Acute Neurologic Syndromes

tPA?

NOT!

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Intravenous t-PA Exclusion Criteria

- Time of symptom onset > 180 (or qualified 270) minutes before treatment would begin.
- Evidence of intracranial hemorrhage on pretreatment computer tomography (CT).
- Clinical presentation suggestive of subarachnoid hemorrhage.
- Only minor or rapidly resolving stroke symptoms.
- Within 3 months of any intracranial operations, serious head trauma, or previous stroke.
- Major surgery within last 14 days.
- History of gastrointestinal or urinary tract hemorrhage within 21 days.
- Recent arterial puncture at a noncompressible site.
- Recent lumbar puncture.
- On repeated measurements, systolic blood pressure > 185 mm of mercury or diastolic blood pressure > 110 mm of mercury at the time treatment is to begin, or patient requires aggressive blood pressure treatment.
This is the worst headache of my life

Subarachnoid Hemorrhage

65 yo man with headache then collapse with right hemiplegia and initial BP of 240/110

Intracerebral Hemorrhage
CASE #1

• 72 yo old woman with history of atrial fibrillation who presents after one hour of progressive aphasia. Exam shows global aphasia but no weakness. Radiologist reports CT negative, all labs negative except INR 2.8

Is she a iv tpa candidate?
Is she an IA tpa candidate?

Subacute Subdural Hematoma
CASE #1
RED FLAGS

72 yo old woman with history of atrial fibrillation who present after one hour of progressive aphasia. Exam shows global aphasia but no weakness. Radiologist reports CT negative, all labs negative except INR 2.8

ALWAYS Look at the scan!!

Acute Ischemic Stroke
Intravenous t-PA Inclusion Criteria

INCLUSION CRITERIA
• Age 18 years or older

• Clinical diagnosis of ischemic stroke causing a measurable neurologic deficit
Objectives

1. Classify common acute stroke syndromes
2. Describe acute non-stroke syndromes including PRES, RCVS, CVT and migraine
3. Distinguish non-stroke neurologic conditions, evaluation and treatment

Disclosures: None

Disclaimer: This is a general clinical pearls talk - there are always exceptions to the rule

Goal of Therapy in all Neurologic Emergencies

• ACUTE Setting
  – Identify syndrome
  – Take immediate action to reduce disability
  – Minimize Risk

• SUBACUTE setting
  – Understand etiology
  – Prevent second event
Review of Acute stroke syndromes

• Large artery strokes
  – Right MCA/PCA
  – Right ACA
  – Left MCA/PCA
  – Left ACA
  – Basilar
  – PICA/AICA/SCA (Cerebellar)

• Lacunar syndromes
  – Dysarthria clumsy hand
  – Pure motor
  – Sensorimotor
  – Pure sensory
  – Ataxia hemisensory

Other Acute Non-stroke Syndromes

• High spinal cord lesion (hemorrhage)
• Seizure
• Subdural hematoma (subacute)
• Conversion Disorder
• Unmasking of old deficit (same symptoms, less severe, identified trigger)
• Transient Global anemia
• Hypoglycemia/ Hyperglycemia/Hypocalcemia
• Syncope/presyncope
• Mass lesion
• Radiculopathy/neuropathy
• Multiple sclerosis/ other acute inflammatory disease
Safety of tPA in Stroke Mimics

Of 56 cases
- 26.5% Conversion Disorder
- 19.5% Complicated Migraine
- 19.5% Seizure

Acute Neurologic Syndromes

- Migraine
- Cerebral Venous Thrombosis
- Reversible Cerebral Vasconstriction Syndrome
- Posterior Reversible Encephalopathy Syndrome
- Meningitis with Vasculopathy
**Features of Stroke**
- Sudden onset; maximal on onset and persistent
  - Exceptions: ie stuttering lacunar
- Respects vascular territories (identifiable syndrome)
- Headache is absent or minor feature (simultaneous)
- Usually have vascular risk factors (previously recognized or unrecognized)

