Disclosures

• Commercial
  ❖ None

• Funding
  ❖ NIH funding for MRI related research in coma after cardiac arrest and intracerebral hemorrhage
Clinical Syndromes

A. Coma
B. Vegetative state
C. Brain death, end of life, organ donation
D. Hydrocephalus
E. Intracranial hypotension
F. Posterior reversible encephalopathy syndrome (PRES)
G. Spinal cord compression
H. Dysautonomia
I. Psychiatric emergencies
J. Intracranial hypertension
K. Herniation syndromes
What is coma?

• Absence of arousal - ARAS - brainstem / thalamus
• Absence of awareness - effective mental functioning – bilateral hemispheres
Classification and causes of coma

Table 1 Syllabus

- Structural
  - Unilateral hemisphere
  - Bilateral hemisphere
  - Brainstem and Cerebellum
- Metabolic-endocrine
- Diffuse brain dysfunction
<table>
<thead>
<tr>
<th>Structural causes</th>
<th>Metabolic-endocrine</th>
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<tr>
<td><em>Unilateral hemisphere</em></td>
<td>Hypo/Hyperglycemia</td>
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<tr>
<td>Intracerebral hemorrhage</td>
<td>Hypo/Hypernatremia</td>
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<tr>
<td>Subdural or epidural hematoma</td>
<td>Addison’s disease</td>
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<tr>
<td>Middle cerebral artery ischemic stroke</td>
<td>Hypercalcemia</td>
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<td>Cerebral venous thrombosis</td>
<td>Acute hypothyroidism</td>
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<td>Traumatic contusion</td>
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<td>Cerebral abscess</td>
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<td>Brain tumor</td>
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<td><em>Bilateral hemispheric</em></td>
<td>Hypercapnia</td>
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<tr>
<td>Subarachnoid hemorrhage</td>
<td>Diffuse brain dysfunction</td>
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<tr>
<td>Traumatic contusion</td>
<td>Generalized seizures</td>
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<tr>
<td>Anoxic-ischemic encephalopathy</td>
<td>Intoxication</td>
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<tr>
<td>Multiple cerebral infarcts</td>
<td>Hypothermia</td>
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<tr>
<td>Bilateral thalamic infarcts</td>
<td>Gas inhalation</td>
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<tr>
<td>Lymphoma</td>
<td>Acute catatonia</td>
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<td>Multiple cerebral metastasis</td>
<td>Malignant neuroleptic syndrome</td>
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<tr>
<td>Meningo-encephalitis</td>
<td>Psychogenic unresponsiveness</td>
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<td>Acute disseminated encephalomyelitis</td>
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<td>Cerebral edema</td>
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<td>Hydrocephalus</td>
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<tr>
<td>Posterior reversible encephalopathy syndrome</td>
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<tr>
<td>Air or fat embolism</td>
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<tr>
<td>Brainstem</td>
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<tr>
<td>Hemorrhage or infarction</td>
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<tr>
<td>Cerebral pontine myelinolysis</td>
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<tr>
<td><em>Cerebellum</em></td>
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<tr>
<td>Hemorrhage or infarction</td>
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<tr>
<td>Tumor</td>
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What is coma?

- Advanced brain failure
- Medical emergency
Emergent evaluation and treatment algorithm of coma

Figure 1 Syllabus
Figure 1. Emergent evaluation and treatment algorithm for comatose patients

Immediate stabilization of cardiopulmonary status and close monitoring of vital signs

Detailed history if possible

Rule out treatable toxic-metabolic causes

- Hypoglycemia/hyperglycemia
- Electrolyte abnormalities
- Hyperammonemia/renal failure
- Drug screen and blood gas

Use antidotes based on history and examination

- Opioids: Naloxone 0.2 – 4 mg I.V.
- Benzodiazepines: Flumazenil 0.2 – 3 mg I.V.
- Thiamine 100-500 mg with or preceding dextrose

Rule out neurological emergencies with focused neurological examination, a head CT and EEG

