History

- **HPI**: 61 y.o. male construction worker experienced acute onset right hemiplegia and aphasia while at work
- **PMHx**: HTN
- **PSHx**: negative
- **SHx**: smoking
- **FHx**: non-contributory
- **Meds**: none
- **Allergies**: NKDA
Physical

- Intubated
- Awake, agitated
- PERRL
- Localizing LUE
- Withdrawing LLE
- R hemiplegia
Primary Intracerebral Hemorrhage (ICH)

Jack M. Klem, M.D.
Neurosurgery Grand Rounds
Thomas Jefferson University Hospital
February 17, 2006
Definition

Rupture of blood vessels within brain parenchyma in absence of preexisting vascular malformation or brain parenchymal lesion
Epidemiology

- 10 - 20 cases of ICH per 100,000 annually in U.S.
- 37,000 to 50,000 Americans annually
- Incidence double among African-Americans and Japanese (50 per 100,000)

National Health and Nutrition Examination Survey Epidemiologic Follow-up Study, 1999
Circadian and Seasonal Variation

- In males, <70 yrs, bimodal distribution w/ peak between 8-10AM and lower peak 6-8PM
- In males >70 yrs and women, single peak 6-10PM
- Peak in winter and trough in summer for all

Risk Factors

Most important contributors to ICH are:

Hypertension (HTN) and Cerebral amyloid angiopathy (CAA)

Broderick et al., Lobar hemorrhage in the elderly: the undiminishing importance of hypertension. *Stroke, 1993.*
Risk Factors (Hypertension)

Prevalence greater among African Americans

Hypertension was present in:
- 67% of patients w/ lobar ICH
- 73% of patients w/ putamenal or thalamic ICH
- 73% of patients w/ cerebellar ICH
- 78% of patients w/ pontine ICH

Broderick et al., Lobar hemorrhage in the elderly: the undiminishing importance of HTN. Stroke, 1993.
Risk Factors
(Cerebral amyloid angiopathy)

- Prevalence:
  4.7% to 9.0% among those 60-69 y.o., but rises to 43% to 58% among those >90 y.o.


- Progressive course:
  2-year cumulative risk of recurrent ICH among survivors of CAA-related ICH is 21% (10-28%)

Risk Factors

- **Excessive EtOH**
  Impair platelet fxn, coagulation, and possibly consistency of endothelial wall

- **Hypocholesterolemia**
  Weakens endothelial wall

- **Tobacco Use**
Risk Factors

Antithrombotic Medications

- 2- to 4-fold increase in rate of ICH among patients treated w/ Coumadin

- Leukoaraiosis and CAA are risk factors for warfarin-related ICH ➔ anticoagulant-related ICH may therefore result from specific vascular pathologies.
  Smith et al., Leukoaraiosis is associated with warfarin-related hemorrhage following ischemic stroke. Neurology, 2002.
Risk Factors

Correlation between cerebral microangiopathy on MRI, clinically silent micro-hemorrhages, and acute spontaneous ICH

Alemany et al., Coexistence of microhemorrhages and acute spontaneous ICH. Radiology, 2006.
Risk Factors

- N=90 (median age 67)
- Enrolled prospectively on suspicion of acute stroke
- Divided into 45 patients w/ ICH and 45 patients control
- Microhemorrhages in 64% of ICH pts, 18% of control pts

Alemany et al., Coexistence of microhemorrhages and acute spontaneous ICH. Radiology, 2006.
Pathophysiology: HTN

Vasculopathy complicating chronic HTN → decrease compliance → rupture at points of dilatation of small penetrating arterioles

Charcot-Bouchard microaneurysms: HTN-related bleeding occurs at or near the bifurcation of affected arteries

Takebayashi et al., Electron microscopic studies of ruptured arteries in hypertensive ICH. *Stroke*, 1983.
Pathophysiology: CAA

Deposition of congophilic material in media and adventitia of cortical and meningeal vessels $\rightarrow$ necrosis of vessel wall $\rightarrow$ ICH
Pathophysiology

- Once ICH occurs, spreads between tissue planes with considerable tissue displacement and minimal destruction
- Majority of hematoma expansion occurs within first 4-hours after Sx onset
- Brain herniation, HCP due to IV extension

Pathophysiology

- Hematoma stabilization and absorption

- Significant vasogenic edema due to deposition of serum proteins → create osmotic gradient

