Progression of Mass Effect After Intracerebral Hemorrhage

Allyson R. Zazulia, MD; Michael N. Diringer, MD; Colin P. Derdeyn, MD; William J. Powers, MD

Background and Purpose—While the evolution of mass effect after cerebral infarction is well characterized, similar data regarding intracerebral hemorrhage (ICH) are scant. Our goal was to determine the time course and cause for progression of mass effect after ICH.

Methods—Patients with spontaneous supratentorial ICH who underwent ≥2 CT scans were identified in our prospectively collected database. CT lesion size and midline shift of the pineal and septum pellucidum were retrospectively measured and correlated with clinical and CT characteristics. Causes for increased midline shift were determined by 2 independent observers.

Results—Seventy-six patients underwent 235 scans (3.1 ± 1.3 per patient). Initial CT was obtained within 24 hours of ICH in 66. Twenty-five scans were repeated on day 1, 80 on days 2 through 7, 31 on days 8 through 14, and 24 >14 days after ICH. Midline shift was present on 88% of the initial scans. There were 17 instances of midline shift progression: 10 occurred early (0.2 to 1.7 days) and were associated with hematoma enlargement, and 7 occurred late (9 to 21 days) and were associated with edema progression. Progression of mass effect due to edema occurred with larger hematomas (P < 0.05). Of 65 scans repeated for clinical deterioration, only 10 were associated with increased mass effect.

Conclusions—Progression of mass effect after ICH occurred at 2 distinct time points: within 2 days, associated with hematoma enlargement, and in the second and third weeks, associated with increase in edema. The clinical significance of later-developing edema is unclear. (Stroke. 1999;30:1167-1173.)

Key Words: cerebral hemorrhage ■ mass effect

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Spontaneous intracerebral hemorrhage (ICH) is associated with greater mortality and more severe neurological deficits than any other stroke subtype.1 To date, no medical or surgical therapy has been shown to improve outcomes2–6; therefore, understanding the manner in which ICH induces brain injury is critical to the development of effective treatments. In addition to the initial mechanical injury produced by the hematoma, further damage is believed to occur after the bleeding stops. The mechanisms underlying this secondary injury are unknown.

Previous reports5 have suggested that hematomas exert clinically significant mass effect in a substantial number of patients. Since progression of mass effect is one of the mechanisms by which ICH may induce ongoing brain injury, we investigated its pattern of evolution and its cause.

The evolution of mass effect after cerebral infarction has been well characterized since the 1950s, when data from pathological examination, angiography, ventriculography, and skull films indicated the development of shift of midline structures and/or ventricular compression during the first week after symptom onset. Shaw and colleagues8 defined the onset and duration of midline shift by combining the results of their own pathological analysis of 15 patients with middle cerebral artery infarcts and 13 cases in the literature. Their results indicated that midline shift developed over the first 3 days, peaked at 3 to 5 days, and subsided by 14 days. Subsequent CT reviews supported this time course of mass effect progression in cerebral infarction.9–11

The evolution of mass effect after ICH, on the other hand, has not been adequately established. Although significant midline shift (>3 mm) was reported in 62% in one CT review,7 the time course of mass effect could not be inferred, since information regarding time of scans relative to symptom onset was not provided. Measuring hemispheric weight in 31 patients with ICH, Clasen et al12 concluded that the time courses of edema in ICH and in ischemic stroke are similar, but changes in mass effect were not reported. Others have suggested that mass effect persists much longer in ICH than in ischemic stroke, not decreasing until after 17 days with small hematomas and even later with larger hematomas,13 or remaining as long as 28 days.14 Methods of estimating mass effect have included comparison of hemispheric weights,12 assessment of ventricular and cisternal compression,13 measurement of transverse widening of the cerebral hemisphere,14 measurement of shift of midline structures,7,15 and descriptions of the presence of “a typical edema pattern” surrounding the hematoma.16,17
Progression of Mass Effect After ICH

To investigate the evolution of mass effect after ICH using an easily quantifiable method, we measured change in midline shift in consecutive patients with ICH admitted to the Neurology/Neurosurgery Intensive Care Unit (NNICU) who underwent >1 CT scan. We recorded the time course of mass effect progression and determined the cause of progression by blinded review of CT scans.

