg} \), or a diastolic blood pressure \( \geq 90 \text{ mm Hg} \) during the chronic stage of the stroke. Hypercholesterolemia was defined as a history of antihypercholesterolemia medication or a serum level of total cholesterol \( \geq 5.69 \text{ mmol/L} \) (220 mg/dL); diabetes mellitus was defined as the use of insulin or oral hypoglycemic drugs, HbA1c \( \geq 6.5\% \), fasting blood glucose \( \geq 7.78 \text{ mmol/L} \) (140 mg/dL), or nonfasting blood glucose \( \geq 11.11 \text{ mmol/L} \) (200 mg/dL). To determine the outcome of MI, the activities of daily living of the patients were assessed twice with the Barthel Index, within 7 days of onset and at approximately 1 month after onset. To compare the contribution of the aforementioned risk factors for LMI and MMI, multiple logistic regression analysis was performed to determine the extent of the contribution of those risk factors to MMI relative to LMI. Age, sex, hypertension, diabetes mellitus, hypercholesterolemia, ischemic heart disease, arrhythmia, and cigarette smoking were used as the covariates to calculate odds ratios (ORs) for MMI relative to LMI. Continuous values, such as age and scores on the Barthel Index, were presented as mean \( \pm \text{SD} \) and analyzed by the Student \( t \) test. Categorized data were presented as a percentage and analyzed by the \( \chi^2 \) test. Statistical analysis was performed with the programmed package SPSS, version 11.0. \( P < 0.05 \) was accepted as statistically significant.

The present study was approved by the Ethical Review Committee of Yamagata University.

### Results

During a period of 5 years (January 1996 to December 2000), a total of 214 patients (159 men and 55 women) with MI were treated at 35 major stroke centers in the Tohoku district, Japan. Of the 214 patients, 167 (78\%) (122 men and 45 women) had LMI, 41 (19\%) (32 men and 9 women) had MMI, and 6 (3\%) (5 men and 1 woman) had LMI plus MMI (Babinski-Nageotte syndrome\(^2\)). The male-to-female ratio was 2.7:1 in LMI and 3.6:1 in MMI. The mean age (\( \pm \text{SD} \)) of onset of MI was 61.3 \( \pm \) 12.4 years. The mean age (\( \pm \text{SD} \)) of onset of LMI and MMI was 60.7 \( \pm \) 12.4 years and 65.0 \( \pm \) 12.3 years, respectively; the onset age of MMI was significantly older than that of LMI (\( P = 0.034 \)) (Figure 1). There was no significant difference in the age of onset of MI between men and women.

On brain MR images, the lesions of LMI were most frequently located in the middle medulla (35\%), and those of MMI were most frequently located in the upper medulla (56\%) (Table 1). The \( \chi^2 \) test showed that there was a significant difference in the preferential location (upper, middle, or lower) of the infarcts between LMI and MMI (\( P = 0.019 \)). On MRA and/or conventional angiography, which were performed in 129 cases of MI, dissection of the VA with images of double lumen, intimal flap, and/or pearl and string sign was found in 31 cases (29\%) of LMI (\( n = 107 \)), in 4 cases (21\%) of MMI (\( n = 19 \)), and in 1 case (33\%) of LMI plus MMI (\( n = 3 \)) (Figure 2). In MMI, VA dissection was observed only in paramedian infarct. The frequency of VA dissection was not significantly different between LMI and MMI (\( P = 0.586 \)) (Figure 2). Most of the remaining cases of LMI and MMI had atherosclerotic changes of VA on MRA and/or conventional angiography.

