Acute Changes in Blood Pressure Following Vascular Diseases in the Brain Stem

BY AKIRA ITO, M.D., TERUO OMAE, M.D., AND SHIBANOSUKE KATSUKI, M.D.*

Abstract: Acute Changes in Blood Pressure Following Vascular Diseases in the Brain Stem

The relationship of the type of acute change in blood pressure to the site of the brain lesion, following cerebral hemorrhage and infarction, were studied in 108 patients in whom autopsy was performed. No significant changes in blood pressure were observed in cases with lesions localized rostral to the midbrain and in the medulla oblongata. The pressor response characteristic in primary pontine lesions, either hemorrhage or infarction, also was demonstrated in the cerebral hemorrhage with fourth ventricular and pontine extension. Blood pressure elevation was more marked with tegmental pontine lesions than when the lesion was in the basilar pons. Extension of the lesion into neighboring portions of the pons did not cause further change in blood pressure. The present results seem to suggest a positive role of the caudal brain stem, especially the pons, in the blood pressure elevation following the cerebrovascular accidents.

Additional Key Words
infarction  pons  cerebrovascular diseases  brain stem  hemorrhage

Introduction
An acute change in blood pressure, either an increase or a decrease, has been observed frequently following an acute episode of cerebrovascular disease. However, only a few clinical reports1-4 have been made correlating patterns of blood pressure response with the site of vascular lesions in the brain. On the other hand, there has been considerable work on this problem in animals with experimentally induced vascular lesions of the brain.4, 5

The present clinicopathological study was undertaken to determine if acute damage in a specific location in the human brain would exert certain patterns of blood pressure response and if strong vasopressor response was characteristic of lesions in the caudal brain stem, especially the pons.

Methods
The case material for this study comprised 108 patients, all of whom had autopsy verification of cerebrovascular disease and information as to the location of the lesion within the brain. Sixty-three of the patients were autopsied in the Department of Pathology, Kyushu University Faculty of Medicine, Fukuoka, Japan, in the period from 1962 to 1965. An additional 45 cases had been reported previously in Japana Centro Revuo Medicina, volumes 24 to 201, 1925 to 1964.

Fifty-one cases were found to have cerebral hemorrhage. Of these, 38 were males and 13 were females, with ages ranging from 30 to 84 (average, 56). The remaining 57 patients had autopsy evidence of cerebral infarction. Forty-two of these were males and 15 were females (mean age, 59), ranging from 23 to 84 years old.

Patients with cerebral hemorrhage caused by head trauma or bleeding disorders were excluded from the present study. Those with widespread subarachnoid hemorrhage or with multiple infarctions were likewise excluded due to the complexity of their blood pressure responses. Patients with lesions in the brain stem, especially in the pons, were collected (as many as possible), since particular attention was given to a comparison of the blood pressure reactions in this group with those in cases with hemispheral lesions. A few cases also were admitted who had hemorrhage in the medulla oblongata.

Ninety-five patients in the present study had records of blood pressure measurements before as well as after the development of cerebral hemorrhage or infarction. Six cases with hemorrhage and seven with infarction both in the midbrain were admitted in the study even though their records contained the measurements only after the stroke.

The location and extent of the vascular lesions in the brain were determined by gross examination at the time of autopsy. The lesions were described as being localized to cerebral hemispheres, midbrain, pons or medulla oblongata.

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BLOOD PRESSURE CHANGES IN CEREBROVASCULAR DISEASES

Cases with cerebellar lesions were not included in the present study because of their scarcity. Hemispherical hemorrhage was then classified into three groups: (1) purely localized, (2) extended into the fourth ventricle, and (3) extended into the fourth ventricle and pons. Midbrain hemorrhage was divided into two categories: (1) purely localized, and (2) extended into the rostral portion of the pons.

Patients with primary pontine hemorrhage were classified into three types: (1) those with the main lesion in the tegmental, intermediate or basal region of the pons, (2) those with extension of bleeding rostrally into the caudal midbrain, and (3) those with extension caudally into the pontomedullary junctional area. Here, hemorrhage which was circumscribed for the most part in the dorsal portion of the medial and lateral lemnisci in the transverse section of the pons was regarded as tegmental bleeding, and hemorrhage which grossly covered ventral to lemnisci as basal and massive hemorrhage involving both areas was regarded as intermediate.

In the pontine infarction, spreading of the main lesion also was grossly studied on the transverse section, such as the tegmental and the basal areas.