Subjects and Methods
We prospectively recorded information on all admissions to the NNICU of a tertiary care academic hospital with a computerized database (QuiC, Space Labs Inc). Data collected include demographic information, past medical history, clinical presentation, diagnoses, complications, and outcome. The database was searched to identify all patients over a 5½-year period (January 1993 through July 1998) admitted with a primary diagnosis of supratentorial ICH who underwent >1 CT scan of the head during their hospitalization. Over 92% of patients with ICH admitted to our institution over this time period were admitted to the NNICU. Patients were excluded from this study if the hemorrhage was associated with trauma, subarachnoid hemorrhage, or known vascular malformation; if >1 hematoma was present; or if the patient had intraventricular hemorrhage (IVH) only. Patients who underwent hematoma evacuation were included as long as 2 or more CT scans were obtained before surgery; only the presurgical CT scans were analyzed.

Clinical Data
The following historical data were obtained from the database and/or hospital records: age, sex, race, and history of hypertension, hematicologic abnormality, or anticoagulant drug use. If any of this information was not specified in the database, hospital records were then consulted. Data collected on arrival to the ICU included interval from ictus to admission (counted from the time the patient was last known to be normal if the symptoms were first noted on waking from sleep) and admission Glasgow Coma Scale (GCS) score, blood pressure, coagulation studies, and platelet count. Time from ictus to each CT scan was recorded. Reasons for obtaining repeat scans were obtained from the physician's written order for the scan or the physicians' and nurses' progress notes. If no reason was specified, the nurses' bihourly clinical assessments were reviewed for changes in GCS score, pupil size and reactivity, or British Medical Research Council motor scale score that might suggest clinical deterioration. In no case did review of nursing assessment reveal neurological decline that was not documented in physicians' progress notes or CT order. Reasons for obtaining repeat CTs were classified as follows: clinical deterioration (decreased consciousness or development of new neurologic deficits), follow-up, transfer from another institution, postangiographic follow-up, ventriculostomy management (to check placement or evaluate ventricular size with raising or clamping of ventricular catheter), and other reasons unrelated to neurological status.

CT Scan Analysis
Cranial CT scans were retrospectively reviewed. ICH location was classified as basal ganglia, thalamic, or lobar. Any hematoma extending into >1 anatomic area (eg, basal ganglia and thalamus) was categorized on the basis of the location from which it appeared to arise or the location containing the largest volume of blood. ICH volume was calculated using the formula A/2, where A and B represent the dimensions of CT hyperdensity in 3 axes perpendicular to each other.18 Midline shifts of the pineal and septum pellucidum were measured in millimeters by 1 observer (A.R.Z.) and corrected for magnification by using the centimeter scale provided on each CT image and then further separating the centimeter divisions into 10 equal millimeter divisions. Pineal shift was calculated as the distance from the center of the pineal calcification to a perpendicular line connecting the anterior and posterior insertions of the falx cerebri. If present on multiple CT slices, the pineal was measured on the slice on which it was the largest. Septum pellucidum shift was similarly measured between the anterior horns of the lateral ventricles on the CT slice containing the third ventricle and/or pineal. Measurements for all scans from an individual patient were made on the slice that provided the most similar image of the midline structures. Because individual measurements were made in millimeters, only changes of ≥2 mm were considered to be significant.

The scans of all patients having an increase in midline shift of either the pineal or septum pellucidum of at least 2 mm from the first to any subsequent scan were then reviewed by 2 independent observers (M.N.D. and C.P.D.), who were blinded to clinical history, time from onset of symptoms, and time interval between scans. An explanation for the increase in mass effect was sought by visual inspection of paired studies. The following categories were used: (1) increase in hemorrhage size, defined as the area of high attenuation; (2) increase in extent of edema, defined as the region with attenuation lower than that of white and/or gray matter in the contralateral normal hemisphere; (3) development of asymmetrical ventricular enlargement, as in the case of a trapped ventricle or asymmetrical ventricular decompression after ventriculostomy; (4) development of a new lesion; and (5) differences in scanning technique or head position. Each observer then made a judgment as to which of the above changes was the primary cause for the increased mass effect. In cases of disagreement between the 2 observers regarding the primary cause of increased midline shift, the cause was determined by consensus of all 4 investigators. In addition to the visual inspection of change in hematoma size, hematoma volume was independently measured by another observer (A.R.Z.) on all scans demonstrating increased midline shift and was compared with hematoma volume on the initial scan. Statistical analysis was performed with SPSS for Windows 7.0 (SPSS Inc).

