Stroke and Seizures in the ICU
Stroke

- Definition
- Imaging features to keep in mind
- When to TPA
- TPA protocol
- ICU management
Stroke

• TIA – transient ischemic attack
  • transient neurologic symptoms without evidence of acute infarction
  • ~10% will have stroke at 90days; ~20x the risk without having had a TIA
  • Should get urgent work-up for stroke and risk factors

• Stroke (cerebral vascular accident – CVA)
  • Neuronal death from decreased blood flow
    • Ischemic –
      • Embolic – major arteries
      • Thrombotic – basilar perforators
    • Hemorrhagic
      • Hypertensive or vascular rupture
      • Hemorrhagic conversion of ischemic

• Other intracranial events to consider
  • SAH – subarachnoid hemorrhage
    • Cerebral aneurysms vs. traumatic
  • SDH – subdural hematoma
    • Usually from trauma

Case courtesy of Dr. David Cuete, Radiopaedia.org
Evaluation of suspected stroke.

Table 8. Immediate Diagnostic Studies: Evaluation of a Patient With Suspected Acute Ischemic Stroke

<table>
<thead>
<tr>
<th>Test采矿内容</th>
<th>T</th>
<th>列表类型</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noncontrast brain CT or brain MRI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood glucose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxygen saturation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum electrolytes/renal function tests*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete blood count, including platelet count*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Markers of cardiac ischemia*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prothrombin time/INR*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Activated partial thromboplastin time*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECG*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selected patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TT and/or ECT if it is suspected the patient is taking direct thrombin inhibitors or direct factor Xa inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatic function tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toxicology screen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood alcohol level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterial blood gas tests (if hypoxia is suspected)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest radiography (if lung disease is suspected)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumbar puncture (if subarachnoid hemorrhage is suspected and CT scan is negative for blood</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electroencephalogram (if seizures are suspected)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CT indicates computed tomography; ECG, electrocardiogram; ECT, ecarin clotting time; INR, international normalized ratio; MRI, magnetic resonance imaging; and TT, thrombin time.
Differential of stroke:

Table 6. Features of Clinical Situations Mimicking Stroke

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychogenic</td>
<td>Lack of objective cranial nerve findings, neurological findings in a nonvascular distribution, inconsistent examination</td>
</tr>
<tr>
<td>Seizures</td>
<td>History of seizures, witnessed seizure activity, postictal period</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>History of diabetes, low serum glucose, decreased level of consciousness</td>
</tr>
<tr>
<td>Migraine with aura (complicated migraine)</td>
<td>History of similar events, preceding aura, headache</td>
</tr>
<tr>
<td>Hypertensive encephalopathy</td>
<td>Headache, delirium, significant hypertension, cortical blindness, cerebral edema, seizure</td>
</tr>
<tr>
<td>Wernicke’s encephalopathy</td>
<td>History of alcohol abuse, ataxia, ophthalmoplegia, confusion</td>
</tr>
<tr>
<td>CNS abscess</td>
<td>History of drug abuse, endocarditis, medical device implant with fever</td>
</tr>
<tr>
<td>CNS tumor</td>
<td>Gradual progression of symptoms, other primary malignancy, seizure at onset</td>
</tr>
<tr>
<td>Drug toxicity</td>
<td>Lithium, phenytoin, carbamazepine</td>
</tr>
</tbody>
</table>

CNS indicates central nervous system.
It is important to recognize the imaging features that differentiate ischemic from hemorrhagic stroke, particularly in the acute phase when these features will help determine whether the patient gets reperfusion therapy with tissue plasminogen activator (TPA).

Imaging features of acute to chronic ischemic stroke. (Radiopedia.org)

Hemorrhagic stroke Non-contrast CT

https://youtu.be/Rb2YPGwwing

Case courtesy of Dr. Rahmoun Fateh, Radiopaedia.org
Stroke management

- ABCs
- Cardiac monitoring (also monitor for arrhythmias like paroxysmal atrial fibrillation that could cause embolism)
- BP control
  - No benefit of immediate blood pressure reduction in acute ischemic stroke (He J et al. JAMA 2014)
  - In hemorrhagic stroke – goal SBP<180; but a goal to <140 may improve physical functioning (Anderson CS NEJM 2013)
  - If patient has new neurologic symptoms with relative hypotension, may need to place on pressors to maintain a MAP high enough to resolve these symptoms
  - Special consideration in patients who could get rtPA (next slide)
- Airway support or ventilation for:
  - Decreased consciousness
  - Bulbar dysfunction
- O2 to keep Sat>94%
- Avoid hypovolemia
- Maintain normoglycemia (140-180mg/dL)

rtPA – recombinant tissue plasminogen activator

• Intravenous rtPA (0.9 mg/kg, maximum dose 90mg) is recommended for selected patients who may be treated within 3 hours of onset of ischemic stroke
  • Up to 4.5 hours unless age >80, NIHSS>25, taking oral anticoagulant, or hx of both diabetes and prior ischemic stroke
• Consider BP goals from Table 9.
• Review exclusion criteria: next slide