Blood pressure was noted from the patients' clinical records in life. The level prior to stroke was that taken at the closest date not preceding more than one month, and that after stroke was the highest recorded throughout the course. Analyses of the average value, the lowest record or the fluctuation of blood pressure after stroke were not possible in the present study due to the lowest record or the fluctuation of blood pressure after stroke being significantly higher than the prestroke level (P < 0.005).

The average response was not significant despite a slight decrease in the systolic pressure. One of the two cases with a pressor reaction was accompanied by distant bleeding in the pons (table 1).

Results

BLOOD PRESSURE IN PATIENTS WITH HEMISPHERAL LESIONS

Hemorrhage

Among six cases with localized hemispherical hemorrhage, three had a depressor response after the stroke developed, two had a pressor response, and the remaining case showed no significant change. The average response was not significant despite a slight decrease in the systolic pressure. One of the two cases with a pressor reaction was accompanied by distant bleeding in the pons (table 1).

Infarction

Thirty-three patients with infarction in the hemisphere revealed variable responses; 23 revealed depressor responses, six revealed pressor responses, and four showed no remarkable change. A significant reduction was calculated in the systolic pressure but not in the diastolic pressure (table 1).

Two of the eight cases with a pressor reaction demonstrated unilateral giant infarction in the cerebral hemisphere accompanied by marked tentorial herniation and distortion of the brain stem.

BLOOD PRESSURE IN PATIENTS WITH BRAIN STEM LESIONS

Hemorrhage

The level of blood pressure before stroke in six patients with localized midbrain hemorrhage was unknown, but the pressure after stroke was 155 ± 13/83 ± 3 mm Hg. In contrast, five cases with hemorrhage extending into the rostral pons all had a remarkable rise in blood pressure, the poststroke level being significantly higher than the prestroke level (P < 0.005).

Two of the 17 with primary pontine hemorrhage showed a reduction after development of the

**TABLE 1**

Blood Pressure* in Cases With Vascular Lesions in the Cerebral Hemispheres

<table>
<thead>
<tr>
<th>Lesion</th>
<th>No</th>
<th>Systolic</th>
<th>Diastolic</th>
<th>Systolic</th>
<th>Diastolic</th>
<th>Δ Systolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhage:</td>
<td></td>
<td>Before</td>
<td>After</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Localized</td>
<td>6</td>
<td>180 ± 16</td>
<td>152 ± 13</td>
<td>-28 ± 12</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>90 ± 12</td>
<td>91 ± 4</td>
<td>- 1 ± 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extended to ventricle</td>
<td>6</td>
<td>173 ± 12</td>
<td>191 ± 7</td>
<td>+18 ± 7†</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>96 ± 4</td>
<td>111 ± 10†</td>
<td>+16 ± 6§</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extended to ventricle and pons</td>
<td>11</td>
<td>195 ± 8</td>
<td>228 ± 8†</td>
<td>+33 ± 4†</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Infarction:</td>
<td></td>
<td>Localized</td>
<td>158 ± 6†</td>
<td></td>
<td>-16 ± 6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>33</td>
<td>174 ± 6</td>
<td>93 ± 3</td>
<td>91 ± 4</td>
<td>- 2 ± 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>124 ± 8†</td>
<td>124 ± 8†</td>
<td>18 ± 4§</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Results are expressed as mean ± SEM, mm Hg.
†P < 0.005 (different from the response in cases with the localized lesion).
§P < 0.05 (different from the prestroke level).
**P < 0.025 (different from the response in cases with the localized lesion).
††P < 0.05 (different from the response in cases with extension only in the fourth ventricle).
‡‡P < 0.01 (different from the prestroke level).
stroke, although the remaining 15 cases displayed a prominent elevation to make the mean response in 17 cases statistically comparable with that in those with midbrain hemorrhage and pontine extension (table 2).

Infarction

The 13 cases with pontine lesions demonstrated reactions similar to those with hemorrhage. Nine of them showed a pressor reaction, three showed a depressor reaction, and the other one showed no significant change. The mean response in these 13 cases was pressor, but the change in the diastolic pressure was less than that observed in patients with pontine hemorrhage. Besides, the poststroke level in these cases was significantly higher than that in those with midbrain infarction who showed a normotensive level similar to the hemorrhage localized in the same area.

Four patients with medullary infarction showed a decrease in blood pressure, especially in the systolic, although it was insignificant (table 2).

LOCALIZATION OF PRIMARY LESIONS IN RELATION TO THEIR BLOOD PRESSURE CHANGES

Gross Localization in the Pons

Primary pontine hemorrhage was found macroscopically from the caudal midbrain to the rostral medulla, and from the ventral surface of the base to the floor of the fourth ventricle. It was most commonly in the tegmentum in the rostral half of the pons.