- Cerebral venous thrombosis
- Epidural and/or subdural hematomas
- Ischemic and/or hemorrhagic strokes
- Non-convulsive status epilepticus
- Meningitis/encephalitis
- Generalized hypoxia/anoxia

Further evaluation, which may include brain MRI, continuous EEG monitoring, endocrine studies, and lumbar puncture.
Emergent evaluation of coma

- General physical examination
- Neurologic examination
- Laboratory values
- Toxscreen
- PMH, Social history, Intoxications
- Imaging
Neurologic examination of the comatose patient

- Vital signs and breathing pattern
- Meningismus
- Level of consciousness
  - Glasgow Coma Scale (GCS) – EMV
  - Four score?
- Cranial nerve examination
- Motor examination - Posturing
Causes of coma

Structural – Unilateral hemisphere
61 year-old man with total R MCA infarct; patient progressed to coma 18 hours following symptom onset
CT - 31 hours after sx onset 50 yo woman
66 year old man w L sided weakness, transferred for management of “R MCA stroke.”

Add’l history: URI c/b possible pneumonia two weeks earlier, rx’d w oral abx. 3 days prior to transfer developed L facial droop, fatigue, increasing confusion. On exam also had L upper and lower extremity weakness.
FLAIR, DWI, ADC. Stroke???
Pattern of enhancement is NOT consistent with infarct (or tumor).

Dx: aggressive demyelination c/w ADEM (acute disseminated encephalomyelitis). Biopsy proven.
T1 WITHOUT CONTRAST
Contrast angiography
Causes of coma

Structural – Bilateral hemisphere
MRI diffusion weighted imaging
Multiple serpiginous hypodensities
Follow-up CT and MRI 4 days later

Wijman, Neurology 1998;51:318-9
MRI with DWI 3 days after symptom onset showed multiple bihemispheric, cortically based areas of restricted diffusion in a gyriform pattern.

MRI with DWI 6 hours after the CT showed multiple areas of restricted diffusion affecting predominantly cortical areas in bilateral hemispheres.
A chest CT angiogram showed no evidence of pulmonary embolism, but air in the right heart and right pulmonary artery.
Discussion
Cerebral Air Embolism

• Incidence unknown, **often not recognized**
• May occur at any time that air can enter the arterial or venous circulation (central lines, cathlab, surgical procedures in particular cardiothoracic surgery, positive pressure ventilation, chest trauma)
• Neurologic manifestations are non-specific: sudden altered consciousness, seizures, and stroke-like symptoms with focal deficits
Cerebral air embolism
Acute management

- Remove air source immediately
- Place the patient in a Trendelenberg position on his/her left side
- Endotracheal intubation
- Provide 100% oxygen
- Hyperbaric oxygen
Causes of coma

Structural – Brainstem and Cerebellum
What to do with those who look clinically good but have large (> 3 cm) hematoma with brainstem compression and/or hydrocephalus?
Cerebellar hemorrhage

• Non-randomized treatment series show
  – patients with small hemorrhages (<3 cm) do well with conservative Tx
  – patients with large (>3 cm) hemorrhages or with brainstem compression or hydrocephalus often have bad outcomes with conservative Tx alone, but may have good outcomes if operated on early
  – Once patients with large (>3cm) hemorrhages decline neurologically they do not do well with surgery
Surgical series: kobayashi 1993

Surgical treatment

Medical treatment
Surgical series: kobayashi 1993

GCS

15

13

10

5

G R | M D | S D, V | DEAD

Surgical treatment

Medical treatment
Surgical series: kobayashi 1993
Controversy
No randomized data available

But what to do with the patient with a great neurologic status but a high risk lesion, like our patient?

“C’mon, c’mon — it’s either one or the other.”
Neurologic deterioration

• Not uncommon
  – 75% (Ott et al 1974)
  – 46% (St. Louis et al 1998)
• Often rapid and unpredictable
• Has been associated with larger (>3 cm) hematomas, midline location, hydrocephalus, brainstem compression, upward herniation/effacement of quadrigeminal cisterns
Who is going to deteriorate?

