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Candidate- The Royal Melbourne Hospital

Stroke Mimics and Differential Diagnosis

ANNA Stroke Seminar 2010
Clinical assessment

Aims

(1) Is it a stroke? (*What is the diagnosis*)
(2) What part of the brain is affected?
(3) Is it a haemorrhage or an infarct?
(4) What caused this stroke? (*Can we prevent a further stroke*)
(5) What are this patient’s problems?
   +
(6) What can we do to treat this patient?
(1) Is it a stroke?

(ii) The nature of the event

• onset: usually sudden
• course: maximal at onset, occasionally evolves over days
• were symptoms focal: focal vs general
• “negative”: loss of function
• associated symptoms: headache - 25% infarcts, seizures & vomiting
What are Focal Neurological Symptoms?

• Weakness of face/ arm/ leg on one side
• Sensory disturbance face/ arm/ leg on one side of the body (NB –Caution if this is the only symptom & Caution if sensory symptoms only last minutes)
• Amaurosis Fugax (transient monocular blindness)
• Language disorder (aphasia)
• Homonymous hemianopia (visual field loss)
• Sudden bilateral blindness
• Diplopia (NB –Caution if this is the only symptom)
• Dysarthria (NB –Caution if this is the only symptom)
Symptoms unlikely to be TIA or Stroke i.e. Non-focal symptoms

- Light headedness/ faintness
- ‘Blackouts’ with altered or loss of consciousness or fainting
- Generalized weakness and/or generalized sensory disturbance
- Incontinence of urine or faeces
- Episode of confusion
- Drop attacks
Symptoms if isolated unlikely to indicate TIA or Stroke

- A spinning sensation
- Vertigo only
- Ringing in ears
- Difficulty swallowing
- Slurred speech
- Double vision
- Loss of balance
Two clinical scenarios

1. The patient with resolved symptoms
   - A completed TIA
   - A pseudo/mimic

2. The patient with symptoms: ‘Brain Attack’
   - More relevant when seeing patient acutely
Difficulties in TIA diagnosis

- There are many causes of transient symptoms which are not due to vascular disease
- Do not make the diagnosis until you have an accurate account of the patients symptoms.
- Ask a witness for details as patients may often forget because symptoms were short, confusion was present, or there was a loss of consciousness
Brain Attack: persistent symptoms

• An open label, not a completed diagnosis
• Implies there are differentials
• Is stroke easy to diagnose?
  – Literature: ~20% of referrals are incorrect
  – Prospective study of consecutive patients presenting to hospital with brain attack
  – 350 presentations:
    241 strokes (69%)
    109 mimics (31%)

Peter Hand et al. Stroke 2006; 37: 769-775
<table>
<thead>
<tr>
<th>Condition</th>
<th>Total Number (%)†</th>
<th>Within 6 hrs‡</th>
<th>After 6 hrs‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure</td>
<td>23 (21.1%)</td>
<td>18 (29.0%)</td>
<td>5 (10.6%)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>14 (12.8%)</td>
<td>6 (9.7%)</td>
<td>8 (17.0%)</td>
</tr>
<tr>
<td>Toxic / metabolic</td>
<td>12 (11.0%)</td>
<td>6 (9.7%)</td>
<td>6 (12.8%)</td>
</tr>
<tr>
<td>Space occupying lesion§</td>
<td>10 (9.2%)</td>
<td>3 (4.8%)</td>
<td>7 (14.9%)</td>
</tr>
<tr>
<td>Syncope / presyncope</td>
<td>10 (9.2%)</td>
<td>9 (14.5%)</td>
<td>1 (2.1%)</td>
</tr>
<tr>
<td>Acute confusional state</td>
<td>7 (6.4%)</td>
<td>3 (4.8%)</td>
<td>4 (8.5%)</td>
</tr>
<tr>
<td>Vestibular dysfunction</td>
<td>7 (6.4%)</td>
<td>3 (4.8%)</td>
<td>4 (8.5%)</td>
</tr>
<tr>
<td>Acute mononeuropathy</td>
<td>6 (5.5%)</td>
<td>4 (6.5%)</td>
<td>2 (4.3%)</td>
</tr>
<tr>
<td>Functional/medically unexplained symptoms</td>
<td>6 (5.5%)</td>
<td>4 (6.5%)</td>
<td>2 (4.3%)</td>
</tr>
<tr>
<td>Dementia</td>
<td>4 (3.7%)</td>
<td>2 (3.2%)</td>
<td>2 (4.3%)</td>
</tr>
<tr>
<td>Migraine</td>
<td>3 (2.8%)</td>
<td>2 (3.2%)</td>
<td>2 (4.3%)</td>
</tr>
<tr>
<td>Spinal cord lesion¶</td>
<td>3 (2.8%)</td>
<td>- (0%)</td>
<td>3 (6.4%)</td>
</tr>
<tr>
<td>Other?</td>
<td>3 (3.7%)</td>
<td>2 (3.2%)</td>
<td>1 (2.1%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>109 (100%)</strong></td>
<td><strong>62 (100%)</strong></td>
<td><strong>47 (100%)</strong></td>
</tr>
</tbody>
</table>
Conditions that mimic stroke
Systematic review of literature (n=1,265 mimics)

