Evaluation & Emergent Treatment of Patients with “Stroke-Like Symptoms”

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Disclosures

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Has no relationships with any entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on patients.
Objectives

1. Discuss differential diagnoses
2. Discuss who should be admitted and who can be safely discharged
3. Review indications & contraindications for rtPA
4. Discuss updates in role of rtPA & other early therapies
Immediate Management Goals

1. Ensure medical stability.
2. Quickly reverse any conditions that are contributing to the patient’s problem.
3. Screen for potential contraindications to thrombolysis in acute ischemic stroke patients.
4. Move toward uncovering the pathophysiologic basis to the patient’s neurologic symptoms.
5. Reduce risk for recurrent stroke.
Stroke vs. TIA

**Stroke:**
- Sudden loss of focal brain function resulting from death of brain tissue.

**Transient Ischemic Attack:**
- Sudden loss of brain function resulting from transient impaired cerebral perfusion that does not result in permanent brain injury, usually limited to 2 hours.
Burden of Stroke

- 4\textsuperscript{th} leading cause of death in US (175,000)
- 2\textsuperscript{nd} leading cause of death worldwide
- 795,000 new strokes each yr; 185,000 recurrent strokes
- 3\% of the US adult population has had a stroke (7 M)
- Main cause of disability
  - ¼ are institutionalized, 70\% are unable to resume usual activities
- $34\text{ Billion}$ in direct costs annually
- Affects minorities disproportionately

Question 1

A 33-year-old woman is evaluated in the ED for paresthesias that began in the left face and spread over 30 minutes to the left arm and leg, clumsiness of the left hand that began 30 minutes ago, and an emerging right-sided throbbing headache. She is otherwise healthy but has a family history of migraine. Her only medication is a daily OCP.

On exam, temp is normal, BP is 140/82, pulse is 110/min, and respiration rate is 20/min. All other exam findings are normal. Results of laboratory studies and a CT scan of the head are also normal.
Question 1

Which of the following is the most likely diagnosis?
A. Migraine with aura
B. Multiple sclerosis
C. Sensory seizure
D. Transient ischemic attack
Differential Diagnoses

Differential for transient focal neurologic deficit

- Stroke/TIA
- Seizure
- Complicated migraine
- Hypoglycemia
- Psychiatric
- Toxins/Drugs
- Benign Positional Vertigo
- Bell’s Palsy
- Delirium
Differential for transient focal neurologic deficit

- Stroke/TIA
- Seizure
  - Postictal drowsiness or confusion with variable degrees of hemiparesis/dysphagia
- Complicated migraine
- Hypoglycemia
- Psychiatric
- Toxins/Drugs
- Benign Positional Vertigo
- Bell’s Palsy
- Delirium
Differential Diagnoses

Differential for transient focal neurologic deficit

- Stroke/TIA
- Seizure
- Complicated migraine
  - Headache with contralateral numbness +/- paresis of face > arm > leg
  - More common in young women
- Hypoglycemia
- Psychiatric
- Toxins/Drugs
- Benign Positional Vertigo
- Bell’s Palsy
- Delirium
Differential Diagnoses

Differential for transient focal neurologic deficit

- Stroke/TIA
- Seizure
- Complicated migraine
- Hypoglycemia
  - Dysarthria, confusion, weakness, decreased LOC
- Psychiatric
- Toxins/Drugs
- Benign Positional Vertigo
- Bell’s Palsy
- Delirium
Differential for transient focal neurologic deficit

- Stroke/TIA
- Seizure
- Complicated migraine
- Hypoglycemia
- Psychiatric
  - Variable and inconsistent physical findings in a younger adult
  - Bizarre pattern of symptoms which do not conform to neuro-anatomy
- Toxins/Drugs
- Benign Positional Vertigo
- Bell’s Palsy
- Delirium
Differential for transient focal neurologic deficit

- Stroke/TIA
- Seizure
- Complicated migraine
- Hypoglycemia
- Psychiatric
- Toxins/Drugs
  - Nystagmus & ataxia with EtOH
  - TCAs, Lithium, & anticonvulsant overdoses
- Benign Positional Vertigo
- Bell’s Palsy
- Delirium
Differential Diagnoses

Differential for transient focal neurologic deficit

- Stroke/TIA
- Seizure
- Complicated migraine
- Hypoglycemia
- Psychiatric
- Toxins/Drugs
- Benign Positional Vertigo
  - May be triggered by sudden movements of the head
  - Nystagmus
- Bell’s Palsy
- Delirium
Differential for transient focal neurologic deficit

- Stroke/TIA
- Seizure
- Complicated migraine
- Hypoglycemia
- Psychiatric
- Toxins/Drugs
- Benign Positional Vertigo
- Bell’s Palsy
- Delirium
An 82-year-old man is evaluated in the office for an episode of hesitancy in speech, word-finding difficulty, right facial droop, and weakness and awkwardness of the right hand and arm. The episode occurred early yesterday, lasted 20 minutes, and was witnessed by his wife. The patient has a history of CAD, HTN, and hyperlipidemia. Current medications are metoprolol, aspirin, & lovastatin. On exam, temp is normal, BP is 148/88, pulse is 70/min. Neuro exam reveals no abnormalities.
Question 2

Which of the following is the most appropriate next step in management?

