Ischemic Stroke and TIA: Mimics and Management

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Disclosures and Relationships

No Conflicts

American Stroke Association
Quality Speakers Bureau
Western/Pacific Region

National Stroke Association
Course Director
Improving In-hospital Stroke Through QI Interventions

Colorado Stroke Alliance
Research Collaboration

Objectives

1. Recognize common conditions which can mimic acute stroke

2. Understand consequences of treating a stroke mimic with tPA

3. Identify appropriate means to manage co-morbid illness in the stroke patient
   - Hyperglycemia
   - Hyperlipidemia
   - Hypertension
Case
- A 55 year old female with HTN and DM II arrives at the Emergency room 20 minutes after onset of trouble speaking and loss of sight in the left visual field
- Symptoms started with a bright light in the left peripheral vision
  - Progression to vision loss on left side
  - 5 minutes later she began having slurred speech and difficulty finding words
  - Now starting to develop a left sided headache and nausea
  - Similar but less severe symptoms 4 times over last 20 years
- No other significant medical history or medications
- Exam confirms left visual field cut and dysarthria.
  - No motor or sensory deficits
  - NIH Stroke Scale Score of 2
- Should the ED call a Stroke Alert?

Neurologic
Chief Complaint
in 911 call
90% will not be strokes
ED Stroke Alerts
For Suspected Stroke
20% will not be strokes
ED Physician
Final Diagnosis
of Stroke
9% will not be strokes
Patient Treated
With Thrombolysis

Patient Treated
With Thrombolysis

Hand PJ. Distinguishing Between Stroke and Mimic at the Bedside. Stroke 2006;37:769-775
Ferro JM. Diagnosis of Stroke by the Non-neurologist. Stroke 1998;29:1106-9
Mimics
Common >10%
- Systemic infection
- Brain tumors
- Toxic/Metabolic
  - Hypoglycemia
  - Hyponatremia
- Complex migraine
- Seizure with post-ictal phenomena

Mimics
Less Common < 10%
- Conversion disorder
- Vestibular dysfunction
- Cardiac
- Hypotension/Syncope
- Trauma
- Subdural hematoma
- Herpes encephalitis
- Transient global amnesia
- Dementia/Acute confusion
- Acute mono-neuropathy
- Demyelinating disease
- Spinal cord injury or lesion
- Myasthenia Gravis
- Parkinsonism
- Hypertensive encephalopathy

Case Continued
- Stroke Alert was called
- Vital signs normal
- Initial labs unremarkable
  - Chem 7
  - CBC
  - Coagulation panel
- EKG normal sinus rhythm
- Non-contrast head CT negative
- Would you administer thrombolysis?
Stroke Mimics Treated With Thrombolysis?

- 3-14% of pts treated with tPA are actually stroke mimics
- Three diagnoses:
  1. Complex Migraine
  2. Seizure
  3. Conversion disorder
- Global aphasia most common symptom of mimics

Get to Know a Mimic
#1 Complex Migraine

- Transient neurologic phenomena “aura”
  - Occur in a quarter of migraineurs
    - Visual changes “fortifications”
    - Scintillations, Scotoma, loss of vision
    - Numbness
    - Weakness (Hemiplegic migraine)
    - Aphasia or mutism

I was playing in the garden when a brilliant, shimmering light appeared to my left — dazzlingly bright, almost as bright as the sun. It expanded, becoming an enormous shimmering semicircle stretching from the ground to the sky, with sharp zigzagging borders and brilliant blue and orange colors. Then, behind the brightness, came a blindness, an emptiness in my field of vision, and soon I could see almost nothing on my left side.

Oliver Sacks M.D.
Distinguishing Migraine from CVA

- History of Migraine
  - Migraine neurologic deficits have a slow migratory or spreading pattern
    - CVA symptoms tend to be abrupt
  - Neurologic aura deficits occur sequentially
  - Biphasic pattern
    - Positive symptoms first followed by negative symptoms
  - Symptoms tend to resolve over 20-60 min

Hemiplegic Migraine Unfortunately Does not Follow These Rules

Get to Know a Mimic

#2 Seizure with Post-ictal Paresis

- Described by Todd in 1849
- Transient post-seizure neurologic deficits reported in 6-40% of seizure patients
- Median duration of post-ictal paresis only 3 minutes and vast majority have resolved within an hour
- Prior theory of “Neuronal Exhaustion”
- Modern theory of “Active Inhibition”