Results
Two hundred fourteen consecutive patients with a primary diagnosis of spontaneous supratentorial ICH who underwent >1 CT scan were identified. Of these, 138 were excluded for the following reasons: 97 had <2 scans available for analysis, 16 were found to have an aneurysm or vascular malformation, 11 had >1 hematoma, 9 had hemorrhagic infarcts, and 5 had IVH only. The remaining 76 patients were enrolled in the study. Table 1 shows the clinical profile of our patients. The study participants underwent 235 scans (3.1±1.3 per patient). Initial CT was obtained within 24 hours of ICH in 66 of the 76 patients, within 35 hours in 76, and within 84 hours in all patients. Mean time to initial CT was 10.8±0.5 hours. Twenty-five scans were repeated on day 1, 81 on days 2 through 7, 31 on days 8 through 14, and 24 >14 days after ICH. (Figure 1.)

Midline shift of ≥1 mm was present in 88.2% of patients on initial CT, including 36 of 39 (92.3%) basal ganglia hematomas, 17 of 18 (94.4%) thalamic hematomas, and 14 of 19 (74%) lobar hematomas. Septum pellucidum shift was a more sensitive measurement of initial mass effect at all hematoma locations, occurring in 64 of 76 (84.2%) overall compared with 51 of 73 (69.9%) for pineal shift. There was no association between initial hematoma location (basal ganglia, thalamic, lobar) and millimeters of initial midline shift at the pineal or septum pellucidum.

There was a significant correlation between size of initial hematoma and millimeters of initial midline shift at both the pineal (r=0.235, P=0.046) and septum pellucidum (r=0.427, P<0.01), with a greater correlation for septum pellucidum than pineal shift. The correlations were significant for basal ganglia hematomas (pineal r=0.430, P<0.01;
TABLE 1. Clinical and CT Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Subjects (n=76)</th>
<th>Increase in Midline Shift of &gt;2 mm (n=15)</th>
<th>No Increase in Midline Shift (n=61)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Mean±SD</td>
<td>61.5±16.4</td>
<td>61.4±15.9</td>
<td>61.5±16.7</td>
</tr>
<tr>
<td>Range</td>
<td>25–97</td>
<td>43–86</td>
<td>25–97</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>38 (50)</td>
<td>8 (53.3)</td>
<td>30 (49.2)</td>
</tr>
<tr>
<td>Female</td>
<td>38 (50)</td>
<td>7 (46.6)</td>
<td>31 (50.8)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>40 (52.6)</td>
<td>8 (53.3)</td>
<td>32 (52.5)</td>
</tr>
<tr>
<td>White</td>
<td>36 (47.4)</td>
<td>7 (46.6)</td>
<td>29 (47.5)</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>54 (71.1)</td>
<td>12 (80.0)</td>
<td>42 (68.9)</td>
</tr>
<tr>
<td>Hematologic abnormality</td>
<td>4 (5.3)</td>
<td>0 (0)</td>
<td>4 (6.6)</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>7 (9.2)</td>
<td>0 (0)</td>
<td>7 (11.5)</td>
</tr>
<tr>
<td>GCS score Mean±SD</td>
<td>11.1±3.6</td>
<td>10.5±3.5</td>
<td>11.2±3.6</td>
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<td>Admission MAP, mm Hg</td>
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</tr>
<tr>
<td>Mean±SD</td>
<td>123.4±30.7</td>
<td>134.3±25.3</td>
<td>131.8±32.1</td>
</tr>
<tr>
<td>Range</td>
<td>74–224</td>
<td>109–200</td>
<td>74–224</td>
</tr>
<tr>
<td>Time from ictus to initial CT, h Mean±SD</td>
<td>10.7±12.9</td>
<td>8.7±9.8</td>
<td>11.2±13.5</td>
</tr>
<tr>
<td>Median</td>
<td>5.5</td>
<td>3.3</td>
<td>5.5</td>
</tr>
<tr>
<td>Range</td>
<td>1.0–83.5</td>
<td>1.0–29.3</td>
<td>1.0–83.5</td>
</tr>
<tr>
<td>ICH location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal ganglia</td>
<td>39 (51.3)</td>
<td>8 (53.3)</td>
<td>31 (50.8)</td>
</tr>
<tr>
<td>Thalamus</td>
<td>18 (23.7)</td>
<td>3 (20.0)</td>
<td>15 (24.6)</td>
</tr>
<tr>
<td>Lobar</td>
<td>19 (25.0)</td>
<td>4 (26.7)</td>
<td>15 (24.6)</td>
</tr>
<tr>
<td>ICH size on initial CT, cc</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>30.0±25.5</td>
<td>34.7±26.5</td>
<td>28.8±25.3</td>
</tr>
<tr>
<td>Median</td>
<td>22.9</td>
<td>23.2</td>
<td>22.4</td>
</tr>
<tr>
<td>Range</td>
<td>1.3–101.6</td>
<td>7.8–101.6</td>
<td>1.3–100.8</td>
</tr>
<tr>
<td>No. of CT scans</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>3.1±1.3</td>
<td>3.4±1.6</td>
<td>3.0±1.2</td>
</tr>
<tr>
<td>Range</td>
<td>2–7</td>
<td>2–7</td>
<td>2–7</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages.