A. Add clopidogrel
B. Admit to the hospital
C. Order outpatient diagnostic studies
D. Schedule a follow-up visit in 1 week
Who should be admitted?

Risk of future stroke after TIA:

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<tr>
<th>ABCD² Score</th>
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2-day risk of stroke

- 6-7 points: 8.1% (high risk)
- 4-5 points: 4.1% (moderate-risk)
- 0-3 points: 1% (low risk)
Who should be admitted?

Aggressive Therapy for TIA

1. SOS-TIA Trial
   - 1,085 pts with TIA admitted to a 24-hr center
   - All treated with standard therapy
   - 74% discharged on same day, stroke risk reduced 80% from ABCD² prediction.

2. EXPRESS Study
   - 80% reduction in risk with urgent TIA clinic visit vs. usual PCP visit in 1,278 pts

Lavallee, PC; et al: Lancet Neurology 2007; 6:953
Who should be admitted?

Aggressive Therapy for TIA

- Patients with TIA require urgent evaluation and treatment (<24-48 hrs).
- Some advocate admitting if ABCD² > 3.
- Admitting all of these pts makes sense unless you have a system of rapid outpatient evaluation.
An 88-year-old woman is evaluated in the ED 1 hour after the acute onset of language disturbance and right-sided weakness. The family members who witnessed the onset say that the symptoms progressed over a few minutes and that there were accompanying symptoms of nausea and vomiting; they describe the patient holding her head as if in pain. She has a 20-year history of hypertension; her only medication is lisinopril.

During the exam, the patient becomes increasingly difficult to arouse and vomits repeatedly. She is afebrile, BP is 220/110, pulse is 110/min. There is no nuchal rigidity. Carotid upstrokes are normal; there are no bruits and no jugular venous distention. Other than tachycardia, the cardiopulmonary exam is unremarkable. Global aphasia and right hemiplegia are noted.
Question 3

On the basis of her preliminary clinical evaluation, which of the following is the most likely diagnosis?

A. Intracerebral hemorrhage
B. Ischemic stroke
C. Meningitis
D. Transient ischemic attack
Classification of Stroke

Stroke

Ischemic (80%)
- Embolic (75%)
  - Rapid/sudden onset
- Thrombotic (25%)
  - Stuttering/progressive sx

Hemorrhagic (20%)
- ICH (90%)
  - ↓LOC, +Emesis
- SAH (10%)
  - HA, N/V, ↓LOC
Symptoms often present upon presentation in acute stroke

<table>
<thead>
<tr>
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<th>Focal Deficit</th>
<th>Severe Headache</th>
<th>Altered Consciousness</th>
</tr>
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<tbody>
<tr>
<td>Infarct</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subarachnoid Hemorrahge</td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Parenchymal Hemorrhage</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
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Accurate ≥90%; useful in quickly triaging patients for thrombolysis. (i.e., do not give thrombolytics to a patient with a severe HA or loss of consciousness even when the CT does not show any evidence of blood.)
Hemorrhagic Stroke (ICH)
Ischemic Stroke (thrombotic)
Ischemic Stroke (embolic)
Hemorrhagic Stroke (ICH + SAH)
Brain Metastasis
Acute Stroke

Initial Evaluation:

• Use H&P to uncover cause of “sudden loss of brain function”
• Ddx:
  – Stroke/TIA
  – Seizure
  – Migraine
  – Hypoglycemia

• History:
  – ? Insulin
  – DM meds
  – h/o sz d/o
  – h/o cancer
  – Medications
  – Recent trauma

• Physical:
  – Head – ? trauma or tongue lac
  – Neck – ? bruits
  – Palpate pulses – ? Absence, asymmetry, irregular
  – Ascultate heart - ? Murmurs
  – Skin – ? Signs of IE, cholesterol emboli, purpura
  – LE – ? signs of DVT
Acute Stroke

Initial Evaluation:

- Non-contrast brain CT
- EKG
- CBC
- Cardiac biomarkers
- Lytes, BUN, creatinine
- Serum glucose
- PT/INR
- PTT
- Oxygen saturation