- Edema presents within few days and lasts up to 2-weeks post-ICH

Zazulia et al., Progression of mass effect after ICH. Stroke, 1999.
Pathophysiology

- Progression of hematoma
  - Mechanical disruption, local coagulation defect
  - Hematoma expanded in 20% of patients (N=204)
  - 36% of those less than 3 hrs out from initial hemorrhage
  - 11% of those presenting > 3hrs out

Common Sites and Sources

Qureshi et al., Spontaneous Intracerebral Hemorrhage. NEJM, 2001
Location

Putamen
Lobar: Hemorrhagic Stroke

Grubb, R. “Spontaneous Cerebral Hemorrhage” in Brain Surgery: Complication Avoidance and Management. Ed. by Apuzzo, 1993
Lobar: Amyloid Angiopathy

Grubb, R. “Spontaneous Cerebral Hemorrhage” in Brain Surgery: Complication Avoidance and Management. Ed. by Apuzzo, 1993
Basal Ganglia Hemorrhage

Grubb, R. “Spontaneous Cerebral Hemorrhage” in Brain Surgery: Complication Avoidance and Management. Ed. by Apuzzo, 1993
Gross Pathology of BG Hemorrhage
Grubb, R. “Spontaneous Cerebral Hemorrhage” in *Brain Surgery: Complication Avoidance and Management*. Ed. by Apuzzo, 1993
Re-Perfusion Hemorrhage
Cerebellar: HTN Hemorrhage

Gross Pathology of Cerebellar Hemorrhage
Cerebellar: Coagulopathic Hemorrhage

Pontine Hemorrhage

Outcome

- 30-day mortality up to 50% despite aggressive mgmt strategies w/ majority of deaths in first 2-days
- Only 20-30% achieve independent status at 6 months

Broderick et al., Guidelines for the management of spontaneous ICH. Stroke 1999.
Prognosis
(Predictors of 30-day mortality)

- Initial Glasgow coma score (GCS)
- Hematoma volume > 30cc
- Age > 80
- Infratentorial origin of ICH
- Intraventricular extension

Hemphill et al., The ICH score: a simple, reliable grading scale for ICH. Stroke, 2001.
Prognosis

- Broderick *et al.* predicts mortality at 30 days
  - 90% in patients w/ GCS<9, Volume > 60cc
  - 17% in patients w/ GCS>=9, volume < 30cc


- Volume = 0.5 (A x B x C)
  - A = greatest diameter on CT
  - B = diameter perpendicular to A
  - C = (number of slices) x (thickness)
Massive Basal Ganglia Hemorrhage
Gross Pathology of Massive Basal Ganglia Hemorrhage
## Clinical Presentation

<table>
<thead>
<tr>
<th>Region (references)</th>
<th>Occurrence (%)</th>
<th>Clinical signs</th>
<th>Associations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Putamen (23–25)</td>
<td>28–42</td>
<td>Sudden onset motor and sensory deficit; headache; depressed conscious state</td>
<td>~90% hypertensive; 20% mortality</td>
</tr>
<tr>
<td>Thalamus (7, 23–25)</td>
<td>10–26</td>
<td>Some motor and sensory deficits; headache, gaze paresis, decreased consciousness, and homonymous hemianopia</td>
<td>~90% hypertensive; 40% mortality</td>
</tr>
<tr>
<td>Lobar (23–25)</td>
<td>19–30</td>
<td>High incidence of headache and seizures; low coma incidence</td>
<td>Aneurysm, arteriovenous malformation, coagulopathy; ~35% hypertensive; 20% mortality</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Frontal lobe (26%): contralateral hemiparesis and headache</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Parietal lobe (25%): motor and sensory deficit, and hemianopia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dominant temporal lobe: fluent aphasia, good repetition, and partial hemianopic visual defect</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Occipital lobe (18%): visual blurring, homonymous hemianopia</td>
<td></td>
</tr>
<tr>
<td>Cerebellum (7, 23–25)</td>
<td>8–15</td>
<td>Ataxias, facial palsy, and gaze paresis</td>
<td>~85% hypertensive</td>
</tr>
<tr>
<td>Brainstem (23–25)</td>
<td>4–11</td>
<td>Coma, decerebrate posturing, pinpoint reactive pupils, and upgoing plantar responses</td>
<td>~70% hypertensive; 85% mortality</td>
</tr>
</tbody>
</table>