Exclusion criteria of considering rtPA:

Exclusion criteria

- Significant head trauma or prior stroke in previous 3 months
- Symptoms suggest subarachnoid hemorrhage
- Arterial puncture at noncompressible site in previous 7 days
- History of previous intracranial hemorrhage
- Intracranial neoplasm, arteriovenous malformation, or aneurysm
- Recent intracranial or intraspinal surgery
- Elevated blood pressure (systolic >185 mmHg or diastolic >110 mmHg)
- Active internal bleeding
- Acute bleeding diathesis, including but not limited to
  - Platelet count <100,000/mm³
  - Heparin received within 48 hours, resulting in abnormally elevated aPTT greater than the upper limit of normal
  - Current use of anticoagulant with INR >1.7 or PT >15 seconds
  - Current use of direct thrombin inhibitors or direct factor Xa inhibitors with elevated sensitive laboratory tests (such as aPTT, INR, platelet count, and ECT; TT; or appropriate factor Xa activity assays)
  - Blood glucose concentration <50 mg/dL (2.7 mmol/L)
  - CT demonstrates multilobar infarction (hypodensity >1/3 cerebral hemisphere)

Relative exclusion criteria

- Recent experience suggests that under some circumstances—with careful consideration and weighting of risk to benefit—patients may receive fibrinolytic therapy despite 1 or more relative contraindications. Consider risk to benefit of IV rtPA administration carefully if any of these relative contraindications are present:
  - Only minor or rapidly improving stroke symptoms (clearing spontaneously)
  - Pregnancy
  - Seizure at onset with postictal residual neurological impairments
  - Major surgery or serious trauma within previous 14 days
  - Recent gastrointestinal or urinary tract hemorrhage (within previous 21 days)
  - Recent acute myocardial infarction (within previous 3 months)

rtPA protocol

• Infuse 0.9 mg/kg (maximum dose 90 mg) over 60 minutes, with 10% of the dose given as a bolus over 1 minute.

• **Admit to ICU.**

• Discontinue the infusion and obtain emergent CT scan if:
  • severe headache, acute hypertension, nausea, or vomiting or has a worsening neurological examination

• BP and Neurocheck q15 min during and after IV rtPA infusion for 2 hours, then q30 min for 6 hours, then q1 hour x24 hours after IV rtPA treatment.

• Increase the frequency of blood pressure measurements if systolic blood pressure is >180 mm Hg or if diastolic blood pressure is >105 mm Hg; administer antihypertensive medications to maintain blood pressure at or below these levels (Table 9).

• Delay placement:
  • nasogastric tubes, indwelling bladder catheters, or a-lines if patient can be managed without

• Obtain a follow-up CT or MRI scan at 24 hours after IV rtPA before starting anticoagulants or antiplatelet agents.
Other management issues

• DVT prophylaxis in those who can

• Large infarcts are at risk for severe edema and increased ICP
  • Transfer to ICU and center with neurosurgical interventions
  • Frank hypodensity on head CT within the first 6 hours, involvement of one third or more of the MCA territory, and early midline shift are CT findings that are useful in predicting cerebral edema
  • Neurosurgical consultation

• Assess swallowing before taking PO

• Stroke work-up in general
  • ECHO, carotid dopplers, ecg monitoring, etc.
SAH – subarachnoid hemorrhage

• Diagnosis:
  • CT head for sudden onset or severe headache
  • If CT head non-diagnostic → LP

• Nimodipine should be administered to all

• SBP<160mmHg with invasive monitoring and titratable meds

• Aggressive targeting of normothermia

• Vasospasm and Delayed cerebral ischemia complications
  • Nimodipine
  • Maintain blood volume to prevent
  • Hypertension to treat?

• Symptomatic hydrocephalus should be treated with CSF diversion (type determined by clinical scenario)
Status epilepticus / Seizure

- Definition
- Differential Diagnosis
- Diagnostic work-up
- Management
- Meds

https://www.healthtap.com/user_questions/530528
Definition

• Status Epilepticus
  • A **clinical** or **electrographic** seizure lasting for 5 minutes or longer
  • or **recurrent** seizure activity without recover between seizures

• Subtypes:
  • Convulsive status epilepticus
    • Generalized tonic-clonic movements, mental status impairment, focal deficits post-ictal
  • Non-convulsive
    • Acutely ill with altered mental status without muscle movements

• Refractory status epilepticus
  • Patients who do not respond to standard treatment – would get neurology involved

