Massive Cerebral Infarction with Severe Brain Swelling:
A CLINICOPATHOLOGICAL STUDY

BY LARRY K. Y. NG, M.D.,* AND JESADA NIMMANNITYA, M.D.†

Abstract: Massive Cerebral Infarction with Severe Brain Swelling

All cases of acute supratentorial cerebral infarction which came to postmortem examination over the past 10 years at the Philadelphia General Hospital were reviewed. Of a total of 353 such cases, 45 showed severe brain swelling.

Seventy-eight percent of these 45 patients died within seven days of the acute infarction. The rapidly fatal outcome appeared to be directly related to the acute brain swelling with transtentorial herniation and brain-stem edema or hemorrhage.

In those patients who survived longer than one week following onset of the ictus (22%), clinical and anatomic findings suggested that increased intracranial pressure probably did not develop until later in the course of the illness. A second massive infarct was probably superimposed upon an earlier one and produced the acute brain swelling noted at the time of postmortem examination. Complicating visceral diseases were more common in this group and seemed to contribute to death in the majority of these patients.

Although it has been established that a large cerebral infarct may produce sufficient brain swelling and simulate an acutely expanding lesion, this is not widely recognized as playing an important part in determining the patient's clinical outcome.

The role of increased intracranial pressure resulting from acute brain swelling should not be overlooked in the management of patients with severe strokes.

ADDITIONAL KEY WORDS: cerebral edema autopsy herniation and stem hemorrhages

Cerebral vascular disorders are probably the most common causes of death among diseases of the central nervous system.¹,² Frequently, however, there is no satisfactory explanation of the causal relationship between the lesion and the fatal outcome. This is particularly true when the location of the cerebrovascular lesion does not directly involve vital centers or when death follows the ictus by hours or days. Apoplectic death following intracerebral hemorrhage is not uncommon, but death in such cases is partially the result of acutely increased intracranial pressure due to massive intracerebral hematoma, often complicated by intraventricular rupture.³,⁴

The possibility that acute brain swelling might also account for death in some patients with cerebral infarction has not been thoroughly investigated. We reviewed all cases of acute

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TABLE 1

<table>
<thead>
<tr>
<th>Age</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 to 39</td>
<td>2</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>40 to 49</td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>50 to 59</td>
<td>6</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>60 to 69</td>
<td>5</td>
<td>6</td>
<td>11</td>
</tr>
<tr>
<td>70 to 79</td>
<td>1</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>80 to 89</td>
<td>1</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>90 and over</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>29</td>
<td>45</td>
</tr>
</tbody>
</table>

The infarction in every brain involved the entire distribution either of one middle cerebral artery (cortical and ganglionic branches) or of the internal carotid artery. In two instances the entire hemisphere was affected because of an anomaly in the circle of Willis (fig. 1). (It should be noted that severe brain swelling was not seen in those cases where the infarction involved only portions of the distribution of the middle or anterior cerebral arteries.) In all 45 brains edema was generalized, but it was more severe in the infarcted hemisphere. Herniation of the parahippocampal gyrus of the infarcted side through the tentorium had occurred in all but five specimens (table 2). In a few instances a lesser degree of tentorial herniation was noted on the contralateral side. Herniation of the cingulate gyrus under the falx on the side of the infarction occurred much less frequently (15 of 45). Much more common were prolapse of the cerebellar tonsils below the rim of the foramen magnum (34 of 45) and severe brain-stem edema with or without hemorrhages (36 of 45). Actual necrosis of parahippocampal or cingulate gyri secondary to herniation was found in nine brains.

To facilitate further study, the patients were divided into two groups on the basis of survival time following the onset of the ictus. Group 1 comprised those who survived one

TABLE 2

Neuropathological Manifestations of Increased Intracranial Pressure in 45 Autopsied Cases

<table>
<thead>
<tr>
<th>Hemispheric swelling</th>
<th>Herniations</th>
<th>Secondary brain stem lesions</th>
<th>Secondary necrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Falcal</td>
<td>Foraminal</td>
<td>Hippocampal gyrus</td>
</tr>
<tr>
<td>Group 1</td>
<td>35</td>
<td>31</td>
<td>31</td>
</tr>
<tr>
<td>Group 2</td>
<td>10</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
<td>40</td>
<td>15</td>
</tr>
</tbody>
</table>
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week or less (35 patients) and group 2 those who lived longer than one week (10 patients).