**Features of Migraine**
- Marching progression
- Time course variable
- Numbness and dizziness are prominent features
- May be associated with visual aura, nausea or confusion (does not respect vascular territories)
- Headache often follows neurologic symptoms
- History of migraine (may be remote)
Case #2

• 28 yo male presents with T 38.1 severe headache, nausea and vomiting and right sided numbness. Thirty minutes after arrival to the ED he develops a nonfluent aphasia.
• CT is negative
• Tpa?
• LP
  – WBC 231 (98% Lymphs) CSF glucose and protein normal, GS negative

HaNDL
Headache and Neurologic Deficit Lymphocytosis in CSF

• Also known as Pseudomigraine with temporary neurological symptoms and lymphocytotic pleocytosis (PMP)
• Pathophysiology unknown (infectious or inflammatory)
• Recurrence unlikely after 12 weeks
Case #3

- 52 yo woman with acute onset aphasia. According to her family she is has no vascular risk factors and is generally healthy but suffered from severe diarrhea 10 days ago that resolved except persistent headache. Exam shows fluent aphasia and questionable right visual field cut.

Tpa or not?
Venous thrombosis

Venous thrombosis misdiagnosed as enhancing tumor
Venous thrombosis

Patient undiagnosed and treated

Decline in LOC but may not develop weakness
Deep Venous thrombosis presents with alteration of consciousness without focal finding

CVT Age and Sex Distribution
Predisposing Conditions for Cerebral Venous Thrombosis

- Hypercoaguability (Factor V Leiden, prothrombin mutation, APS, Protein C/S deficiency, hyperhomocysteinaemia)
- OCP and postpartum
- Severe dehydration
- Medications: androgen, danazol, lithium, Vitamin A, IVIG, ectacy, tamoxifen, L-asparaginase
- Cancer
- Perimeningeal infection (mastoiditis, otitis media, sinusitis)
- Intracranial hypotension
- PNH, iron deficiency anemia, nephrotic syndrome, polycythemia, thrombocythemia
- SLE, Behcet, Inflammatory bowel disease, thyroid disease, sarcoidosis
Case #3

Red Flags and Take home

• 52 yo woman with acute onset aphasia. According to her family she is has no vascular risk factors and is generally healthy but suffered from severe diarrhea 10 days ago that resolved except persistent headache. Exam shows fluent aphasia and questionable right visual field cut

• Imaging appearance (edema and hemorrhage) often looks much worse than clinical picture

Case #4

• 64 yo man presents to ED with acute onset confusion. He is agitated can speak fluently but confabulates. His BP is 200/120

• Labs show new elevation of creatinine of 3.4

• Head CT read as bilateral subacute occipital lobe strokes
Posterior Reversible Encephalopathy Syndrome

- Posterior reversible encephalopathy syndrome (PRES), also known as reversible posterior leukoencephalopathy syndrome (RPLS), is a syndrome characterised by headache, confusion, seizures and visual loss. It may occur due to a number of causes, predominantly malignant hypertension, eclampsia and some medical treatments. On magnetic resonance imaging (MRI) of the brain, areas of edema (swelling) are seen. The symptoms tend to resolve after a period of time, although visual changes sometimes remain.
PRES

- PRES occurs due to the use of drugs like tacrolimus and cyclosporine, hence it may occur in people who have undergone an organ transplant, in which these drugs may be used to suppress transplant rejection. It also occurs due to eclampsia, severe high blood pressure and hypercalcemia. Low magnesium levels can augment PRES.