Distinguishing Post-ictal Paresis from Stroke

- Pre-existing epilepsy should raise suspicion of post-ictal paresis
- Distinction made difficult by shared risk factors
  - Prior stroke can be a seizure focus
  - Most common cause of epilepsy in the elderly is stroke
- Early seizure can also complicate acute stroke
  - 2-5% of stroke pts have a seizure at onset of ischemia
- Seizure prior to onset of symptoms suggests post-ictal paresis
  - Used as an exclusion criteria in original thrombolytic NINDS trial
Get to Know a Mimic

#3 Conversion Disorder
- Psychiatric condition manifesting with transient motor or sensory deficits
  - Hemiplegia
  - Paralysis
  - Blindness
  - Diplopia
  - Aphonia
  - Others

- Manifestation of major emotional stress
  - Not the same as factitious disorder or malingering

- Can look VERY convincingly like stroke

Distinguishing Conversion Disorder from Stroke
- Give-way weakness
  - May be unreliable as this is "seen" in 30% of organic neurologic disease

- "La belle indifférence"
  - Unreliable in differentiating conversion from organic disease

- "Hoover sign"
  - Involuntary extension of a pseudo-paralyzed leg when the ‘good leg’ is flexing against resistance

- Neurologic deficits which do not match vascular distribution
  - Can mislead with multiple infarcts or entities such as dural venous sinus thrombosis

- Inconsistency in exam

- "Teddy Bear Sign"??

What Happens if Mimic is Treated with Thrombolysis?
- Stroke patients receiving tPA had some complication in 19% of cases
  - 5% symptomatic ICH
  - 12% asymptomatic ICH
  - 1% angioedema

- None of the stroke mimics had symptomatic ICH
  - Overall prognosis much better for stroke mimics
CASE CONTINUES
- 10 years later your patient, now 65 years old re-presents with
  - Sudden onset right sided weakness
  - Numbness of the right arm, leg, and face
  - Difficulty forming sentences
- Unfortunately she waits 5 hours before coming in to the hospital
  - BP 195/110
  - Blood glucose 240
  - LDL 102
- How do we manage her co-morbidities?

CO-MORBIDITIES
- Hyperglycemia
  - Sugar
- Hypertension
  - Salt
- Hyperlipidemia
  - Loco Moco Burger

Hyperglycemia
- Common on presentation with stroke
  - Seen in 1/3 of admissions
- Associated with bad outcome
  - Larger infarctions
  - More disability
  - Increased mortality
- Is this causation or correlation
  - Stress response → cortisol/catecholamines → high blood sugar
  - Pre-existing Diabetes (recognized or unrecognized)
  - Hyperglycemia harms ischemic brain tissue

Potential Mechanisms Of Harm From Hyperglycemia

- May reduce recanalization
  - Increased thrombin and tissue factor
  - Decreased activity of tPA

- May decrease reperfusion
  - Impaired vasodilation via impact on nitric oxide

- May increase re-perfusion injury
  - High glucose can increase oxidative stress

Harm of Intensive Insulin Regimens

- Hypoglycemia
  - Reported in average of 31% of patients in 7 trials of IV insulin in stroke patients

- Effect of hypoglycemia may be more significant in stroke patient than in the general medicine patient

Glycemic Control Recommendations

- Recommendation is to control to <200
  - Goal of 80-140

- How to achieve this goal and whether intensive insulin drip therapy will end up proving beneficial is not clear

- Large trials in stroke patients using clinical outcomes are needed
The Pendulum Swings


Management of Co-morbidities Glycemic Control

PEARLS

- Rarely a need for dextrose in IVF in the first 24 hrs
- Metformin problematic-contrast/lactic acidosis
- Sulfonylurea medications associated with hypoglycemia when oral intake interrupted
- Sliding scale insulin alone is a poor choice for more than 24 hours

Evidence-Based Suggestions

For the Hyperglycemic Stroke Patient

- For the critically ill stroke patient
  - IV insulin drip titrated to BG 140-180

- For the stroke patient on the general medical ward
  - Anticipatory short acting SQ insulin prior to meals
  - Correction factor based on blood glucose
  - Long acting SQ insulin as basal control
  - Adjust daily if not at goal BG

- Long term glycemic control to A1c <7

American Association of Clinical Endocrinologists and American Diabetes Association Consensus Statement on Inpatient Glycemic Control
Diabetes Care. 2009;32:1119-1131
Hyperlipidemia

Population studies find a weak association between cholesterol and risk of stroke

Lesser evidence that some lipid lowering agents reduce risk of stroke alone or added to other agents
  - Fibrates
  - Niacin
  - Ezetimide

Statins do reduce stroke
  - And reduce stroke severity when already treated

How Do Statins Work

HMG CoA reductase inhibitors block conversion of HMG-CoA to mevalonate.

Mevalonate is a precursor to many classes of sterols and non-sterols including the primary product, cholesterol.