**GROUP 1**

Thirty-five patients (78%) died within one week of the ictus, the majority within the first four days. In this group, the most common presentation was sudden onset of hemiplegia, with or without accompanying hemihypesthesia, homonymous hemianopia or aphasia. Conjugate deviation of the eyes toward the side of the cerebral lesion (described in 17 cases) suggested the presence of a massive destructive lesion in the cerebral hemisphere. Disturbance in sensorium was invariably present early in the course, with coma often supervening precipitously within 24 to 72 hours following the ictus. Not all the patients were examined by neurologists, so comparisons were not strictly reliable, but certain observations were of interest with regard to evidence suggesting increased intracranial pressure, especially transtentorial herniation.

Observations concerning pupillary size were specifically noted in 24 cases. The pupil was dilated ipsilaterally to the cerebral lesion in 19 and contralaterally in two, and was normal in only three cases. Funduscopic findings were recorded in seven and, of these, papilledema was noted in two. Cardiorespiratory disturbances included an acute rise in blood pressure (often above previous hypertensive levels) in 15 patients; bradycardia (pulse rate of 50 or less per minute) in three; and periodic respiration (including Cheyne-Stokes) in six. Terminally, the temperature rose abruptly (105° or above) in six patients. Decerebrate rigidity was described in five cases.

Lumbar puncture was performed in 24 patients. In only seven was the pressure elevated (215 to 320 mm water) even though pupillary or cardiorespiratory abnormalities as well as changes in sensorium were present at the time of the procedure.

The cause of death in 25 patients was seemingly attributable only to the acute cerebral infarction, with increased intracranial pressure and transtentorial herniation. In 10 patients, there were also significant visceral complications which could have contributed to death. These complications were primarily cardiovascular or pulmonary; acute myocardial infarction (two); auricular fibrillation with cardiac decompensation (one); ventricular tachycardia (one); pulmonary embolism (four); acute cor pulmonale (one); and gram negative sepsis with shock (one). In five of these patients, the visceral factors appeared to be causally related to the development of the stroke, since there was a significant decrease in cardiac output and the development of shock before the stroke.

**GROUP 2**

The clinical picture in this group differed significantly from group 1, although postmortem intracranial pathology did not. The duration of survival varied from 10 days to five weeks. The initial motor deficit was usually not severe and the clinical course was generally one of gradual or stepwise deterioration. It was difficult to determine when increased intracranial pressure developed, since clinical signs usually associated with increased intracranial pressure were not as obvious in this group. Clouding of the sensorium was present, but progression to coma was more gradual and tended to occur after the first week. Dilation of a pupil was noted in three patients; the dilation was ipsilateral to the cerebral lesion in two and contralateral in one. The pupils were equal in four others. No mention was made of decerebrate rigidity or cardiorespiratory or thermoregulatory disturbances. Lumbar puncture was performed on two patients; the findings were normal.

Major systemic diseases were frequent in this group. In eight of 10 patients, catastrophic complications occurred during the course of the illness: myocardial infarction in two, cardiac decompensation with arrhythmia in two, massive pulmonary embolism in two, uremia with chronic and acute pyelonephritis in one, and diabetic acidosis in one.

**Discussion**

Death due to acute brain swelling resulting from cerebral infarction is uncommon. The true incidence is difficult to ascertain, since significant visceral complications not frequently develop which may contribute to the patient's death. In this survey, acute hemispheric swelling occurred in 13% (45 of 353) of autopsy-verified cases of strokes. Of these, only 7% (27 of 353) could be judged to have died from acute brain swelling with transten-
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Posterior herniation. Since these figures are computed from patients who died and came to autopsy, the actual incidence of acute swelling in a clinical stroke population is obviously considerably lower.

Our study indicates that acute brain swelling in cerebral infarction occurs only in those patients in whom the necrosis involves the entire vascular distribution of the internal carotid or the middle cerebral artery. This finding is consistent also with the observation of others that the degree of brain swelling is proportional to the size of the infarct; the larger the infarct, the greater the likelihood of acute brain swelling with transtentorial herniation.

The rapidly fatal outcome which characterized most of these cases with massive cerebral infarction appears to be related to the effects of transtentorial herniation. The significance of transtentorial herniation in this condition received little attention from early investigators. Shaw et al. were among the first to recognize its prevalence and importance. Trottenburg and Vinken similarly stressed its role in their report of two cases of cerebral infarction which led to a rapidly fatal issue. In 12 cases of fatal cerebral infarction reported by Adams and Graham the duration of survival varied from 32 hours to eight days after the onset of stroke, and transtentorial herniation was present in 10 (83%). In our series of 45 cases, transtentorial herniation was present in 40 (89%).