septum pellucidum $r=0.557, P<0.01$) but not for thalamic or lobar hematomas.

In 25 instances in 23 patients, a $>2$-mm increase in midline shift of the pineal and/or septum pellucidum occurred between any 2 consecutive scans. In the 8 instances with a 2-mm increase, blinded visual inspection detected no alteration to explain the increase other than differences in head positioning or scanning technique. Reasons for the increase were identified in all of the 17 instances with $>2$-mm increase. There was a clear clustering of cases into 2 distinct groups: 10 with early increase (0.2 to 1.7 days after ICH; $\mu=0.8$ days) all showed hematoma enlargement, and 7 with late increase (9 to 21 days after ICH; $\mu=14.3$ days) all showed progression of edema. (Two patients had both early hematoma enlargement and late edema progression.) Among the patients with late increase in midline shift, 6 had predominantly white matter edema and 1 had edema of the basal ganglia and surrounding structures. Figure 2 shows the timing and cause of increased mass effect in relation to ictus.

The 2 blinded independent observers were in complete agreement about cause of increased midline shift in 23 of the 25 cases. Two cases (both with a 2-mm increase) required consensus of the 4 investigators. Among those patients whom the 2 independent observers judged to have hematoma enlargement ($n=10$), all had an increase in measured hematoma volume ($\mu=207\%$; range, 30% to 919%; Figure 3). Among those whom the independent observers judged to have no hematoma enlargement, all had either a decrease or no change in measured hematoma volume. All cases judged to have edema progression showed either a decrease or no change in the volume of the CT hyperdensity and extensive lucency.
There was no relationship between initial hematoma location (basal ganglia, thalamic, lobar) and progression of mass extending well away from the original hematoma border (Figure 4).

Figure 3. Sequential CT scans from a patient with hematoma enlargement. Scans were obtained at (A) 1.3 hours and (B) 8.8 hours after ICH. There was an increase in midline shift from 0 to 6 mm for the pineal and from 0 to 14 mm for the septum pellucidum. Volume of the hyperdensity increased by 481%. Note the development of contralateral hydrocephalus.

Figure 4. Sequential CT scans from a patient with edema. Scans were obtained at (A) 56 hours and (B) 493.3 hours after ICH. There was an increase in midline shift from 4 to 6 mm for the pineal and from 4 to 7 mm for the septum pellucidum. Note reduction in volume of the central hyperdensity and evolution of expansive white matter lucency extending well away from the hematoma.
effect. Those with and without progression of mass effect did not differ in terms of initial hematoma size (35.3±26.2 cc versus 28.8±25.3 cc), initial pineal shift (3.13±2.7 mm versus 2.3±2.2 mm), or initial septum pellucidum shift (3.2±2.2 mm versus 4.5±3.4 mm). However, the subset of patients who had progression of mass effect due to edema were significantly more likely to have larger initial hematoma size (49.5±28.6 cc versus 28.8±25.3 cc; 2-tailed t test, −2.025; \( P = 0.047 \)).

Early ipsilateral ventriculostomy was performed in 4 patients, 2 of whom showed mass effect progression and 2 of whom did not.

The reasons for obtaining repeat CT scans are shown in Table 2. Progression of mass effect was rarely found in patients rescanned for clinical deterioration. Only 10 of the 65 scans (15.3%) repeated for clinical deterioration were associated with increased mass effect (increase in midline shift >2 mm). In contrast, 7 of the 94 scans (7.4%) repeated for other reasons showed increased mass effect.