Nine cases with tegmental hemorrhage (52.9%) had a remarkable rise in blood pressure, and five with the intermediate area involved (29.4%) revealed a similar pressor response coming after the former, while no significant change was detected in three patients with hemorrhage into the base of the pons (17.7%).

The response was similar in pontine infarction. Seven patients with tegmental infarction (53.8%) demonstrated a pressor change equivalent to that in hemorrhage in the same portion, while three patients with basal infarction had no significant alteration. Difference in the response between these two groups was statistically evident as in cases with hemorrhage ($P < 0.05$) (table 3).

Extension Into the Caudal Midbrain in Cases With Primary Pontine Hemorrhage

Ten patients with such extension (53.8%) and six without (35.3%) revealed a prominent and equivalent pressor response, although the systolic change was greater in the former and the diastolic change was greater in the latter (table 3).

Extension Into the Tegmental Portion at the Pontomedullary Junction in Cases With Primary Pontine Hemorrhage

Although the pressor response in three patients with the spread in such caudal direction (17.7%) was not significant, perhaps due to scarcity of cases, the magnitude of their reactions was similar to that observed in seven patients without such large lesions (41.2%) (table 3).

---

**TABLE 2**

<table>
<thead>
<tr>
<th>Blood Pressure* in Cases With Vascular Lesions in the Brain Stem</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Hemorrhage:</td>
</tr>
<tr>
<td>Midbrain:</td>
</tr>
<tr>
<td>Localized</td>
</tr>
<tr>
<td>Extended to rostral pons</td>
</tr>
<tr>
<td>Pons</td>
</tr>
<tr>
<td>Infarction:</td>
</tr>
<tr>
<td>Midbrain</td>
</tr>
<tr>
<td>Pons</td>
</tr>
<tr>
<td>Medulla oblongata</td>
</tr>
</tbody>
</table>

*Results are expressed as mean ± SEM, mm Hg.
†$P < 0.01$ (different from the prestroke level).
‡$P < 0.05$ (different from the prestroke level).
§$P < 0.1$ (different from the response in cases with midbrain hemorrhage with extension in the rostral pons).
‖$P < 0.25$ (different from the prestroke level).
**$P < 0.025$ (different from the prestroke level).
***$P < 0.1$ (different from the prestroke level).
TABLE 3

Localization of Primary Vascular Lesions in the Pons Related to Blood Pressure* Responses

<table>
<thead>
<tr>
<th>Lesion</th>
<th>No</th>
<th>Before Systolic</th>
<th>Before Diastolic</th>
<th>After Systolic</th>
<th>After Diastolic</th>
<th>Δ Systolic</th>
<th>Δ Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhage:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sphere in the pons</td>
<td>9</td>
<td>180 ± 10</td>
<td>227 ± 7†</td>
<td>+46 ± 7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tegmental</td>
<td>94 ± 1</td>
<td>125 ± 8†</td>
<td>+32 ± 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>5</td>
<td>190 ± 14</td>
<td>222 ± 15</td>
<td>+32 ± 9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal</td>
<td>3</td>
<td>192 ± 8</td>
<td>116 ± 8</td>
<td>+19 ± 4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extended bleeding in the caudal midbrain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>10</td>
<td>190 ± 9</td>
<td>223 ± 10†</td>
<td>+28 ± 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>6</td>
<td>171 ± 12</td>
<td>196 ± 12</td>
<td>+27 ± 6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unclassified</td>
<td>1</td>
<td>96 ± 3</td>
<td>128 ± 12**</td>
<td>+32 ± 6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extended bleeding in the pontomedullary junctional area</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>3</td>
<td>182 ± 14</td>
<td>218 ± 18</td>
<td>+36 ± 9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>7</td>
<td>186 ± 11</td>
<td>223 ± 12‖</td>
<td>+38 ± 6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unclassified</td>
<td>7</td>
<td>94 ± 5</td>
<td>122 ± 7***</td>
<td>+28 ± 5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infarction:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sphere in the pons</td>
<td>7</td>
<td>172 ± 7</td>
<td>225 ± 6†</td>
<td>+53 ± 5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tegmental</td>
<td>97 ± 5</td>
<td>119 ± 7‖</td>
<td>+22 ± 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal</td>
<td>3</td>
<td>198 ± 10</td>
<td>226 ± 18</td>
<td>+28 ± 10‡‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unclassified</td>
<td>3</td>
<td>107 ± 6</td>
<td>105 ± 5</td>
<td>−2 ± 4‡‡</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Results are expressed as mean ± SEM, mm Hg.
†P < 0.005 (different from the prestroke level).
‡P < 0.025 (different from the response in cases with a tegmental lesion).
§Record of the diastolic blood pressure was found only in two of all cases. Blood pressures before and after stroke are described only with the mean values, and the response was not calculated.
‖P < 0.05 (different from the prestroke level).
**P < 0.025 (different from the prestroke level).
††P < 0.01 (different from the prestroke level).
‡‡P < 0.05 (different from the response in cases with a tegmental lesion).