- Miscellaneous: 15.0%
- Wernicke's alcohol: 2.5%
- Meningitis/encephalitis: 5.0%
- PN palsy: 7.5%
- Dementia: 10.0%
- Psychogenic: 12.5%
- Migraine: 15.0%
- Vertigo: 17.5%
- Syncope/presyncope: 20.0%
- Sequelae of old stroke: 0.0%
- Toxic/metabolic: 2.5%
- Wernicke's/alcohol: 5.0%
- Miscellaneous: 7.5%
- Miscellaneously: 10.0%
- Miscellaneous: 12.5%
- Miscellaneous: 15.0%
- Miscellaneous: 17.5%
- Miscellaneous: 20.0%

Peter Hand et al. 2000.
The miscellaneous group

- Cardiac cause (ischaemia, heart failure etc.) 24
- Spinal cord lesion 13
- Multiple sclerosis 12
- Transient global amnesia 11
- Parkinson’s disease 8
- Subarachnoid haemorrhage 6
- Trauma 4
- Hypertensive encephalopathy 3
- Myasthenia gravis 3
- Acute confusional state 2
- Aortic dissection 2
- Herpes encephalitis 2
- Motor neuron disease 2
- Parasthesia of unknown cause 2
- Vertebral artery dissection 1
- Friedreich’s ataxia 1
- Multiple systems atrophy 1
- Cerebral sarcoidosis 1
- Normal pressure hydrocephalus 1
- Sleep apnoea 1
- Perforated duodenal ulcer 1
- Weakness of unknown cause 1
- Arm stiffness of unknown cause 1
- Arm pain of unknown cause 1
- Sudden death 13

- No details provided 76
- Total 193
Stroke mimics

- 42% of pts had previous stroke
  - Around half had no residual symptoms
  - Many might have an abnormal scan
- 26% of pts had cognitive impairment
- 75% of mimics were neurological conditions
  - Many of these would have normal scans
- *This highlights the importance of the neurologist and or Nurse Practitioner in acute assessment*

Peter Hand et al. Stroke 2006; 37: 769-775
Reliability of clinical assessment

• Reliability is the likelihood of 2 observers finding the same thing (i.e. agreement)
  – Accuracy depends on validity & reliability

• Reliability sub-study
  – 98 non-consecutive patients
  – 4 different observers, blind to history

• Kappa – measure of agreement
  – Allows for agreement expected by chance
  – $\kappa < 0.2$ poor agreement; 0.21–0.40 = fair; 0.41–0.60 = moderate; 0.61–0.80 = good; 0.81–1.00 = excellent agreement
### Vascular Risk Factors:

<table>
<thead>
<tr>
<th>Item</th>
<th>K value</th>
<th>95% CI</th>
<th>Crude Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>0.47</td>
<td>0.32 – 0.62</td>
<td>65/97 (67%)</td>
</tr>
<tr>
<td>Smoker within 12 months</td>
<td>0.69</td>
<td>0.55 – 0.83</td>
<td>81/97 (84%)</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>0.64</td>
<td>0.50 – 0.78</td>
<td>77/97 (79%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>0.54</td>
<td>0.38 – 0.70</td>
<td>73/96 (76%)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>0.44</td>
<td>0.27 – 0.62</td>
<td>69/97 (71%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.65</td>
<td>0.45 – 0.84</td>
<td>75/86 (87%)</td>
</tr>
<tr>
<td>Past history of a focal neurological deficit</td>
<td>0.51</td>
<td>0.36 – 0.66</td>
<td>69/98 (70%)</td>
</tr>
</tbody>
</table>