- 72 pts. with spontaneous cerebellar hemorrhage
  - 56 initially alert patients (GCS 13-15)
  - 12 initially drowsy/stuporous patients (GCS 8-12)

- Assessed for
  - Decreasing level of consciousness
  - Evolution of new brainstem signs
  - Worsened motor response on the GCS

### Presenting features predictive of deterioration in 72 patients with cerebellar hemorrhage

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients with finding</th>
<th>Patients who deteriorated with finding</th>
<th>Odds ratio (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td>Absent</td>
<td>Not available</td>
<td>Present</td>
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<tr>
<td><strong>Clinical features</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Admission SBP &gt; 200</td>
<td>34 (47)</td>
<td>38 (53)</td>
<td>20 (59)</td>
<td>13 (34)</td>
</tr>
<tr>
<td>Absent/asymmetric CR</td>
<td>9 (13)</td>
<td>44 (61)</td>
<td>7 (78)</td>
<td>15 (34)</td>
</tr>
<tr>
<td>Abnormal OCR or EOM</td>
<td>23 (32)</td>
<td>45 (63)</td>
<td>14 (61)</td>
<td>16 (36)</td>
</tr>
<tr>
<td><strong>Neuroimaging features</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Hydrocephalus</td>
<td>30 (42)</td>
<td>37 (51)</td>
<td>23 (77)</td>
<td>7 (19)</td>
</tr>
<tr>
<td>Intraventricular hemorrhage</td>
<td>25 (35)</td>
<td>35 (49)</td>
<td>18 (72)</td>
<td>11 (31)</td>
</tr>
<tr>
<td>Involvement of the vermis</td>
<td>45 (63)</td>
<td>16 (22)</td>
<td>26 (58)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Upward herniation</td>
<td>12 (17)</td>
<td>22 (31)</td>
<td>38 (53)</td>
<td>10 (83)</td>
</tr>
<tr>
<td>Brainstem distortion</td>
<td>19 (26)</td>
<td>20 (28)</td>
<td>14 (74)</td>
<td>6 (30)</td>
</tr>
<tr>
<td>Fourth ventricular distortion</td>
<td>10 (14)</td>
<td>57 (79)</td>
<td>1 (10)</td>
<td>29 (51)</td>
</tr>
<tr>
<td>Size &gt; 3 cm</td>
<td>40 (56)</td>
<td>18 (25)</td>
<td>14 (19)</td>
<td>22 (55)</td>
</tr>
</tbody>
</table>
Why do patients deteriorate?

- Brainstem compression by direct mass effect
- Evolution of obstructive hydrocephalus from compression of the 4th ventricle
- Occlusion of the cerebral aqueduct
  - A secondary phenomenon accompanying upward herniation of vermian cerebellar tissue through the tentorial notch
What to do with those who look clinically good but have large (> 3 cm) hematoma with brainstem compression and/or hydrocephalus?
1. Cerebellar hemorrhage > 3cm with deterioration or brainstem compression and/or hydrocephalus (Class I, level B)
Causes of coma

Non-structural
Causes of coma

Non-structural – Diffuse brain dysfunction
non-convulsive status epilepticus
toxins
drugs
metabolic-endocrine
infections
hypothermia
hypercapnia
malignant neuroleptic syndrome, etc
Causes of coma
Post-operative patient
that may not be so obvious
Causes of coma
Post-operative patient that may not be so obvious
(because CT findings do not account for coma)

- Non-convulsive status epilepticus
- Wernicke’s encephalopathy
- Narcotic overdose
- Hypothyroidism
- Addison’s crisis
- Fat embolism
- Air embolism
(Behavioral) states that may be misdiagnosed as coma, but that are distinct clinical entities
(Behavioral) states that may be misdiagnosed as coma, but that are distinct clinical entities

- Persistent vegetative state
- Brain death
- Locked-in syndrome
- Akinetic mutism (extreme abulia)
- Psychogenic unresponsiveness
- Complete peripheral paralysis (ethyleen glycol, GBS, botulism)
Persistent Vegetative State
Case

22 yo woman found down at home in a comatose state
Non-contrast head CT
She develops a fever on hospital day 4 and a cardiac murmur is noted.
Mycotic aneurysm
Case

55 y/o woman with lupus found down at home in a comatose state
What is your differential diagnosis?