The manifestations of transtentorial herniation vary considerably. Some degree of herniation, particularly when it develops slowly, may be asymptomatic; rapid herniation, however, may seriously influence the outcome. The clinical condition of patients in group 1 of our series was characterized by early and rapid development of signs and symptoms related to transtentorial herniation—dilation of the pupil and loss of pupillary light reflex on the side of herniation, precipitous onset of coma, cardiorespiratory or thermoregulatory disturbances, and various motor manifestations of decerebration. Death usually ensued within the first week, the majority of patients dying within four days. These findings are in accord with those of Shaw et al. who found that increased intracranial pressure resulting from cerebral infarction was manifested within 24 hours and reached a maximum in three to five days.

It is of interest to speculate on the mechanism of fatal outcome in patients who die presumably without visceral disease, since lesions in the area of infarction should not be physiologically incompatible with life. In these cases death appears to be related directly to increased intracranial pressure, with rapid transtentorial herniation. In our series there was a high incidence of brain-stem edema (80%) and secondary brain-stem hemorrhage (60%).

Secondary brain-stem hemorrhage is usually associated with transtentorial herniation due to increased intracranial pressure from an expanding supratentorial lesion. The first comprehensive description was given by Attwater in 1911. In 67 cases of traumatic and apoplectic hemorrhage, 30% were accompanied by pontine hemorrhages. Dill and Isenhout produced pontine hemorrhages in dogs by supratentorial expanding lesions. They suggested that mechanical distortion of the arterial and venous systems of the brain stem resulted from transtentorial herniation and caused the bleeding. However, the mechanism of these hemorrhages has still not been entirely resolved. Some investigators believe that the brain-stem lesions are secondary to venous engorgement while others are of the opinion that they are produced by arterial rupture.

The incidence of secondary brain-stem hemorrhage due to supratentorial expanding lesions varies. Poppen reported 258 deaths due to supratentorial tumors, with brain-stem hemorrhages in 36 (14%). Postmortem examination was not carried out in all cases and the true incidence may have been higher. The same author found 56 deaths due to supratentorial intracerebral hemorrhage and noted brain-stem hemorrhage in six (10.7%). Marks, in a study of 253 cases of massive intracerebral hemorrhage at Philadelphia General Hospital, found that brain-stem hemorrhage occurred in 30% of the entire group but was limited to those dying within three days after ictus. In this latter group, 76 (47%) had secondary brain-stem hemorrhage. Berry and Alpers reviewing the brain changes in 21 cases of carotid occlusion in the neck, found brain-stem hemorrhage in six of 10 cases with massive cerebral infarction. In Adams and Graham's series of fatal massive cerebral
infarction, only two of 12 had brain-stem hemorrhage (16.6%).

In group 2 of our series the illness lasted 10 days to five weeks, although there was massive infarction with brain swelling. In view of the findings of Shaw et al. that brain swelling resulting from massive infarction recedes after one week, it seems unlikely that the brain changes found at autopsy were present throughout the illness. This supposition is strengthened somewhat by the clinical course of these patients. The initial motor deficit was never as severe as in group 1. Clouding of consciousness occurred, but coma developed later and evolved in a less precipitous manner. Pupillary disturbances were rare and occurred late. Cardiorespiratory or thermoregulatory disturbances and decerebrate rigidity were not observed. One could speculate, as did Shaw et al., that in cases with greater swelling than expected for the duration of illness a recent massive infarct may have been superimposed upon an earlier one.

The chief diagnostic problem in acute massive cerebral infarction is its differentiation from intracerebral hemorrhage, usually distinguishable by lumbar puncture. This procedure is considered dangerous by some in the presence of increased intracranial pressure due to a massive unilateral supratentorial lesion because of the risk of transtentorial herniation; however, the findings of two extensive studies indicate that the risks may be more presumptive than real.

In the management of massive cerebral infarction the primary objective would appear to be reduction of intracranial pressure. Therapeutic measures must be instituted early, since attempts to control brain-stem edema after transtentorial herniation may be futile. Once herniation has been established, treatment should be aimed at prevention of secondary brain-stem edema and hemorrhage. This may entail emergency surgery with radical removal of the infarcted area or excision of herniated tissue. The value of such radical surgical intervention has yet to be established, but encouraging results have been reported by Scarcella and more recently by Greenwood.

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