Neuroimaging in Stroke

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Setting - Community ED with no on-call neurologist. Nighttime radiologist is available, but lives 65 minutes away from the hospital. No teleradiology is available.

A 58 year-old female presents via EMS with acute onset exactly 2 hours and 15 minutes prior to arrival of aphasia and right-sided weakness. The patient is found to be dysarthric with unintelligible speech. She has marked right upper and lower extremity weakness, with toes upgoing bilaterally. Her NIHSS is 18. She handles secretions without problems, and is only mildly obtunded. Her family relates that the patient had complained over the past few weeks of left arm tingling and clumsiness.

The patient is found to have no contraindications to thrombolysis. She is sent for a cranial CT, and returns within 15 minutes from CT with her films accompanying her. Laboratory studies return and are normal. The nurse asks what the CT shows and if TPA will be administered. You are now at 2 hours, 45 minutes from the patient’s symptom onset. If you wait for the radiologist to come and interpret the CT, it will be beyond three hours from the stroke ictus.
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## Introduction

Computed tomography (CT) has revolutionized the assessment of patients who present with an acute neurologic deficit with the head CT scan now playing an integral role in the screening and treatment of stroke patients. The non-contrast head CT scan remains the first-line imaging study in suspected stroke patients due to its ubiquity and exquisite sensitivity for the detection of blood. On the initial emergency CT scan, overt nonstroke processes must be confidently excluded. These “stroke mimics” include tumor, subdural or epidural hematoma, subarachnoid hemorrhage, and intraparenchymal hemorrhage.

Since thrombolytic therapy may produce lethal bleeding in patients with intracranial hemorrhage, exclusion of hemorrhage has been the key criterion in the major thrombolytic trials. While detection of hemorrhage is the most fundamental and critical step in the evaluation of the head CT, the ECASS trial demonstrated that early signs of major cerebral infarction (e.g. sulcal effacement, mass effect, edema, and loss of the insular ribbon) are also important features to look for, since they are associated with an increased risk for intracerebral hemorrhage in patients who receive thrombolytic therapy. Some guidelines have incorporated these more subtle signs into recommendations against thrombolysis when present. The NINDs trial, however, did not use these CT criteria for making decisions regarding thrombolysis.

Developing expertise in reading cranial CT requires education and practice, but this has been demonstrated to be a teachable skill. Importantly, like other areas in the field of emergency medicine, the clinician may be called upon to make a time-critical decision based on the CT scan without the benefit of a radiologic consultant.

## CT Findings

There are three possible classes of CT diagnoses when a patient presents with an acute neurologic deficit:

1. **Non-ischemic stroke lesion:**
   
   A: Hemorrhagic:
   
   1. SDH
   2. EDH
   3. SAH
   4. Intracerebral hemorrhage (cortical, subcortical, cerebellar, and brainstem)

   B: Non-hemorrhagic:
   
   1. Tumor
   2. Abscess
II. Ischemic Stroke Signs
   A. Hyperdense Artery Sign
   B. Loss of Insular Ribbon (“Insular ribbon sign”)
   C. Loss of cortical gray-white differentiation
   D. Mass effect

III. Normal CT

Non-ischemic stroke lesions

Fundamental to cranial CT interpretation in potential stroke cases is the identification of non-stroke lesions, particularly hemorrhage. The NINDs trial used the determination of hemorrhage vs. no hemorrhage as the major CT criterion for study inclusion. Acute hemorrhage will usually appear hyperdense to gray matter, and have a heterogeneous appearance. It also tends to have less mass effect than would be predicted for the size of the lesion. All hyperdensities, however, are not necessarily acute hemorrhage. Calcification, proteinaceous material, and lesions with a high nucleocytoplasmic ratio (e.g. GBM) can all appear hyperdense to normal brain.

Epidural hematoma (lens shaped/ do not cross suture lines), subdural hematoma (falx shaped/ can cross suture lines) and intraparenchymal hematoma (supra/infratentorial) are all clinical possibilities which are usually readily apparent on CT scanning. Subarachnoid hemorrhage can be more difficult to diagnose. SAH typically appears as a hyperdense (white) collection, most commonly in the basal cisterns (including circummesencephalic, suprasellar, sylvian, and quadrigeminal). The ability to diagnose a SAH on CT scan depends on the volume of blood present and the duration of its presence. Typically, CT scan loses sensitivity for detecting subarachnoid hemorrhage as time from the SAH ictus increases.

Tumor and abscess can have similar appearances on non-contrasted scans. Both can demonstrate mixed densities within them, and both are frequently associated with edema in the surrounding brain matter.