The neurological symptoms and signs are summarized in Table 2. The sensory disturbance of the extremities and face
of LMI with information of sensory function, 40 cases (25%) had a central pain syndrome (thermal hypesthesia with touch and thermal allodynia) without any correlation with a specific topographical subgroup. Horner’s syndrome usually showed ipsilateral miosis and ptosis, but anhidrosis was relatively unusual (17% of LMI cases). Of the 167 cases of LMI, 41 cases (25%) had limb paresis. Eleven cases (7%) had an ipsilateral spastic hemiplegia, consistent with Opalski syndrome. In our series, no case had cruciform paralysis or facial pain, which was reported by Fisher et al.24 Other presentations such as nystagmus, dysphagia, and vertigo were noted in each subgroup of MI, as shown in Table 3, without any specific predominance. On the other hand, dysphagia was found more often in the infarcts of the rostral than caudal medulla among various clinical presentations.

In our series the VA alterations were predominant in all topographical subgroups of LMI (Table 3). Among them, small midlateral and olivary infaracts had no posterior inferior cerebellar artery (PICA) lesions, while dorsal and large inferodorsolateral infarcts had PICA occlusions more often than the other subgroups. Cerebellar hemispheric infarctions were associated with 34 of 167 LMI cases (20%), 6 of 41 MMI cases (15%), and 1 of 6 hemimedullary infarcts (Babinski-Nageotte syndrome) (17%). On the other hand, pure medullary infarctions were seen in 76 of 167 patients (46%) with LMI, 15 of 41 (37%) with MMI, and 1 of 6 (17%) with LMI plus MMI. Cerebellar infarcts were noted predominantly in dorsal infarcts (42%) of LMI. Inferolateral infarction rarely had cerebellar infarcts (Table 3).

MMI also showed topographical subgroups: paramedian (23 cases), bilateral paramedian (6 cases), and unilateral pyramidal (10 cases) infarcts were identified. There were 2 cases of unclassified pattern. Bilateral paramedian infarct showed bilateral paralysis of 4 limbs, while other topographical subgroups of MMI usually had contralateral hemiplegia. Patterns and extent of sensory disturbance were poorly correlated with the subgroups of MMI. Similar to the cases of LMI, Horner’s sign usually consisted of ipsilateral miosis and ptosis.

Figure 3 illustrates the results of the multiple logistic regression analysis to show the contribution of medical conditions to MMI relative to LMI. Among several covariates such as age, sex, hypertension, diabetes mellitus, hypercholesterolemia, arrhythmia, ischemic heart disease, and cigarette smoking, only age and diabetes mellitus were independent risk factors for MMI relative to LMI; the OR was 1.467 (95% CI, 1.017 to 2.115; P=0.041) for age and 2.476 (95% CI, 1.104 to 5.549; P=0.028) for diabetes mellitus. Other variables were not shown to be independent risk factors for MMI relative to LMI. In MMI, there was no significant difference in the frequency of diabetes mellitus between rostral and caudal medulla.

Discussion

In the present study a total of 214 cases of MI, including 167 cases of LMI and 41 cases of MMI, were examined; this number is the largest reported thus far. For MMI in particular, most reports have dealt with 1 or a few cases of MMI.1–3,11–13 Some larger studies included 18 and 14 cases of MMI (Kim et al14,18) and 11 cases of MMI (Toyoda et al15 and Kumral et

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**TABLE 2. Neurologic Symptoms and Signs of LMI and MMI**