**Discussion**

Although the evolution of mass effect after ischemic stroke is well characterized, mass effect after ICH has not been studied as thoroughly. Part of the difficulty in determining the time course of mass effect in ICH lies in attempts to use changes in the perihematomal CT lucency as an indicator of mass effect. Measurement of this area is complicated by the fact that the borders of both the high- and low-attenuation regions become increasingly indistinct over time. In addition, the etiology of the perihematomal lucency remains controversial. It is variably thought to be due to clot retraction (with separation of the clot into a central mass of red blood cells and a surrounding area of serum),\(^{19–21}\) interstitial edema (caused by increased osmotic pressure exerted by serum proteins derived from the clot),\(^{22}\) cytotoxic edema (due to effects of blood-derived proteases),\(^{23–25}\) or ischemic edema.\(^{26–28}\)

Because of the difficulties in assessing the pathophysiological importance of signal characteristics around the hematoma, we chose not to attempt to measure changes in the perihematomal lucency as an indicator of mass effect; rather, we measured change in midline shift over time. We chose midline shift because it is easily quantifiable, and its correlation with clinical deterioration has been well described.\(^{29}\) In addition, measurement of increased midline shift allows for direct comparison with data on cerebral infarction. Although there are other manifestations of mass effect exerted by hematomas, including ventricular compression, sulcal effacement, obliteration of basal cisterns, and local tissue pressure effects, these are difficult to quantify. While a gross assessment of effacement of ventricles, sulci, or basal cisterns can be made when looking at an individual scan, appraisal of change in degree of effacement between any 2 scans is more subjective than is midline shift. The fact that we limited our definition of mass effect to include only midline shift means that we may have underestimated the number of patients who had mass effect on initial CT, especially in cases of superficial hemorrhages, which are far removed from the deep midline structures. This should have had little effect on our ability to document progression of mass effect, however, because midline shift was present on initial CT in 88% of patients, and any further increase in mass effect would be expected to be manifest through further midline shift, not just changes in ventricles, sulci, or basal cisterns.

Although any given degree of pineal shift may be more clinically significant than a similar degree of septum pellucidum shift, we chose to measure midline shift of both the pineal and septum pellucidum because (1) our primary goal was to identify all patients with progression of mass effect rather than to assign weight to the degree of shift based on the structure involved, and (2) we anticipated that there might be a relationship between hematoma location and which midline structure is shifted.\(^{15}\) Although our results did not demonstrate any relationship between location of hematoma and location of maximal midline shift, they did indicate that septum pellucidum shift is a more sensitive marker of mass effect after ICH than is pineal shift.

We chose CT as our neuroimaging modality because it remains the most readily available and widely used imaging tool in the assessment of ICH and its complications at our institution, and thus it provided a means of studying a large number of patients over time. Our method was technically limited in that measurement of midline shift off CT films rather than online restricted our resolution capabilities to

<table>
<thead>
<tr>
<th>Reason</th>
<th>All Scans</th>
<th>Scans With Increased Midline Shift</th>
<th>Scans With Increased Shift Due to Hematoma Enlargement</th>
<th>Scans With Increased Shift Due to Edema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical deterioration</td>
<td>65</td>
<td>10</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Follow-up</td>
<td>34</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Transfer from other hospital</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postangiographic follow-up</td>
<td>10</td>
<td>2</td>
<td>2</td>
<td></td>
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<tr>
<td>Ventriculostomy management</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>14</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>159</td>
<td>17</td>
<td>10</td>
<td>7</td>
</tr>
</tbody>
</table>

**TABLE 2. Reasons for Repeat CT Scans**

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changes in midline shift of >2 mm. Our resolution capabilities, however, were similar to those of Ropper in his study of lateral displacement of the brain and level of consciousness in acute hemispheral mass.

Within the constraints of our methodology, we were able to show that progression of mass effect in our series of patients with ICH was an uncommon phenomenon, occurring in only 15 of 76 patients. This is despite the potential selection bias in our study of including only patients with >1 CT scan, a population that may have had a longer or more complicated course. On the other hand, it excluded patients who underwent immediate hematoma evacuation and may have had a higher incidence of very early deterioration. Because of the retrospective nature of our study, we may have underestimated the number of patients who had progression of mass effect. Without systematic repetition of CT scans at regular intervals, we could judge for progression of mass effect only if a repeat CT was obtained on any given patient. Our study was limited to patients admitted to the NNICU; however, >92% of patients with ICH at our institution during the time period of our study were admitted to the NNICU. Our series is therefore reasonably representative of patients with ICH admitted to a tertiary care hospital and is not biased toward only large hemorrhages or clinically devastated patients. This is supported by the fact that the clinical profile of our patients is similar to that reported in other population-based studies of ICH (with the exception that our patients are younger).