Normal CT Scan

Even with state-of-the-art 3rd and 4th generation scanners, most ischemic strokes will go undetected for the first few hours. Hence, the “Normal CT Scan” is perfectly compatible with acute ischemic stroke. Unfortunately, a normal scan is also perfectly compatible with seizure, metabolic disease (hypoglycemia, hyponatremia), and TIA as etiologies for a neurologic deficit.

In general, gray matter is more susceptible to ischemia than white matter, as it is more metabolically active. Hence, loss of gray-white differentiation due to the influx of edema into the gray matter is the earliest change to be noted. Subtle edema has been detected as early as 46 minutes from the ictus, but changes this early are the exception. By 6 hours from the ictus,
of patients with MCA strokes will show early edema in the insular cortex. After 6-12 hours, additional edema is recruited into the area, making the lesion more conspicuous on CT imaging. Early on, it is NOT POSSIBLE to distinguish between ischemia and frank infarction by imaging techniques.

Ischemic Stroke Signs

The Hyperdense Artery Sign:

When an artery (typically MCA, PCA, or ACA) appears hyperdense, this is indicative of a major occlusion of the vessel with thrombus formation. The specificity of the hyperdense MCA (HMCAS) is 98%. False-positives can occur in the case of unilateral calcification of the MCA trunk. The sensitivity of the HMCAS, however, is only about 50%. Variability in blood volume and composition of the thrombus are responsible for the frequent false-negative findings. The hyperdense artery sign suggests that a major cerebral vessel is occluded and that this vessel’s territory is at risk for hypoperfusion. ICA and MCA trunk occlusions have more serious clinical implications than occlusions of the MCA branches, the PCA, or the ACA because the threatened territory is larger. Whether the affected territory will undergo ischemic necrosis is a matter of collateral blood supply. Therefore, this is not an infarct sign, rather it indicates volume of tissue that will die if the collateral blood supply fails and recanalization is not achieved. Clinically, ischemic stroke patients with an HMCAS have a poorer prognosis than those without this radiographic finding.

The Insular Ribbon Sign

The insular ribbon is an area of extreme gray-white differentiation that is readily examined on the CT scan. Located between the Sylvian fissure and the basal ganglia, it is supplied by small perforating branches of the MCA. Loss of the insular stripe is one of the more subtle early indications of MCA stroke. The normal insular cortex appears as a thin white line (gray-matter) adjacent to a darker gray subcortical area (white-matter). With ischemia, the metabolically active gray matter is affected first, resulting of intracellular edema, with resulting hypodensity. Thus, the insular ribbon or stripe is lost, and a homogeneous appearance is noted. This finding alone is not an exclusion criterion for intravenous thrombolytic therapy.

Mass Effect

Brain swelling is very subtle during the first hours after arterial occlusion. Swelling of brain tissue is assessed on CT scans by looking for compression of CSF spaces and asymmetry of cortical sulci. In ECASS, 21% of initial CT scans demonstrated focal brain swelling. Moreover, this finding was associated with a poorer outcome. Swelling visible within the first 6 hours indicates severe edema and indicates a poor prognosis for the majority of patients.

A retrospective evaluation of CTs from the ECASS study suggested that if ischemic changes were present in greater than 1/3 of the MCA territory, the patient was at increased risk of hemorrhage. Other studies have supported this conclusion, but it has been demonstrated that the interobserver variability for identifying greater than 1/3 of the MCA distribution is very poor.
For this reason, this criterion is difficult to rely on for clinical decision making, even when the CT is interpreted by a neuroradiologist.\textsuperscript{6,17,21-23}

**Future Trends in Stroke Imaging**

While CT is the current brain-imaging method of choice for determining qualification for thrombolysis, this may change in the future. MRI, especially diffusion-weighted and perfusion-weighted MRI are exquisitely sensitive to early pathologic changes of ischemic infarction and subtle brain edema.\textsuperscript{16,24,25} These techniques are superior to CT in that they can detect abnormalities much sooner than a conventional non-contrast CT scan. The major limitation of MRI remains its relative insensitivity to detecting hemorrhage, which is the key neuroimaging branch point in a clinical protocol. PET scanning, Xenon CT scanning, and cranial doppler are all being investigated in the stroke arena, but are all currently considered to be experimental.\textsuperscript{16,18}

**Key Points for Cranial CT Evaluation in Potential Acute Stroke:**

- The cranial CT must be reviewed by someone with expertise in its interpretation.

- Presence of intracranial hemorrhage on CT scan is the key contraindication to thrombolysis, based on the NINDs trial data.