<table>
<thead>
<tr>
<th>LMI</th>
<th>%</th>
<th>MMI</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensory dysfunction</td>
<td>89</td>
<td>Limb weakness</td>
<td>93</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>75</td>
<td>Sensory dysfunction</td>
<td>68</td>
</tr>
<tr>
<td>Vertigo/dizziness</td>
<td>73</td>
<td>Diminished pharyngeal reflex</td>
<td>56</td>
</tr>
<tr>
<td>Horner’s syndrome</td>
<td>72</td>
<td>Vertigo/dizziness</td>
<td>56</td>
</tr>
<tr>
<td>Cerebellar ataxia</td>
<td>69</td>
<td>Dysarthria</td>
<td>53</td>
</tr>
<tr>
<td>Diminished pharyngeal reflex</td>
<td>64</td>
<td>Nystagmus</td>
<td>51</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>58</td>
<td>Nausea or vomiting</td>
<td>44</td>
</tr>
<tr>
<td>Nystagmus</td>
<td>57</td>
<td>Cerebellar ataxia</td>
<td>33</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>57</td>
<td>Facial palsy</td>
<td>30</td>
</tr>
<tr>
<td>Headache</td>
<td>47</td>
<td>Lingual palsy</td>
<td>30</td>
</tr>
<tr>
<td>Limb weakness</td>
<td>25</td>
<td>Dysphagia</td>
<td>29</td>
</tr>
<tr>
<td>Facial palsy</td>
<td>18</td>
<td>Consciousness disturbance</td>
<td>24</td>
</tr>
<tr>
<td>Consciousness disturbance</td>
<td>16</td>
<td>Horner’s syndrome</td>
<td>16</td>
</tr>
<tr>
<td>Hiccups</td>
<td>15</td>
<td>Headache</td>
<td>13</td>
</tr>
<tr>
<td>Lingual palsy</td>
<td>9</td>
<td>Central respiratory dysfunction</td>
<td>5</td>
</tr>
<tr>
<td>Limitation of ocular movement</td>
<td>6</td>
<td>Taste disorder</td>
<td>3</td>
</tr>
<tr>
<td>Central respiratory dysfunction</td>
<td>2</td>
<td>Limitation of ocular movement</td>
<td>2</td>
</tr>
<tr>
<td>Topographical Pattern</td>
<td>Sensory Dysfunction</td>
<td>Horner’s Sign</td>
<td>Cerebellar Ataxia</td>
</tr>
<tr>
<td>-----------------------</td>
<td>---------------------</td>
<td>---------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Small midlateral n = 19</td>
<td>cross 53%</td>
<td>unilat. 37%</td>
<td>face 0%</td>
</tr>
<tr>
<td>Dorsolateral n = 60</td>
<td>cross 55%</td>
<td>unilat. 16%</td>
<td>face 4%</td>
</tr>
<tr>
<td>Inferolateral n = 45</td>
<td>cross 55%</td>
<td>unilat. 18%</td>
<td>face 3%</td>
</tr>
<tr>
<td>Large inferodorsolateral n = 15</td>
<td>cross 75%</td>
<td>unilat. 8%</td>
<td>face 0%</td>
</tr>
<tr>
<td>Dorsal n = 12</td>
<td>cross 50%</td>
<td>unilat. 25%</td>
<td>face 8%</td>
</tr>
<tr>
<td>Olivary n = 16</td>
<td>cross 40%</td>
<td>unilat. 20%</td>
<td>face 7%</td>
</tr>
<tr>
<td>Hemimedullary n = 6</td>
<td>cross 83%</td>
<td>unilat. 17%</td>
<td>face 0%</td>
</tr>
<tr>
<td>Paramedian n = 23</td>
<td>cont. 50%</td>
<td>ipsi. 25%</td>
<td>face 0%</td>
</tr>
<tr>
<td>Bilateral paramedian n = 6</td>
<td>bilat. 25%</td>
<td>ipsi. 0%</td>
<td>face 0%</td>
</tr>
<tr>
<td>Unilateral pyramidal n = 10</td>
<td>cont. 38%</td>
<td>ipsi. 49%</td>
<td>face 0%</td>
</tr>
</tbody>
</table>

Hemimedullary indicates Babinski-Nageotte; cross, crossed sensory disturbance; unilat., unilateral sensory disturbance; face, restricted to the ipsilateral facial region; none, not present; cont., contralateral to infarct; ipsi., ipsilateral to infarct; bilat., bilateral; hori., horizontal nystagmus; verti., vertical nystagmus; rota., rotatory nystagmus; VA, vertebral artery (number in the parentheses indicates the percentage of the dissection among the cases of the VA alteration); PICA, posterior inferior cerebellar artery; BA, basilar artery.
The lesion never involved the surface of the medulla, suggesting that the perforator occlusion would result in the unique topographical pattern. Furthermore, our study disclosed the frequency of topographical subgroups of LMI. In our series, dorsolateral (36%) and inferolateral (27%) infarctions were frequent, while small midlateral (11%), large inferodorsolateral (9%), dorsal (7%), and olivary infarcts (9%) were relatively few.