Lipid Management in Stroke Evidence

SPARCL trial- first RCT with stroke as 1° outcome
  - 16% RRR with statin over 5 yrs following CVA
  - No change in mortality
  - Small increase in hemorrhagic strokes

ASA Guidelines
  - Cholesterol lowering therapy recommended for LDL>100
  - (NEW) target goal 50% reduction or LDL<70
Evidence-Based Suggestions

- Avoid interrupting prior statin use during hospitalization for stroke
- High-dose high-potency statin therapy for stroke patients with LDL $>100$
  - Statin rec to 50% reduction of LDL or $<70$
    - Especially in very high risk patients
    - Unclear if benefit if LDL already $<70$
  - For low HDL consider niacin or gemfibrozil
- Start prior to hospital discharge
- Unclear if recommendations apply to hemorrhagic strokes

Management of Co-morbidities

Hypertension

Ischemic Penumbra

- Zone of at risk tissue susceptible to reduction below the threshold of viability in response to relatively small drops in MAP.

Objective of Blood Pressure Control

Maximize perfusion to the ischemic penumbra
Minimize risk of hemorrhagic transformation
Natural History of BP after Stroke

- 80% of stroke admissions have elevated BP.
- Even without intervention, the pressure tends to fall 10-15% in the first 24 hours.
- By day 10 BP will fall 13-20%

Relationship Between Admit BP and Outcome

- Observational trials suggest a U shaped curve
  - SBP on admit of 140-179 do best
- However multiple reports demonstrate harm of overcorrection in the acute setting
- Key Clinical Questions:
  1. At what threshold should I start new BP meds acutely
  2. Should I stop or continue home anti-hypertensives
  3. When should I begin lowering BP to long term goals

Question #1

What do the Guidelines Say

- Pre-Thrombolysis BP must be <185/110
- Post Thrombolysis- Goal BP<180/105
  - About 1/3 of patients who receive tPA require antihypertensive therapy in the first day
- Ischemic Stroke without Thrombolysis
  - Goal BP <220/120
  - “Permissive Hypertension”
In the setting of acute stroke auto-regulation is lost,
Cerebral blood flow becomes linear relationship with MAP

Question #2
Continue or Stop Home Meds?
- COSSACS Trial
  - Randomized 763 patients to continue or hold
  home antihypertensives for 2 weeks
  - No change in disability or death
  - No benefit or harm demonstrated

Question #3
When Should I Start New Meds?
- CHIPPS trial
  - Lisinopril or Labetolol vs placebo
  - BP on entry averaged SBP 181 mm Hg
  - SBP fell 21 points with b vs 11 in placebo group
  - No difference in outcome at 2 wks
  - Longer term the group with lowered bp did better
    - 60% reduction in mortality at 3 months
  - Caveat- Underpowered study of only 179 pts
Evidence-Based Suggestions

- Reasonable to continue home antihypertensives
  - Thiazides may be held acutely given risk of hyponatremia after CVA

- Avoid overcorrection of BP in hyperacute period
  - Permissive HTN still permitted in first 24 hours

- Modest bp reduction (10-15%) likely safe but no clear evidence it is of acute benefit
  - Timing of initiation may vary based on size of penumbra

- Long term benefit of lowering bp is well established
  - Diuretic or Diuretic+ACE-I have best evidence
  - Goal NORMAL blood pressure

Chronic Blood Pressure Control

- UK TIA study demonstrated a 28% decrease in long term stroke risk for every 10mm drop in systolic BP.

- By comparison- How much risk reduction do you get with aspirin?
  - 15%

The Treatment Imperative Does Not End At Hospital Discharge

- Outpatient use of secondary prevention measures suboptimal
  - 43% not regularly exercising
  - 36% not getting dietary counseling
  - 23% not regularly using anti-platelet agent
  - 19% not having cholesterol monitoring
  - 9% not on antihypertensive
With Aggressive Treatment
Impact can be Huge

- Mathematical Model of Risk Reduction
  - 5 year intensive control of 5 risk factors
    - Diet, and exercise
    - High potency anti-platelet agent
    - High-dose statin
    - Aggressive BP control

- Relative Risk Reduction: 90%
  - NNT = 5


Conclusions

- Many Stroke Mimics
  - Focus on migraine, seizure, and conversion to avoid being fooled in the decision to give lytics

- Permissive HTN still appropriate after CVA
  - But long term-- Normotensive is the goal

- Statins indicated after ischemic stroke
  - Target LDL <70 or 50% reduction

- Targeting normoglycemia after stroke can not be recommended based on current evidence
  - Moderate control is reasonable to BP<200