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**TABLE 1:** Presenting Symptoms and Causes of Posterior Reversible Encephalopathy Syndrome (PRES) in 76 Patients

<table>
<thead>
<tr>
<th>Presenting Symptoms</th>
<th>No. of Patients</th>
<th>Primary PRES Cause</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizures</td>
<td>58</td>
<td>CSA for transplant</td>
<td>34</td>
</tr>
<tr>
<td>Mental status change*</td>
<td>10</td>
<td>Hypertension</td>
<td>17</td>
</tr>
<tr>
<td>Visual symptoms or loss</td>
<td>3</td>
<td>Eclampsia</td>
<td>5</td>
</tr>
<tr>
<td>Severe headache</td>
<td>3</td>
<td>Tacrolimus</td>
<td>4</td>
</tr>
<tr>
<td>Aphasia</td>
<td>1</td>
<td>Cocaine, methamphetamine use</td>
<td>3</td>
</tr>
<tr>
<td>Facial numbness</td>
<td>1</td>
<td>TTP/ITP</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Combined chemotherapy</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Systemic lupus erythematosus</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chronic renal failure</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PEG-1- asparaginase</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hemolytic urtic syndrome</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NOE, anasythastis?</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NOE, alcohol withdrawal?</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NOE, steroids?</td>
<td>1</td>
</tr>
</tbody>
</table>

Note—CSA = cyclosporine A, TTP/ITP = thrombotic or idiopathic thrombocytopenic purpura, PEG = polyethylene glycol, NOE = not otherwise specified.

*Include acute increase in consciousness or in responsiveness or acute confusion.
Classical MRI Appearance of PRES

PRES imaging variants
Regional Involvement of PRES

![Bar graph showing regional involvement by posterior reversible encephalopathy syndrome (PRES) in 76 patients. Number of patients in each region are listed in or above each bar.](image)

**Case # 5**

- 49 yo female who presents with a sudden severe headache and progressive visual changes. PMH is negative. She denies drug use but consumes energy drinks daily and smokes marijuana. Exam shows mild word finding difficulties, right visual field cut
- Head CT is negative
- Tpa?
Reversible Cerebral Vasoconstriction Syndrome (RCVS)

- **Reversible cerebral vasoconstriction syndrome (RCVS)**, sometimes called Call-Fleming syndrome or by a number of other names) is a poorly understood disease in which the arteries of the brain develop vasospasm without a clear cause (such as hemorrhage or trauma).
- Vasospasm narrows arteries and can trigger severe headaches that wax and wane. When the vasospasms subside the headaches are relieved.
- Symptoms result from vasospasms that narrow arteries, especially those around the circle of Willis, which can lead to a dramatic headaches that are often of the thunderclap headache (sudden-onset) character.
- Ischemia damage in these patients which presents 3–4 days after headache onset as focal neurological symptoms.
### Table 1. Conditions Associated with Reversible Cerebral Vasoconstriction Syndromes

<table>
<thead>
<tr>
<th>Condition</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy and puerperium</td>
<td>Early puerperium, late pregnancy, eclampsia, preeclampsia, and delayed postpartum eclampsia</td>
</tr>
<tr>
<td>Exposure to drugs and blood products</td>
<td>Phenylpropanolamine, pseudoephedrine, ergotamine tartrate, methergine, bromocriptine, lisuride, selective serotonin reuptake inhibitors, sumatriptan, isometheptine, cocaine, ecstasy, amphetamine derivatives, marijuana, lysergic acid diethylamide, tacrolimus, FK-506, cyclophosphamide, erythropoetin, intravenous immune globulin, and red blood cell transfusions</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Hyperalactemia, porphyria, pheochromocytoma, bronchial carcinoid tumor, unruptured saccular cerebral aneurysm, head trauma, spinal subdural hematoma, postcardiac endarterectomy, and neurosurgical procedures</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>No identifiable precipitating factor</td>
</tr>
<tr>
<td></td>
<td>Associated with headache disorders, such as migraine, primary thundertap headache, benign exertional headache, benign sexual headache, and primary cough headache</td>
</tr>
</tbody>
</table>


