



Management of Intracerebral Hemorrhage

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Case Presentation

A 67-year-old female with a history of uncontrolled hypertension and hyperlipidemia presents after sudden onset of headache followed by vomiting and progressive left hemiparesis over 2 h. Vital signs were notable for a systolic blood pressure of 230 mmHg. Laboratory values upon arrival, including coagulation parameters and toxicology screen, were unrevealing. CT head imaging was performed on arrival and the pertinent images are shown below (Fig. 38.1).

Question

Would early surgical intervention be appropriate in the initial management of this patient?

Answer Certain patients may benefit from early neurosurgical intervention in the setting of intracerebral hemorrhage [2].

However, the International Surgical Trial in Intracerebral Haemorrhage (STICH) did not demonstrate improved 6-month functional outcome or mortality with the early evacuation of supratentorial hematomas [3]. Furthermore, STICH II did not demonstrate any significant difference in combined death or disability in patients undergoing evacuation of supratentorial hematoma volumes of 10–100 cm³ without intraventricular hemorrhage (IVH) when compared with the maximal medical management group [4]. However, patients with cerebellar hemorrhages >3 cm with fourth ventricular effacement and/or hydrocephalus should undergo

urgent surgical intervention given elevated morbidity and mortality with conservative management in this group [2, 4, 5]. Younger patients with rapid neurological decompensation secondary to hematoma expansion, or with underlying lesions such as aneurysms, AVMs and tumors may also be surgical candidates [2, 4, 5]. The Minimally Invasive Surgery Plus Recombinant Tissue-Type Plasminogen Activator for Intracerebral Hemorrhage Evacuation II (MISTIE II) trial demonstrated a reduction in perihematomal edema and a trend towards improved outcomes in the hematoma evacuation group [6]. The MISTIE III trial is currently in progress. Phase 3 of Clot Lysis: Evaluating Accelerated Resolution of Intraventricular Hemorrhage (CLEAR III) IVH trial is a randomized control study, which aims to evaluate clearance of clot and outcome in patients with large intraventricular hemorrhage receiving scheduled injections of rt-PA through EVD [7]. Study results are expected in the near future.

This patient's CT scan demonstrates a large right basal ganglia hemorrhage without intraventricular extension. Current guidelines would advocate for maximal medical management [2, 5].

Principles of Management

Clinical Presentation

The onset of acute severe headache, vomiting, seizure, significant hypertension (often >220 mmHg), and rapid deterioration in consciousness with possible accompanying pupillary dilatation, posturing and abnormal respiratory pattern should provoke a high suspicion for intracerebral hemorrhage (ICH) [2].

Diagnosis

The rapid onset of focal neurological symptoms warrants brain imaging on an emergent basis [2, 5]. CT scans provide

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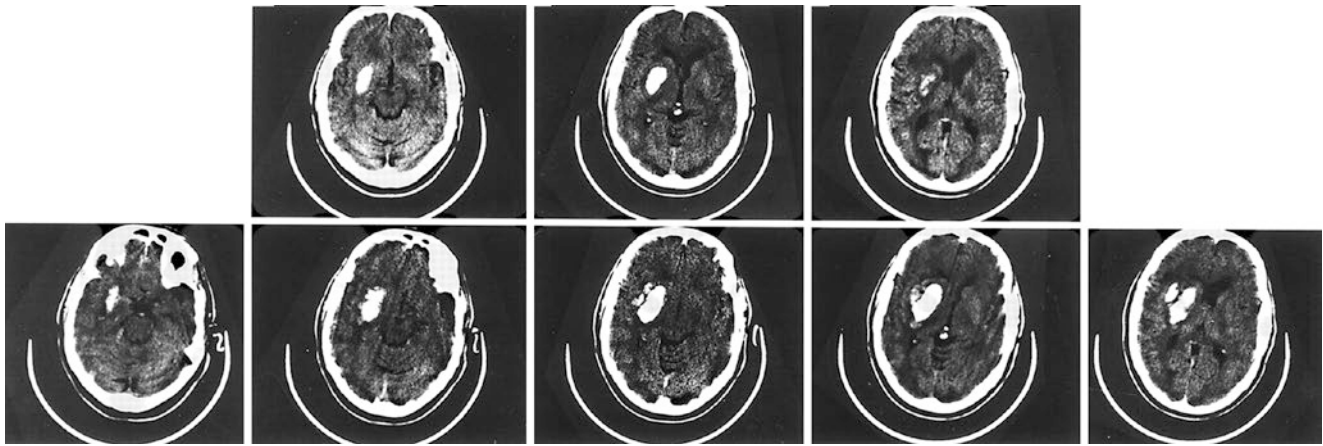