In our series, mass effect had a bimodal time course, with an early (<2 days) and a late (>9 days) increase. Among cases of increased mass effect developing within 2 days of ICH, all were associated with hematoma enlargement. It should be noted that although our data indicate that increase in mass effect in association with hematoma enlargement was seen for up to 2 days, it is clear from the literature that hematoma enlargement almost always occurs within the first few hours. There are likely many more patients who had hematoma enlargement before their first CT was obtained. The early expansion in hematoma size is attributable to the addition of more blood rather than edema, because edema fluid would lead to a decrease in the attenuation of the hematoma, which was not seen.

Because this was not a prospective study with scans obtained at predefined regular time points, the intervals between scans had wide variation, and we cannot state with certainty when exactly the increased mass effect occurred in these patients. We did not find early progression in mass effect from edema similar in time course to that seen in ischemic stroke, despite the fact that most patients had repeat scans during the first week. A potential explanation for this is that prophylactic treatment effectively prevented its development. Of the possible treatments, we eliminated the effect of surgical debulking by excluding patients once hematoma evacuation was performed. Osmotic agents, steroids, and hyperventilation are used infrequently in ICH at our institution. Early ipsilateral ventriculostomy was performed in only 2 patients who did not show progression of mass effect, so ventricular drainage cannot account for the lack of early progression in mass effect due to edema in our series.

Our results do, however, support the occurrence of late edema progression in the second and third weeks after ICH. Because of insufficient sampling toward the end of the first week and into the second week, we cannot identify exactly when these changes began to develop in our patients. Pathophysiological explanations for this late edema formation are speculative. Radionuclide and CT studies showing pertechnetate uptake and contrast enhancement, respectively, 1 to 14 weeks after ICH indicate blood-brain barrier (BBB) breakdown to macromolecules, which lack a fully developed BBB. Thus, late edema progression after ICH might represent vasogenic edema associated with angiogenesis. Only 1 of our patients received contrast for the CT scan on which edema was seen (ring enhancement was present), so we are unable to address the hypothesis of BBB breakdown as a cause for late edema formation.

The association of clinical deterioration with hematoma enlargement is well-documented. The role of edema in producing clinical deterioration is less clear. Our series shows that only 3 of 65 CT scans repeated for documented clinical deterioration demonstrated increased mass effect associated with increased edema and that all of these occurred after the first week. Of 7 patients with mass effect associated with increased edema, only 3 had concomitant clinical deterioration. Because our data on clinical change were obtained retrospectively and there are other possible concurrent explanations for clinical deterioration in patients with ICH, we cannot with certainty ascribe their decline to increased mass effect. A recent series of 97 patients reported that edema growth within 20 hours of symptom onset occurred in 61% and was not associated with early neurological deterioration. In another series of 46 patients, in-hospital worsening occurred in 15, 9 of which were ascribed to edema. Deterioration secondary to edema occurred in 3 patients on day 1, 4 on days 2 through 6, and 2 on days 7 through 14. It is unclear, however, what criteria were used to define edema and how many patients had similar neuroimaging findings without neurological deterioration. Finally, in a series of 7 patients with ICH, changes in the volume of the high-signal-intensity area on T2-weighted MRI scans (increasing relative to initial CT hyperdensity at 1 week, peaking at 2 weeks, and declining at 4 weeks) did not correlate with clinical status.

In conclusion, our data suggest that the time course of progression of mass effect in ICH does not follow the same pattern as that of ischemic stroke. Progression of mass effect in our series was infrequent and occurred at 2 distinct time points: within the first 2 days and during the second and third weeks after symptom onset. All cases with early progression were associated with hematoma enlargement, and all cases with late progression were associated with the development of extensive edema. The clinical importance of hematoma enlargement is well established; the clinical significance of later-developing mass effect with edema will require further study. Progression of mass effect due to edema was more likely to occur in those with larger initial hematoma size. We acknowledge that these are preliminary observations based on a retrospective, possibly biased review. A prospective study in which patients are assessed and scans obtained at regular,
prespecified intervals is required to validate the incidence and time course of mass effect progression and to correlate changes in mass effect with clinical status.

Acknowledgments

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References


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