Non contrast head CT
MRI T1 weighted image, without contrast
The 2010 guidelines continue to recommend therapeutic hypothermia in these patients, now as Class I and Class IIB recommendations, respectively.
Outcome and at 6 months

Good outcome = live independently and work at least part-time at 6 months

NNT = 6 to avoid 1 unfavorable outcome
Good outcome = hospital discharge to home or rehabilitation facility

Bernard S. et al, NEJM 2002;346:557
Complications/side effects of systemic hypothermia

- **Shivering**
  - Sedation / Paralysis
- **Coagulopathies**
  - Thrombosis, thrombocytopenia, prolonged PT/PTT, decreased platelet and clotting factor function
- **Infections**
  - Pulmonary, systemic
- **Hemodynamic**
  - Hypotension, Bradycardia, VT, V Fib, CHF, Myocardial infarction
- **Metabolic / Systemic**
  - Hypokalemia, hyperglycemia, ileus, renal/hepatic dysfunction, pancreatitis
Adverse Event Rates

No statistically significant difference (p=0.09)

• 58 yo Female
• Recent History of Migraine Headaches
• No History of HTN
• Admission GCS 15, NIHSS 0

Highly Probably
Vascular Malformation
Highly Probable Reversible Vasoconstriction Syndrome
35 yr old F, post-partum, w L sided neglect and visual field defect.
RCVS

- Sudden onset “thunderclap” headache
  - Ischemic stroke or ICH may occur
- Vascular imaging: multifocal vasoconstriction
  - Improves with nifedipine
- F>M, associated with post-partum state
  - Also associated with SSRI’s, nasal decongestants, sympathomimetic drugs
- Need to distinguish from vasculitis or vasculopathy
Three different patients with the same diagnosis

Patient #1. Renal tubular acidosis
Patient #2. Liver transplant, weakness, confusion
Patient #3. Hyponatremia with correction. Confusion $\rightarrow$ coma and quadriparesis.

Trident-shaped; sparing of CST’s and ventrolateral pons; typically no enhancement.
Osmotic Myelinolysis

- Recognized for decades as complication of rapid correction of hypoNa\(^+\)
  - Variety of other associated conditions
    - EtOH, liver tx, AIDS, malnutrition, severe burns
- Classically affects pons (CPM), but also BG and capsules (EPM)
- Loss of myelin sheaths, relative sparing of axons and neurons
Case

66 y/o woman with fever, agitation and respiratory distress after hip replacement surgery

ORIF of left acetabular fracture with bone graft

Postoperatively, initially awake and extubated, but became over hours progressively confused/agitated, febrile, respiratory distress.
Head CT normal
Dx: fat embolization syndrome (the “starfield” pattern)
“Starfield pattern”
Fat Embolization Syndrome (FES)

- Can occur when fat enters the circulatory system
  - Usually due to surgery or trauma
  - Especially with long bone such as femur, or pelvis
- Usually small + multiple, WM > GM
  - Petechial hemorrhage common
- FES: 1-3 days post injury
  - Pulmonary (SOB, hypoxemia)
  - Neurological (agitation, delirium, coma)
  - Derm (rash)
Fat Embolism Syndrome
Pathophysiology

• Fat forced in venous system due to trauma leads to increased lipase ➔

• Increases SERUM FFAs ➔

• End organ injury (SIRS, complement system activation, DIC, ARDS)
Case

A 19 y/o woman underwent a liver and small bowel transplant for short gut syndrome.

