Imaging ischemic strokes: Correlating radiological findings with the pathophysiological evolution of an infarct

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Patient A: history

91 y.o. woman

Acute onset R sided weakness and aphasia
DDx

Stroke (Ischemic ~80% or Hemorrhagic ~20%)

Transient ischemic attack (TIA)

Seizure with post-ictal paralysis

Intracranial tumor (with secondary hemorrhage, seizure, or hydrocephalus)

Migraine

Metabolic encephalopathy
## Acute Stroke Management

### Non-contrast head CT

Quickly identifies hemorrhagic strokes (fresh blood is bright on CT)

<table>
<thead>
<tr>
<th>Ischemic stroke</th>
<th>Hemorrhagic stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Can administer tPA within 3 hrs (systemic) or 6 hrs (intra-arterial)</td>
<td>DO NOT administer tPA</td>
</tr>
<tr>
<td>Identify source of ischemic stroke: Embolic, Thrombotic, Low-flow</td>
<td>Mildly reduce blood pressure</td>
</tr>
<tr>
<td>Prevent secondary damage and expansion of infarct</td>
<td>Administer products to reduce interstitial fluid levels (eg. Mannitol)</td>
</tr>
</tbody>
</table>
**Patient A: Non-contrast CT**

**Findings**

*** No evidence of hemorrhage***

Loss of gray-white matter distinction in L MCA territory

Sulcal effacement

Slight mass effect on L lateral ventricle

No midline shift

PACS, BIDMC
Patient A: Progression of Infarct

Findings

No evidence of hemorrhagic transformation

Hypodensity in region of L MCA infarct

Mass effect on L lateral ventricle with midline shift
# Mechanisms of ischemic stroke injury

<table>
<thead>
<tr>
<th>Event in Neurons</th>
<th>Time</th>
</tr>
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<tbody>
<tr>
<td>Loss of blood supply</td>
<td>0</td>
</tr>
<tr>
<td>$O_2$ depletion</td>
<td>10 sec</td>
</tr>
<tr>
<td>Glucose depletion</td>
<td>2-4 min</td>
</tr>
<tr>
<td>Conversion to anaerobic respiration</td>
<td>2-4 min</td>
</tr>
<tr>
<td>Exhaustion of cellular ATP</td>
<td>4-5 min</td>
</tr>
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</table>

NEURONS have very limited stores of energy in the forms of phosphocreatine and glycogen. In contrast, GLIAL cells have greater energy reserves and are less energy demanding.
Mechanisms of ischemic stroke injury

- ATP depletion
- Na\(^+\) -K\(^+\) ATPase dysfunction
- Loss of electrochemical gradient: Anoxic depolarization
- Massive glutamate release
- Ca\(^{++}\) influx
- Phospholipase and protease activation
- Necrosis
- Apoptosis pathway
- Mitochondrial dysfunction
- Edema, FAS death ligands, cytokine release, free radical generation, acidosis
Early CT changes from intracranial edema

1. Effacement of gray-white matter distinction as edema reduces the small difference in gray and white matter attenuations

2. Effacement of sulci due to swelling within limited space

3. Mass effect on ventricles due to swelling within limited space

* Earliest CT changes seen several hours to days after initial loss of blood supply depending on size of infarct and volume of edema.

Edema: 0-20 HU;  Gray matter: ~46 HU;  White matter: ~40 HU
**Progression of an ischemic infarct**

Increase in infarct size over time is possible

Ischemic Penumbra - the region surrounding the infarcted tissue is subjected to numerous stresses:

- Decreased perfusion
- Abnormal cerebrovascular pressure autoregulation
- Compression by neighboring edema
- Active inflammation
- Free radical damage from infarcted region and neutrophils, astrocytes, microglia
- Induction of apoptosis by FAS death ligands
Pt B: Progression of an ischemic infarct

Time = 3.25 hr
Late CT changes:

Increased infarction area, mass effect on ventricle, loss of sulci, hypodensity in infarcted tissue

* Hypodensity due to replacement of tissue by fluid

[Figure from Pantano et al. 1999. Stroke 30:502-507]
Hemorrhagic transformation of ischemic stroke results from reperfusion injury.

**Reperfusion injury:** Restoration of blood flow through a previously occluded intracranial vessel that results in vessel wall destruction and hemorrhage.

- Spontaneous or tPA-induced clot lysis
- O$_2$ combines with toxic metabolites to generate superoxide O$_2^-$
- Invading neutrophils convert O$_2$ to O$_2^-$
- Blood-brain barrier destruction from free radical damage to endothelial cells AND ischemic endothelial cell death (3-4 hrs)
Patient C: Hemorrhagic transformation of an ischemic stroke

[Figure from http://www.strokecenter.org/education/ais_pathogenesis/16_hemorrhagic_conversion.htm]
tPA-induced hemorrhagic transformation: potential treatment

1. tPA treatment for ischemic stroke often leads to secondary hemorrhagic transformation due to reperfusion injury.

2. Current models state that reperfusion injury occurs in large part from free radical damage following clot-lysis.

3. Therefore, delivery of tPA WITH anti-oxidants should reduce the probability of hemorrhagic transformations.

Animals models support co-administration of tPA with anti-oxidants in the prevention of secondary hemorrhagic transformation:

Ischemic strokes: imaging with MRI
Diffusion-Weighted Imaging (DWI)

Loss of blood supply

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<th>ATP depletion</th>
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<tbody>
<tr>
<td>Massive depolarization</td>
</tr>
<tr>
<td>↑ intracellular ions</td>
</tr>
<tr>
<td><strong>INTRACELLULAR EDEMA</strong></td>
</tr>
<tr>
<td>Cell death</td>
</tr>
<tr>
<td><strong>EXTRACELLULAR EDEMA</strong></td>
</tr>
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</table>

DWI signal intensity is related to the apparent diffusion coefficient (ADC) of water molecules (independent of the amount of water).

ADC(water) decreases by ~50% within 5-10 min of ischemic stroke due to intracellular edema and also possibly decreased temperature—recall that ATP is depleted from neurons within 4-5 min.

*** DWI changes can be seen within minutes of an ischemic stroke.***
Pt D: Imaging ischemic strokes with MRI Diffusion-Weighted Imaging (DWI)

Left inferior temporal/occipital lobe ischemic infarct
Summary slide

Loss of blood supply

ATP depletion

Cell Death

Edema, cytokine release, free radical damage, FAS death ligands

Early CT changes:
GW & sulcal effacement, mass effect (hrs to days)

Late CT changes:
Hypodensity, mass effect, possibly enlarged infarct region

Reperfusion injury

Hemorrhagic transformation

Bright lesion on CT

DWI:
increased signal intensity
(5-10 min post-ischemic injury)
References


http://www.strokecenter.org/education/ais_pathogenesis/16_hemorrhagic_conversion.htm

All websites as of 9/20/04
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