Brophy GM Neurocrit Care 2012
Rapid seizure control is important

**Mortality Associated with Prolonged Seizures and Status Epilepticus**

<table>
<thead>
<tr>
<th>DURATION</th>
<th>STAGE</th>
<th>%</th>
<th>INTERVENTIONS</th>
<th>SETTING</th>
<th>MORTALITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2 min</td>
<td>Seizure</td>
<td>100%</td>
<td>Supportive measures</td>
<td>Community</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>&gt;2 min</td>
<td>Prolonged</td>
<td>10%</td>
<td>Benzodiazepine</td>
<td>Com/Amb/ER</td>
<td>&lt;5%</td>
</tr>
</tbody>
</table>
| >30 min  | SE          | 5-7%| 1st line: Benzodiazepine  
2nd line: Fosphenytoin/Phenytoin  
3rd line: Phenobarbital/Valproate/Levetiracetam | ER            | 10-20%    |
| 2 hours  | RSE         | 1-2%| Continuous Infusion therapy  
Midazolam/Propofol/Pentobarbital | ICU           | 40%       |
| >48 hours| HRSE        | <1% | Alternative Continuous Infusion Therapy  
Novel Therapeutic Options | ICU           | >60%      |
Differential Diagnosis

- Acute processes
  - Metabolic disturbances: electrolyte abnormalities, hypoglycemia, renal failure
  - Sepsis
  - Central nervous system infection: meningitis, encephalitis, abscess
  - Stroke: ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, cerebral sinus thrombosis
  - Head trauma with or without epidural or subdural hematoma
  - Drug issues
    - Drug toxicity
    - Withdrawal from opioid, benzodiazepine, barbiturate, or alcohol
    - Non-compliance with AEDs
  - Hypoxia, cardiac arrest
  - Hypertensive encephalopathy, posterior reversible encephalopathy syndrome
  - Autoimmune encephalitis (i.e., anti-NMDA receptor antibodies, anti-VGKC complex antibodies), paraneoplastic syndromes

- Chronic processes
  - Preexisting epilepsy: breakthrough seizures or discontinuation of AEDs
  - Chronic ethanol abuse in setting of ethanol intoxication or withdrawal
  - CNS tumors
  - Remote CNS pathology (e.g., stroke, abscess, TBI, cortical dysplasia)
  - Special considerations in children
    - Acute symptomatic SE is more frequent in younger children with SE
    - Prolonged febrile seizures are the most frequent cause of SE in children
    - CNS infections, especially bacterial meningitis, inborn errors of metabolism, and ingestion are frequent causes of SE

Brophy GM Neurocrit Care 2012
Diagnostic Work-up

• Complete ASAP and simultaneously with management and treatment
• All patients
  1. Fingerstick glucose
  2. Vital signs.
  3. Head computed tomography (CT) scan (appropriate for most cases)
  4. Order laboratory test: blood glucose, complete blood count, basic metabolic panel, calcium (total and ionized), magnesium, AED levels.
  5. Continuous electroencephalograph (EEG) monitoring
• Consider based on clinical presentation
  1. Brain magnetic resonance imaging (MRI)
  2. Lumbar puncture (LP)
  3. Comprehensive toxicology panel including toxins that frequently cause seizures (i.e. isoniazid, tricyclic antidepressants, theophylline, cocaine, sympathomimetics, alcohol, organophosphates, and cyclosporine)
  4. Other laboratory tests: liver function tests, serial troponins, type and hold, coagulation studies, arterial blood gas, AED levels, toxicology screen (urine and blood), and inborn errors of metabolism
Management

• ABCs
  • Airway – open and protect airway (head positioning – do not put fingers in mouth); may need intubated
  • Breathing – administer O2
  • Circulation – may need vasopressor support if hypotensive

• Monitor Vitals

• IV access
  • Emergent AED – benzos (within 5 minutes)
  • Fluids
    • Thiamine → glucose if needed

• Urgent control AEDs – Phenytoin vs Levetiracetam

• Urinary catheter

• Cont EEG

• Further diagnostic testing
  • CT, MRI, ?LP

• Possibly intracranial pressure monitoring – depending on situations
Meds

• Emergent AEDs
  • 1st line: Ativan or midazolam (preferred if IM)
  • Other options: Propofol (if intubated), diazepam (preferred if rectal is the only route)

• Control AEDs
  • First line in SE:
    • Phenytoin: 20mg/kg loading – hypotension, bradycardia, arrhythmia
      • (fosphenytoin – more soluble, may have less acute side effects)
    • Levetiracetam: 20mg/kg loading
  • Other options
    • Carbamazepine
    • Valproate
    • Phenobarbital
    • Lamotrigine
    • Topiramate

Brophy GM Neurocrit Care 2012; Chakravarthi S J Clin Neurosci 2015
Take home points

• Change in neurologic status concerning for stroke or seizure should be evaluated early on with a head CT
• Differentiate ischemic from hemorrhagic stroke
• rtPA for ischemic stroke within 3 hours of onset (4.5 hours in some circumstances)
• Status epilepticus should be evaluated and treated immediately and simultaneously
• Stop seizures as soon as possible - Benzodiazepams for seizures within minutes