In the past she had undergone bowel resection for a volvulus. Her liver failure was secondary to chronic use of TPN.
• Her postoperative course was complicated by gastric perforation with peritonitis requiring abdominal washout, high blood pressures (SBP 160 mmHg), high Prograf (tacrolimus) levels, and low platelets (54,000).

• On POD# 7 while intubated and sedated in the ICU, it was noted that her R pupil was fixed and dilated.
Emergent non-contrast head CT
Follow-up FLAIR MRI 6 weeks later
Reversible posterior leukoencephalopathy syndrome (RPLS/PRES)

Discussion

- 3 main groups of patients:
  - Hypertensive encephalopathy
  - Eclampsia
  - Immunosuppressant drugs / cytotoxic agents, relative hypertension, w/wo renal failure
Typical lesions are hyperintense on T2 and are hyperintense or isointense on DWI, with an increase of the ADC, indicating vasogenic edema.
The RPLS is not always reversible, not always posterior, and not always confined to the white matter.
Reversible posterior leucoencephalopathy syndrome
Treatment and Prognosis

• Blood pressure control to baseline blood pressures
• Substitution or reduction of immunosuppressant or cytotoxic agent
• ? Short term anti-epileptic drug (1-2 weeks)

• Clinical improvement starts in 24-48 hours, but imaging findings may take weeks to resolve
• If patients are left untreated irreversible brain injury may develop due to cerebral ischemia or hemorrhage.
Hemicraniectomy might be considered in patients with a “malignant” MCA infarction

- large MCA (+ACA/PCA) infarction with edema formation, midline shift, and clinical signs of herniation
- leading cause of death in the 1st week of stroke
  - Case fatality rate of 80% in ICU based series
- survivors often dependent
Management of space-occupying stroke
De compressed Surgery Goals

1. prevention of brain herniation
2. decrease ICP
3. increase CPP → prevention further ischemia
Pooled analysis of 3 RCT of early decompressive surgery in malignant MCA infarction (N=104)

Inclusion Criteria

- Age 18-60
- Complete MCA (+/- ACA or PCA)
- NIHSS > 15
- Surgery < 48 hours of symptom onset
- Drowsiness
- CT evidence of at least 50% of MCA territory infarct

Lancet Neurol 2007 Mar;6(3):200-
Pooled analysis of 3 RCT of early decompressive surgery in malignant MCA infarction (N=104)
Pooled analysis of 3 RCT of early decompressive surgery in malignant MCA infarction (N=104)

“In conclusion, decompressive surgery increases the probability of survival without increasing the number of very severely disabled survivors. Still, the decision to perform decompressive surgery should be made on an individual basis in every patient.”

Lancet Neurol 2007 Mar;6(3):200-1
“Paradoxical” Transtentorial Herniation Syndrome

- Complication of chronic large craniectomy
- Clinical hallmark: Neurological deterioration and a sunken skull defect in presence of a large craniectomy
- Presentation may be subacute over hours or days or more abrupt like in our case
- May occur spontaneously, but can be precipitated/aggravated by CSF drainage (LP or CSF shunt)
Paradoxical Transtentorial Herniation syndrome

**Pathophysiology**

- Intracranial contents are exposed to atmospheric pressure due to a large skull defect.
- CSF pressure opposes atmospheric pressure, preventing brain herniation.
- If CSF pressure decreases, brain contents will shift away from the craniotomy site resulting in subfalcine and transtentorial herniation.
Paradoxical Transtentorial Herniation Management

• Standard measures to lower ICP should be avoided!!
• Place patient supine or in Trendelenberg position
• Clamp CSF drain if present
• IV fluids, intrathecal fluids, epidural blood patch
• Cranioplasty is definitive therapy
In conclusion

• Coma is a medical emergency, life threatening condition

• Expeditiously rule out reversible and treatable causes.

• Use all available clinical information ESP if your imaging findings do not account for coma.