- Dense MCA sign, ischemia in $> 1/3$ of the MCA distribution, and obscuration of the insular ribbon/basal ganglia are evidence for large or more advanced strokes.

- Ischemic changes in $> 1/3$ of the MCA distribution may suggest an increased risk for hemorrhagic conversion after TPA administration, but the interobserver variability in identifying this finding make it unreliable on which to base clinical decision making.

- Diffusion- and perfusion-weighted MRI are very sensitive for early detection of cerebral ischemia, but remain relatively insensitive for hemorrhage.
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Case Outcome

You interpret the cranial CT correctly as demonstrating an early stroke in the left MCA distribution with obscuration of the insular ribbon on that side. Unfortunately for the patient, however, you also identify a right frontal mass lesion with significant edema surrounding it. You wisely withhold tPA in the presence of the presumed tumor.

The patient is transferred to a nearby tertiary care center with neurosurgical expertise, where he undergoes craniotomy. A diagnosis of Astrocytoma is made, and the patient is ultimately discharged to a rehabilitation hospital.
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Annotated Bibliography


   Administration of CT scan test to emergency physicians, neurologists, and neuroradiologists. Highlights the fact that none of the studied groups were extremely skilled at CT scan interpretation (emergency physicians = 67% correct, neurologists = 83% correct, radiologists = 83% correct).


   Study to look at the kappa (inter-rater agreement) for ischemic changes in either greater than or less than 1/3 of the MCA distribution. At best there was fair to moderate agreement among observers for these changes. Highlights the fact that this criterion is difficult to accurately reproduce and use as a clinical criterion.


   Excellent, brief review text on essential head CT findings in the most common clinical situations in the emergency department. Clearly labeled CT scans demonstrate key pathological entities and brief text delineates important findings.


   Multicenter teaching intervention with emergency medicine residents designed to assess baseline skill at reading cranial CT, and then improve this skill with a teaching intervention. At baseline, residents interpreted 59% of scans correctly. At 3 months after the intervention, residents interpreted 76% of the scans correctly.


   Excellent review article on the state of the art in detection of neurological emergencies, with particular attention to stroke diagnosis. Also looks at what is coming for the near future.
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Questions

1. **NINDs CT scan criteria for exclusion from thrombolysis included:**
   a. Dense MCA sign
   b. Hemorrhage
   c. Edema in > 1/3 of MCA distribution
   d. a&c
   e. All of the above

2. **Current treatment guidelines specify that the cranial CT must be read by a:**
   a. Neuroradiologist
   b. Neurologist
   c. Radiologist
   d. Physician skilled in cranial CT interpretation

3. **The normal cranial CT scan:**
   a. Is incompatible with acute stroke
   b. Is pathognomonic of acute stroke
   c. Is compatible with the diagnosis of acute stroke

4. **The “Hyperdense Artery sign” is:**
   a. Highly sensitive for ruling out major vessel occlusion
   b. Highly specific for ruling in a major vessel occlusion
   c. Neither sensitive nor specific for major vessel occlusion

5. **Ischemic changes in > 1/3 the distribution of the MCA:**
   a. Have a poor inter-rater reliability (kappa)
   b. Suggest an increased risk for intracranial hemorrhage
   c. Was not used as a radiographic thrombolysis criteria in the NINDs study
   d. All of the above
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Answers

1. **Answer b.**

   The NINDs study used hemorrhage as an exclusion criterion for thrombolysis. Dense MCA is not an exclusion criterion, but indicates a large area at risk for ischemia. Edema in > 1/3 of the MCA territory was looked at in ECASS, but not used in NINDs, in part due to poor inter-rater reliability.

2. **Answer d.**

   Treatment guidelines specify that the CT be interpreted by a “physician skilled in cranial CT interpretation.” Who does this is left up to the individual physicians and treatment teams at a particular hospital.

3. **Answer c.**

   The finding of a normal CT scan is perfectly compatible with acute ischemic stroke, and in fact, should be the most common reading for those receiving thrombolysis. Most ischemic changes aren’t seen for 4-6 hours, at which point the patient is out of the thrombolysis window.

4. **Answer b.**

   The hyperdense artery sign is highly specific for major vessel thrombosis (98%). It is not an infarct sign, as the area of infarction will depend on any collateralization that may exist. It indicates a large area that is at risk for infarction.

5. **Answer d.**

   Ischemic changes in > 1/3 of the MCA were looked at in the ECASS study as being at risk for increased chance of ICH with thrombolysis. Most studies, however, have shown that the kappa (agreement between observers) is poor for determining whether > 1/3 of the MCA is involved. This was not used as a radiographic criterion in the NINDs study.