As shown in Figure 3, age and diabetes mellitus were independent and significant risk factors for the occurrence for LMI relative to LMI, with ORs of 1.467 and 2.476, respectively. The other factors were not significant, independent risk factors contributing to the MMI. The previous reports also described a high prevalence of diabetes mellitus in patients with MMI (11 of 18 cases of MMI by Kim et al\textsuperscript{14} and 6 of 11 cases of MMI by Toyoda et al\textsuperscript{15}), although they did not analyze it or comment on it. In an autopsy study, the frequency of severe atherosclerosis of the intracranial VA was reported to be greater in diabetic patients than in nondiabetic ones.\textsuperscript{25} This may explain why the prevalence of diabetes mellitus is high in MI. However, it remains unclear why diabetes mellitus is more frequent in MMI than in LMI.

FIGURE 3. Multiple logistic regression analysis, showing that age and diabetes mellitus are independent risk factors for MMI relative to LMI.

Another implication of the present study is reconfirmation of the wide spectrum of LMI in topographical patterns. In addition to the topographical subgroups of LMI reported by Vuilleumier et al,\textsuperscript{7} we identified an unrecognized pattern that showed an infarction restricted to the inferior olivary nucleus. The lesion never involved the surface of the medulla, suggesting that the perforator occlusion would result in the unique topographical pattern. Furthermore, our study disclosed the frequency of topographical subgroups of LMI. In our series, dorsolateral (36%) and inferolateral (27%) infarctions were frequent, while small midlateral (11%), large inferodorsolateral (9%), dorsal (7%), and olivary infarcts (9%) were relatively few.

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frequency of diabetes mellitus in MMI at present, one can speculate that the anteromedial medullary arteries may possibly be more susceptible to the condition of diabetes mellitus than the lateral medullary arteries.

In conclusion, the present study revealed that (1) the mean age of onset of MMI is higher than that of LMI, (2) the dissection of the VA is an important cause not only of LMI but also of MMI, and (3) diabetes mellitus is frequently associated with MMI. The present results will provide a new research field of MMI and diabetes mellitus.

Appendix
Stroke Centers of the Study Group of the Association of Cerebrovascular Disease in Tohoku for providing the MI database in Tohoku district, Japan, that contributed to this study are as follows: Aomori Rosai Hospital, Hatinohe City Hospital, Akita Prefectural Cerebrovascular Research Center, Iwate Medical University Hospital, Iwate Prefectural Central Hospital, Iwate Prefectural Koku Hospital, Morioka Red Cross Hospital, General Hanamaki Hospital, Iwate Rosai Hospital, Tohoku University Hospital, National Sendai Hospital, Kohman Hospital, Ishinomaki Red Cross Hospital, Senseki Hospital, National Miyagi Hospital, Furukawa Municipal Hospital, Kesen-numa General Hospital, Southern Tohoku General Hospital, Sendai East Neurosurgical Hospital, Sendai Tokusyukai Hospital, Saiseikai Yamagata Hospital, San-yudo Hospital, Okitama Public General Hospital, Yamagata Prefectural Central Hospital, Yonezawa Municipal Hospital, Yamagata Prefectural Nihonkai Hospital, Kitamura-rayama General Hospital, Yamagata University Hospital, Yamagata City Hospital Saiseikan, Yamagata Prefectural Kaho Hospital, Fukushima Medical University Hospital, Fukushima Red Cross Hospital, Shirakawa Kosei Hospital, Takeda General Hospital.

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References
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