Fig. 38.1 Axial CT brain demonstrating right putaminal hemorrhage (From Brott et al. [1]. Reprinted with permission from Wolters Kluwer Health, Inc.)

a rapid method of evaluating the head for acute pathology, including intracerebral hemorrhage (ICH). Brain CT imaging in the latter often demonstrates intra-axial, focal area(s) of hyperdensity with mass effect and effacement of the surrounding parenchyma [2]. Hemorrhage location(s) provide clues to the underlying pathology. In addition to trauma, multiple etiologies of non-traumatic ICH exist, and include hypertension, vascular malformations, trauma, cerebral amyloid angiopathy, brain neoplasm, infarction, vasculitis, illicit drug-related, bleeding diathesis, and anticoagulation [2, 5]. Hypertension is the most common cause of non-traumatic ICH. Typical locations suggestive of a hypertensive bleed include the basal ganglia (most commonly putamen) and thalamus, as well as the pons and cerebellum [2, 5]. Hematoma volume can be estimated using the ABC/2 method (Fig. 38.2) [9]. Large hematoma volumes and evidence of heterogeneous attenuation are predictive of subsequent hematoma expansion [1, 2, 5, 10].

Acute Management

In addition to emergent brain imaging, initial laboratory assessments should include coagulation parameters and toxicology screen, with elevations in the former requiring rapid normalization with appropriate reversal agents. Contrast-enhanced head imaging, often CT angiography, can provide additional information about the presence of underlying vascular malformations, aneurysms, as well as the presence of contrast extravasation within the hematoma [1, 10, 11]. The latter “spot sign” is suggestive of active bleeding and predicts hematoma expansion, as well as likely higher morbidity and mortality [1, 10, 11]. Demchuk et al. found a positive predictive value of 61% for hematoma expansion in the presence of the spot sign [10]. Exacerbating factors for expansion also include antithrom-

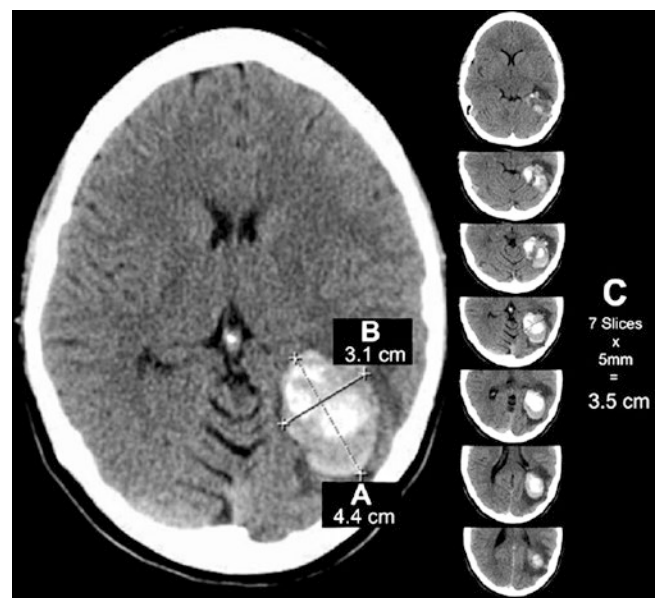


Fig. 38.2 Example of ICH calculation using ABC/2 formula. (a) Greatest hemorrhage diameter by CT. (b) Diameter 90° to A. (c) The approximate number of CT slices with hemorrhage multiplied by slice thickness (From Beslow et al. [8]. Reprinted with permission from Wolters Kluwer Health, Inc.)

botic and anticoagulation therapy, as well as persistent hypertension, and therefore aggressive management with anticoagulation reversal and antihypertensive therapy is warranted [1, 2, 5, 10].