- LFTs**
- Toxicology**
- EtOH level**
- β-hCG**
- ABG**
- LP**
- EEG**

** may be useful on case-by-case basis
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<th>Treatment</th>
<th>Evidence</th>
<th>Summary</th>
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<tr>
<td>0 – 3 hrs</td>
<td>IV-tPA</td>
<td>IA</td>
<td>Proven Approved</td>
</tr>
<tr>
<td>3 – 4.5 hrs</td>
<td>IV-tPA</td>
<td>IB</td>
<td>Proven Unapproved</td>
</tr>
<tr>
<td>0 – 6 hrs</td>
<td>IA-tPA</td>
<td>IB</td>
<td>Proven Unapproved</td>
</tr>
<tr>
<td>0 – 8 hrs</td>
<td>Mechanical Embolectomy</td>
<td>IIA</td>
<td>Unproven Approved</td>
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<tr>
<td>&gt; 8 hrs</td>
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IV-rtPA in Acute Stroke

Pivotal IV tPA NINDS trial (0-3 hrs)

- 30% increase in minimal or no disability at 90 days
- Symptomatic hemorrhage risk increased 0.6 – 6.4%; half were serious or fatal
- No change in mortality
- Multiple recent studies confirm this result in diverse settings

THE EARLIER THE BETTER!!!

IV-rtPA in Acute Stroke

ECASS III Trial (3-4.5 hrs)
- 821 pts randomized to tPA vs placebo
- Median time: 3 hrs 59 min
- Favorable outcome: 52% vs 45%, p=0.04
- Symptomatic ICH: 2.4% vs 0.2%, p=0.008
- No mortality difference

THE EARLIER THE BETTER!!!

IV-rtPA in Acute Stroke

The Safe Implementation of Treatments in Stroke – SITS-ISTR (3-4.5 hrs)

## IV-rtPA in Acute Stroke

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<th>NINDS (0 – 3 h)</th>
<th>ECASS III (3 – 4.5 h)</th>
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<tbody>
<tr>
<td>Benefit/100</td>
<td>32.3</td>
<td>16.4</td>
</tr>
<tr>
<td>Harm/100</td>
<td>3.3</td>
<td>2.7</td>
</tr>
<tr>
<td>Net Benefit/100</td>
<td>29</td>
<td>13.7</td>
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<tr>
<td>Rate of Sx ICH</td>
<td>6.4%</td>
<td>7.9%</td>
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**Inclusion:**
- Stroke with measureable deficit
- < 4.5 hrs onset
- No spontaneous improvement
- Not minor deficit
- CT without hemorrhage
- CT hypodensity ≤ ⅓ hemisphere
- BP < 185/110
- Glucose ≥ 50
- Platlets ≥ 100,000
- INR ≤ 1.7
- PTT in normal range

**Exclusion:**
- Active systemic bleeding
- Prior ICH
- Trauma < 3 months
- Stroke < 3 months
- GI/GU hemorrhage < 21 days
- Surgery < 14 days
- Seizure with postictal state

**Exclusion 3-4.5 hrs:**
- Age > 80
- NIHSS > 25
- Combination of previous stroke and diabetes
- Oral anticoagulant treatment
Timing of Recanalization

70% of those that recanalize with rtPA do so in the first hour

Recanalization

- 43% within < 1 hr
- 11% within 1-2 hr
- 7% within 2-6 hr
- 39% no recanalization

179 cases with MCA occlusion < 3 h, IV rtPA + 2 h TCD

Odds Ratio for recanalization with IV rtPA

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<tr>
<td>1 – 1.5</td>
<td>2.8</td>
<td>&lt; 0.0001</td>
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<td>1.4</td>
<td>&lt; 0.02</td>
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<tr>
<td>4.5 – 6</td>
<td>1.2</td>
<td>&lt; 0.26</td>
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For non IV rtPA candidates or for those who do not improve with IV rtPA, advanced neuroimaging can select patients that may benefit from endovascular approaches.
**Synthesis Trial**

- IV rtPA vs. IA thrombectomy (n=362)
- No difference in 90 d outcome free of disability (mRS ≤1)
- Time to Rx 2.75 & 3.75 h
- Similar rate of hemorrhage
- Limitations: stent retrievers used rarely

Ciccone et al. NEJM, 2013; 368:904-913.
Rescue Endovascular Tx

IMS 3 Trial
- IV rtPA +/- IA thrombectomy
- n=656
- No difference in 90 d functional independence (mRS ≤2)
- No subgroup benefitted
- No safety concerns
- Limitations: time to IA 4 h; stent retrievers used rarely

Conditions that may mimic acute stroke or TIA

- Seizure
- Complicated migraine
- Hypoglycemia
- Psychiatric
- Toxins/Drugs
- Benign Positional Vertigo
- Bell’s Palsy
- Delirium
## Summary

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### 2-day risk of stroke

- **6-7 points**: 8.1% (high risk)
- **4-5 points**: 4.1% (moderate-risk)
- **0-3 points**: 1% (low risk)
Rapid assessment is crucial for patients with acute neurological symptoms suggestive of stroke because the opportunity for a positive outcome from rtPA diminishes rapidly within the first few hours.

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