Medical Treatment

- Maintain pre-morbid blood pressure
  AHA guidelines: treat only for SBP>180, DBP>105, MAP>130

- Normovolemic hydration

- Reversal of coagulopathy

- ICP control

- Dexamethasone of no benefit (NEJM, 1987)

Emerging Medical Treatment

- Recombinant factor VIIa (NovoSeven)
  - N=399 w/ acute ICH
  - Randomized into to rFVIIa vs. placebo within 1-hr after baseline CT scan
  - Dose-dependent effect on reducing hematoma growth over 24-hrs (29% growth w/ placebo, 11% w/ rFVIIa)
  - 90-day mortality: 29% placebo vs. 18% rFVIIa
  - Modified Rankin Scale: 69% of placebo patients dead or severely disabled vs. 49-55% for rFVIIa patients
  - Thromboembolic complications (2% vs. 7%)

Surgical Therapy

- **N = 52** (surgical = 26, medical = 26)
- Inclusion: severe neurologic deficits and/or decreased consciousness
- Craniotomy within 48 hrs of symptom onset
- 6-month mortality:
  - Surgery = 46%
  - Medical = 36%
- 6-month functional independence:
  - Surgery = 7%
  - Medical = 31%
- Odds ratio 5.95 (95% CI, 0.64 to 55)
- Surgery group had lower presenting GCS and higher rate of IVH

- N = 17 (surgical = 8, medical = 9)
- Inclusion: putaminal hemorrhage > 3 cm in diameter
- Craniotomy performed
- 6-month mortality:
  - Surgery = 75%
  - Medical = 78%
- Odds ratio 0.86 (95% CI, 0.09 to 8.1)

- N = 20 (surgical = 9, medical = 11)
- Inclusion: volume > 10cc, GCS > 4, hypertensive ICH
- Craniotomy within 24 hrs of symptom onset
- 6-month mortality:
  - Surgery = 22%
  - Medical = 27%
- 3-month NIHSS:
  - Surgery = 4
  - Medical = 14
- Odds Ratio = 0.48 (95% CI, 0.09 to 2.69)

- N = 1033 (surgical = 503, medical = 530)
- Patients with extensive IVH excluded
- Craniotomy within 12 hrs of symptom onset
- 6-month mortality:
  - Surgery = 17%
  - Medical = 24%
- Good recovery or moderate disability:
  - Surgery = 26%
  - Medical 24%
- Odds Ratio = 0.53 (95% CI, 0.13 to 2.21)

No overall benefit of early surgical evacuation
Meta-analysis of the randomized controlled trials slightly favor surgical management. There is no significant difference.

Emerging Surgical Therapies

- Transparent endoscopic tools for hematoma evacuation (Nishihara et al., 2005)
- Frameless stereotactic aspiration and thrombolysis using rtPA (Vespa et al., 2005)
- Decompressive craniectomy (Murthy et al., 2005)
- Minimally invasive surgery plus rtPA for ICH (NIH-sponsored safety study)
Upshot of the Literature

- Prevention is key given new understanding of pathophysiology
- Few definitive conclusions can be drawn from the randomized studies when considered individually or with meta-analysis
- Most conservative interpretation → no difference between surgical and medical management of ICH
- Direction emerges when patient and treatment variables are considered

“Take-Home” Message

Non-Surgical Candidates

- Small hemorrhages < 10cc
- Minimal neurologic deficit
- Dominant-hemisphere hematomas near or involving eloquent cortical structures
- CAA patients
- History and CT morphology classic for BG or thalamic ICH
  - Exception: “young,” no co-morbidity, rapid neurologic decline, non-dominant hemisphere, no intra-ventricular extension and significant mass effect not due to hydrocephalus
- GCS < 4
  - Exception: cerebellar hemorrhage w/ brainstem compression

* ICP mgmt via ventriculostomy may be warranted in some non-surgical candidates*
“Take-Home” Message

Surgical Candidates

- Non-dominant hemisphere subcortical ICH meeting following criteria:
  - Age < 60 yrs
  - Minimal co-morbidity
  - Volume > 10cc
  - Significant mass effect on CT
  - GCS > 5

- Dominant hemisphere subcortical ICH not encroaching on eloquent cortex meeting above parameters or rapidly deteriorating young patient

- Cerebellar hemorrhage >3 cm, neurologically deteriorating w/ brain stem compression and hydrocephalus

- Timing of surgery important (within 4-12hrs of ictus)