Serial CT head imaging, usually within 4–6-h, is critical for the evaluation of hematoma expansion and obstructive hydrocephalus. Brott and Broderick found 38% of hematomas expand by 33% of original volume or at least 6 cm³ within 24-h of symptom onset, with most reaching significant expansion within 4 h [1]. Intraventricular hemorrhage is a risk factor for development of the hydrocephalus [12]. The initial presence or subsequent development of ventricular

system enlargement warrants rapid neurosurgical intervention with external ventricular drain (EVD) placement and drainage of cerebral spinal fluid (CSF) [2, 5, 12].

Airway patency should be monitored carefully. Large or rapidly expanding hematomas, particularly with evidence of obstructive hydrocephalus, often result in depressed mental status and compromised airway protection [2]. Emergent intubation is warranted in these circumstances with utilization of agents such as propofol and lidocaine to blunt potential intraprocedural intracranial pressure crises [2].

Brain herniation is the most dreaded outcome of ICH, leading to increased morbidity and mortality, particularly in the absence of rapid intervention and reversal. Clinical manifestations include the development of new or worsening neurological deficits, including depressed mental status and pupillary abnormalities, thus mandating frequent monitoring of the patient's neurological exam in acute setting [2, 5]. Rapid intervention is critical and includes elevating the head to 30°, hyperventilation (with rapid sequence intubation in the setting of an unsecured airway), and administration of hyperosmolar therapy [2, 5, 13]. Repeat head imaging is warranted when the patient is stabilized with insertion of an EVD if obstructive hydrocephalus is present [1–5, 11]. Ultimately the patient may require decompressive hemicraniectomy to improve odds of survival, even though the data for functional outcome amelioration amongst survivors is not nearly as robust as for large hemispheric ischemic strokes [2–6].

Natural History

The ICH score is a risk stratification scale using the Glasgow Coma Score (GCS), age, ICH volume, infratentorial loca-

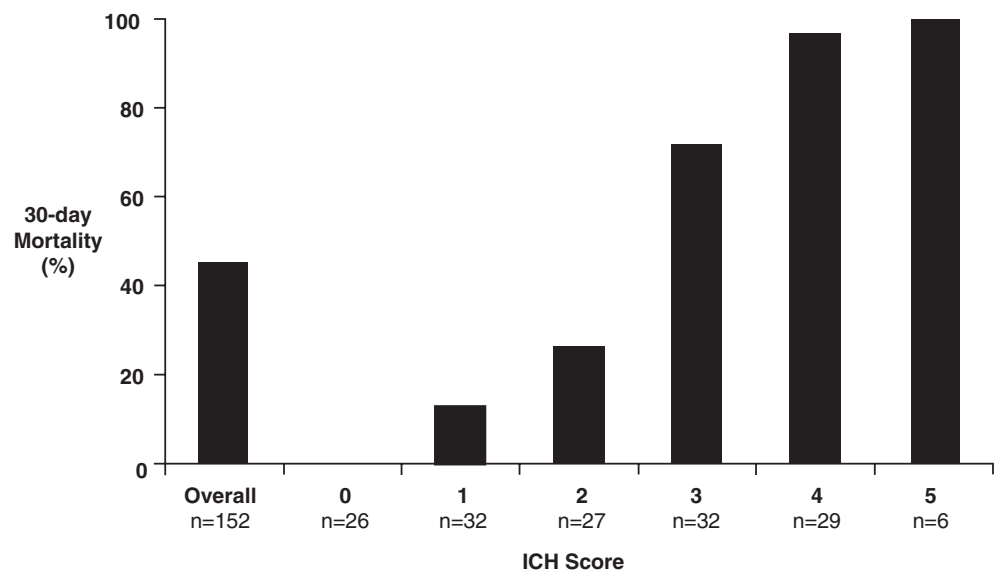
tion, and presence of IVH to predict 30-day mortality (Table 38.1 and Fig. 38.3) [14]. The tissue at the epicenter of the hematoma undergoes rapid destruction causing clinical neurological insult and is unlikely to be salvaged [15]. Hematoma expansion and perihematomal edema can worsen mass effect and may contribute to further injury and higher mortality. Edema develops early after ICH and peaks up to 2 weeks after onset, although the most rapid increase occurs in first 2 days on MRI imaging [16]. The degree of edema is predictive of poor outcome. Secondary injury as a consequence of blood–brain-barrier damage, inflammation, and reticulocyte lysis can further worsen injury to the surrounding parenchyma [15, 16].