Discussion

An elevation in blood pressure after development of a stroke in the brain stem, especially in the pons, has been frequently noticed,1 4 5 and the response was reportedly prominent following that in the pontine tegmentum.4 5

There also have been some reports on the pressor reaction following infarction in the brain stem, especially in its rostral portions.2 5

While change in blood pressure following vascular lesions in the cerebral hemispheres appears to remain so far obscure, a relatively low incidence of hypertension after stroke was observed in patients with occlusion of the internal carotid artery.5

These clinical findings seem to reflect to some extent functional differences in vasoregulatory activities according to regions in the brain, although only few reports have been presented on the type of change in blood pressure as affected by the location of the cerebrovascular lesion. Therefore, this study was done.

There are several difficulties in a clinicopathological analysis. First, the temporal profile of the localization of the lesion during life is made on clinical judgments. In fact, it remains unknown whether the influence of these lesions on blood pressure could arise from destruction or stimulation of the local functions, functional interruption between rostral and caudal portions of the brain, or even some peripheral changes. How these factors might develop during the course of vascular disease such as hemorrhage or infarction is uncertain.

Another difficulty is the complexity of the central reflex-integrating mechanisms controlling blood pressure, either phasic or tonic, which are
generally considered to be responsive to alteration in various afferent impulses.\textsuperscript{7-9} Therefore, it is difficult to establish a firm relationship between autopsy findings and blood pressure changes during life. The method in this study is one approach to this problem.

Other investigators, mainly using local electrical stimulation, have reported vasoactive reactions in a variety of regions in the central nervous system rostral to the midbrain, e.g., from the premotor cortex to the deep segmental nuclei of the midbrain.\textsuperscript{7, 8, 10-13} However, the actual relationship of these drives to human blood pressure regulation or to vasomotor functions in the pontomedullary region\textsuperscript{7, 8, 14} has not yet been clarified. In fact, several reports on section of the brain stem demonstrated no significant change in blood pressure until the procedure reached to the rostral or mid pons.\textsuperscript{15, 16}

In the present study, localized hemispheral lesions, either hemorrhage or infarction, tended to decrease the systolic pressure, with no significant change in the diastolic pressure. While an elevation of blood pressure was demonstrated in hemispheral infarction accompanied by marked tentorial herniation and compression of the caudal brain stem and also in hemispheral hemorrhage with extension of bleeding into the fourth ventricle, the pressor response of the latter was significantly intensified by accompanying secondary pontine hemorrhage. In primary pontine lesions, both hemorrhage and infarction, a prominent pressor reaction occurred.

The results in the present study suggest that the pons is responsible for the poststroke elevation in blood pressure following cerebrovascular events. In the cases with vascular lesions limited to other portions of the brain stem, there was no significant pressor response. In five cases where midbrain hemorrhage extended into the rostral pons, there was a pressor response.

The vasoregulatory function of the pons has been considered as a pathway between rostral structures and the medulla oblongata or the spinal cord,\textsuperscript{7, 8} although some reports\textsuperscript{5, 15-17} describe the caudal pons as a sympathetic promotive area probably accelerating the medullary vasomotor activities\textsuperscript{7-9, 14} under inhibitory influences from the rostral pons and vagal afferents.

In the present study, the pressor response in primary pontine lesions, mainly located in the rostral tegmentum, was more remarkable than with basal lesions and appeared not statistically affected by bleeding extending into the caudal midbrain or in the pontomedullary junction. These observations seem to suggest that the pressor reaction following pontine vascular lesions could originate in some inherent functions in the pons, which might override activities in the neighboring regions, reserving the possibility that principal drives in the medulla oblongata may be involved also.

**Acknowledgments**
The authors would like to express their thanks to Dr. Kenzo Tanaka, Professor of Pathology, Kyushu University Medical Faculty, Fukuoka, Japan, for his kind arrangement in reviewing the pathological protocols. We are indebted also to Dr. Albert Heyman, Professor of Neurology, Duke University Medical Center, Durham, North Carolina, for his kind criticisms and suggestions.

**References**

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