### Table 2. Summary of Critical Elements for the Diagnosis of Reversible Cerebral Vasoconstriction Syndromes

- Transfemoral angiography or indirect CTA or MRA documenting multifocal segmental cerebral artery vasoconstriction
- No evidence for aneurysmal subarachnoid hemorrhage
- Normal or near-normal cerebrospinal fluid analysis (protein level < 80 mg/dL, leukocytes < 10 mm³, normal glucose level)
- Severe, acute headaches, with or without additional neurologic signs or symptoms
- Reversibility of angiographic abnormalities within 12 weeks after onset. If death occurs before the follow-up studies are completed, autopsy rules out such conditions as vasculitis, intracranial atherosclerosis, and aneurysmal subarachnoid hemorrhage, which can also manifest with headache and stroke

*CTA = computed tomography angiography; MRA = magnetic resonance angiography.
Case #6

- 18 year old female two weeks postpartum from normal vaginal delivery (epidural anesthetic) who presents with severe headache, fever and aphasia and right sided weakness.
- Non-contrast Head CT negative
- LP
  - WBC 4200 (89% PMNs) glucose low and protein normal, GS + coccidian
- Lumbar MRI – epidural abscess
Meningitis—Stroke (KT)

Meningitis—Stroke (KT)
Meningitis—Stroke (KT)

Transcranial Doppler in Bacterial Meningitis
Red Flags

• Headache as a prominent feature
• FEVER
• No vascular risk factors
• Non-anatomic symptoms (mute and left sided weakness but not left handed)
• ANY CT findings
• Disconnect between imaging and clinical findings

Final case

• 32 year old with history of migraine, who has had one week of atypical left sided headache then presents with ED with nausea, vomiting, diplopia, severe dysarthria and first left, than right-sided hemiparesis. Exam shows dysconguate gaze severe dysarthria but no facial droop, right sided moderate weakness
• Noncontrast head CT is negative, labs are normal.
• Tpa?
• Diagnosis?
Acute Basilar Thrombosis from Vertebral dissection

Cerebrovascular Dissection

- Disruption of intima with infiltration of blood between mural layers
- Common cause of stroke in young and middle-aged adults
  - 5-20%
- Associated with trauma, neck manipulations, or can be spontaneous.
- More common in patients with collagen vascular diseases.

Schievink, NEJM 2001; 334:898
Cerebrovascular Dissection

- Features
  - Wall thickening
  - Stenosis & occlusion
  - Pseudoaneurysms
  - Intimal flaps
  - Thrombus & emboli

- Common Sites
  - Carotid: 1-2 cm beyond bifurcation to skull base
  - Vertebral: Below C6 (V1) or above C2 level (V3, V4)

MRI/MR Angiography

- MRI
  - Diffusion imaging for acute stroke

- MR Angiography
  - Flame-shaped occlusion
  - Long segment stenosis
  - Luminal irregularity
  - Pseudoaneurysm

- Intramural hematoma
  - T1 fat sat neck
  - Crescent shape or round rim
  - Methemoglobin

34 yo woman, right ICA dissection
Final case
Take Home

• 32 year old with history of migraine, who has had one week of atypical left sided headache then presents with ED with nausea, vomiting, diplopia, severe dysarthria and first left, than right-sided hemiparesis. Exam shows dysconjugate gaze, severe dysarthria but no facial droop, right sided moderate weakness.

• Diagnosis: Migraine vs Conversion disorder-----but only after dissection is ruled out!
Conclusion

- TPA is a safe effective intervention in a select population
- Ischemic stroke is clinical diagnosis
- Explore the history and physical to exclude or include nonstroke or atypical syndromes
- Order the right test
- Look at the imaging!!!
- Limit Disability

References


Tsivgoulis G, et al. Safety Outcomes of Intravenous Thrombolysis in Stroke Mimics A 6 year, single-Care Center Study and a Pooled Analysis of Reported Studies Stroke (2013) 42:00-00


ENLS
Emergency Neurological Life Support