Table 38.1 ICH score for predicting 30-day mortality

Component	ICH score points
<i>GCS</i>	
3–4	2
5–12	1
13–15	0
<i>ICH volume (mL)</i>	
≥30	1
<30	0
<i>Intraventricular hemorrhage</i>	
Yes	1
No	0
<i>Infratentorial origin of ICH</i>	
Yes	1
No	0
<i>Age (year)</i>	
≥80	1
<80	0
Total ICH score	0–6

From Hemphill et al. [14]. Reprinted with permission from Wolters Kluwer Health, Inc.

Fig. 38.3 ICH score and 30-day mortality (From Hemphill et al. [14]. Reprinted with permission from Wolters Kluwer Health, Inc.)



Complications

Damage or irritability of the cerebral cortex in the setting of ICH can manifest as seizures. Although occasionally a presenting symptom, seizures can develop at any point after the inciting event and therefore antiepileptic drugs are a mainstay in the initial treatment [2, 5, 17, 18].

ICP can be measured via an EVD or a dedicated ICP monitor. Persistent ICP elevations can further complicate the management of ICH, often manifesting as herniation events. ICP crises are treated algorithmically, as noted above, often beginning with raising the head of the bed, hyperventilation with a goal PCO_2 of 30–35, and hyperosmolar therapy [2]. Additional iatrogenic interventions include the use intravenous agents to drive down the ICP, such as propofol and pentobarbital, as well as systemic body temperature cooling [2, 5].

Evidence Contour

Hyperosmolar Therapy

Urgent intervention is warranted in the setting of increased intracranial pressure as assessed by invasive monitoring techniques or changes in the neurological examination, such as the rapid development of pupillary dilation and absent reactivity. In addition to head elevation and hyperventilation, hyperosmotic agents are often utilized for rapid ICP reduction, effectively removing free water and dehydrating the brain parenchyma [2, 5, 13]. Mannitol and hypertonic saline are two commonly utilized agents. Mannitol, typically administered in 1 g per kilogram boluses, increases serum osmolality and induces an osmotic gradient between the serum and brain parenchyma, resulting in osmotic diuresis. Despite being widely available and easily administered through a peripheral line, caution should be used given the potential for hypotension, volume depletion and electrolyte disturbances [13]. Serum osmolality >320–340 mOsm/kg or poor renal function may be limiting factors. Mannitol can cross the blood–brain-barrier and extravasate into the damaged parenchyma especially given the lower reflection coefficient than hypertonic saline (0.9 and 1.0, respectively), posing the theoretical risk of “rebound” elevations in ICP secondary to a reversal of the osmotic gradient in the setting of recurrent use [13].

Alternatively, hypertonic saline, used in widely varying volume and tonicity, is also utilized for urgent ICP reduction [13]. The mechanism of action is similar to mannitol although without the accompanying diuresis and subsequent hypovolemia [13]. Hypertonic saline is less likely to cross the damaged BBB and cause worsening mass effect and shift with recurrent use. Given the risk of thrombophlebitis, solutions of 3% or greater should be administered via central IV access [13].

Several randomized control trials evaluating various etiologies of increased ICP have compared the efficacy of

hypertonic saline and mannitol, with a meta-analysis of these trials demonstrating marginally greater efficacy of hypertonic saline (16% more likely to decrease ICP <20 mmHg 1 h post administration) in the management of elevated ICP, although clinical outcomes were not measured [13]. Current guidelines advise clinician discretion in the utilization of either agent and do not recommend one over the other [5, 13].

Seizure Prophylaxis

Brain injury involving the cortex increases the risk of epileptogenic activity. The incidence of electrographic seizures may be as high as nearly 1/3 of patients with ICH, with most occurring within 24-h of the inciting event [2, 5, 17, 18]. Vespa et al. reported a relatively high frequency of seizures after lobar (28%) and deep (21%) ICH [18]. Lobar location and small hematomas may be early predictors of early seizures. Although management often involves the use of seizure prophylaxis, current guidelines recommend otherwise [5]. Furthermore the agent of choice and duration of treatment remain areas of debate. One prospective review found phenytoin to be associated with a higher incidence of fever and worse outcomes [17]. The association of seizures with clinical outcomes remains unclear, however. Alterations in mental status incongruent with the degree of cerebral injury certainly warrant continuous EEG monitoring [2, 5, 18]. Seizures should be managed with anticonvulsant therapy, although the choice of anticonvulsant remains debatable. Prophylactic anti-epileptic medication is not recommended by current AHA guidelines [2, 5].

Hypothermia

Fever has been strongly associated with poorer neurological outcomes in patients with brain injury [2, 5, 19, 20]. Investigation into temperature reduction as a neuroprotective treatment began in the 1950s and has subsequently been most studied in the context of traumatic brain injury. Multiple studies have postulated the beneficial effects of mild to moderate hypothermia to be secondary to the reduction of cerebral metabolism and potential reduction of ICP and CBF [19, 20]. The attenuation of several secondary injury mechanisms, including free radical generation, excitotoxicity, and inflammation, may also be contributory [15, 19, 20]. However, limiting side effects of systemic cooling have included coagulopathy and cardiac arrhythmias [19, 20]. Furthermore, an optimal method of cooling, target core temperature, and duration of cooling has not been established [19, 20].

In comparison to standard medical or surgical treatment, hypothermia has not been shown to improve outcomes in patients with traumatic brain injury. The National Acute Brain Injury Study: Hypothermia II, a randomized control

trial comparing normothermia and hypothermia in patients with traumatic brain injury, did not demonstrate a difference in functional outcome between the two groups at 6-months [20]. In 2015, the Hypothermia for Intracranial Hypertension after Traumatic Brain Injury study, a randomized control trial of elevated ICP management comparing standard care to hypothermia plus standard care, did not find better outcomes in the hypothermia group [19]. At this time, ensuring strict normothermia remains the standard in this patient population [5].

Hypertension Management

Elevated blood pressure, defined as SBP > 140 mmHg, is present in approximately 75% of patients with acute ICH. Proposed mechanisms include stress activation of neuro-endocrine systems and damage to central autonomic centers, including the insular cortex. Hypertension is a strong predictor of early mortality in ICH [2, 5, 21]. However, the intensity of blood pressure control in this setting has remained a topic of debate. Proponents for aggressive control cite hematoma expansion, early neurological deterioration and higher mortality as the basis for targeting systolic blood pressures of <140 mmHg. Conversely, rapid reduction and aggressive targeting of blood pressure may run the theoretical risk of perihematomal and perhaps more global ischemia [21]. The Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial 2 (INTERACT2) compared early intensive blood pressure lowering with SBP < 140 mmHg to target SBP < 180 mmHg and did not demonstrate any significant difference in death or major disability at 90-days between groups, but did demonstrate better 90-day modified Rankin scores [21]. Aggressive blood pressure strategies have not been found to reduce hematoma volumes or perihematomal cerebral blood flow [21, 22]. Furthermore, the Intracerebral Hemorrhage Acutely Decreasing Arterial Pressure Trial (ICH-ADAPT) study, did not find that intensive blood pressure reduction precipitated perihematomal ischemia [22]. The results of the Antihypertensive Treatment of Acute Cerebral Hemorrhage II (ATACH II) trial, which will randomize participants to target blood pressure goals of SBP <140 mmHg or SBP < 180 mmHg, are pending. Current AHA guidelines suggest that early aggressive blood pressure management strategies with target SBP < 140 mmHg appear to be safe and may maximize patient outcomes, especially in patients with smaller ICH volumes (<20 cm³), admission GCS 12–15, and initial SBP < 220 [5]. In others, a more conservative approach may be reasonable.

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