### History of the presenting complaint:

<table>
<thead>
<tr>
<th>Item</th>
<th>K value</th>
<th>95% CI</th>
<th>Crude Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>An exact time of onset can be determined</td>
<td>0.63</td>
<td>0.47 – 0.78</td>
<td>80/98 (82%)</td>
</tr>
<tr>
<td>Patient woke from sleep with deficit</td>
<td>0.55</td>
<td>0.40 – 0.69</td>
<td>70/97 (72%)</td>
</tr>
<tr>
<td>Patient can recall what he/she was doing at time of onset</td>
<td>0.37</td>
<td>0.20 – 0.53</td>
<td>60/97 (62%)</td>
</tr>
<tr>
<td>Improvement since onset</td>
<td>0.54</td>
<td>0.39 – 0.68</td>
<td>69/98 (70%)</td>
</tr>
<tr>
<td>Symptoms are now stable</td>
<td>0.59</td>
<td>0.42 – 0.77</td>
<td>81/98 (83%)</td>
</tr>
<tr>
<td>Patient well in the week before onset</td>
<td>0.40</td>
<td>0.24 – 0.57</td>
<td>64/98 (65%)</td>
</tr>
<tr>
<td>A definite history of focal neurological deficit</td>
<td>0.59</td>
<td>0.42 – 0.75</td>
<td>79/98 (81%)</td>
</tr>
<tr>
<td>Hemianopia/quadrantanopia</td>
<td>0.63</td>
<td>0.47 – 0.79</td>
<td>72/89 (81%)</td>
</tr>
<tr>
<td>Loss of speech/language</td>
<td>0.64</td>
<td>0.50 – 0.77</td>
<td>68/89 (76%)</td>
</tr>
<tr>
<td>Loss of sensation</td>
<td>0.62</td>
<td>0.48 – 0.76</td>
<td>68/89 (76%)</td>
</tr>
<tr>
<td>Loss of power</td>
<td>0.59</td>
<td>0.44 – 0.75</td>
<td>68/89 (76%)</td>
</tr>
<tr>
<td>Headache</td>
<td>0.65</td>
<td>0.51 – 0.79</td>
<td>78/97 (80%)</td>
</tr>
</tbody>
</table>
Timing of symptom onset

• Good reliability for whether there was an exact time of onset (κ=0.63)

• Agreement for:
  – date, hour and minute in 19/42 (45%)
  – date and hour in 11/42 (26%)
  – date only in 9/42 (21%)
  – complete disagreement for date & time in 3/42 (7%)

• Median difference in onset times for the 23 patients where there was disagreement was 30 minutes (IQR: 10 – 90 minutes)

• Methods to improve timing…
Factors that caused poor reliability

- Experience of clinician:
  - Greatest difference for neurological exam
- Clinician confidence:
  - Lower reliability when clinician uncertain
- Time since symptom onset:
  - Worse in those presenting very early or late
- Patient factors:
  - Much worse when patient had aphasia (not so bad for confusion or older age)

Peter Hand et al. Stroke 2006; 37: 776-780
Clinical features that distinguish between stroke & mimic

- **Stroke predicted by**
  - exact time of onset
  - patient could recall exactly what he/she was doing at symptom onset
  - well in the last week
  - definite focal symptoms or signs

- **Mimic predicted if**
  - known history of cognitive impairment
  - lost consciousness or had a seizure at onset
  - the patient could still walk
  - no lateralising symptoms
  - examination revealed confusion, signs in other non-vascular systems and no neurological signs
Stroke vs Mimic:
value of the OCSP classification

Peter Hand et al. Stroke 2006; 37: 769-775
Stroke vs Mimic: value of the NIHSS

Peter Hand et al. Stroke 2006; 37: 769-775
<table>
<thead>
<tr>
<th>Clinical Item</th>
<th>Importance</th>
<th>Suggests the likely diagnosis is:</th>
<th>Odds Ratios - Multivariable Logistic regression:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>History</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Definite history of focal neurological symptoms</td>
<td>★ ★</td>
<td>STROKE</td>
<td>7.21</td>
</tr>
<tr>
<td>• An exact onset of symptoms can be determined</td>
<td>★</td>
<td>STROKE</td>
<td>2.59</td>
</tr>
<tr>
<td>• Known cognitive impairment</td>
<td>★</td>
<td>MIMIC</td>
<td>0.33</td>
</tr>
<tr>
<td><strong>Examination</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Any abnormal vascular findings</td>
<td>★</td>
<td>STROKE</td>
<td>2.54</td>
</tr>
<tr>
<td>• Any abnormal findings in other systems</td>
<td>★</td>
<td>MIMIC</td>
<td>0.44</td>
</tr>
<tr>
<td>• Either</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIHSS 1-4</td>
<td>★</td>
<td>STROKE</td>
<td></td>
</tr>
<tr>
<td>NIHSS 5-10</td>
<td>★</td>
<td>STROKE</td>
<td></td>
</tr>
<tr>
<td>NIHSS &gt;10</td>
<td>★ ★</td>
<td>STROKE</td>
<td>7.23</td>
</tr>
<tr>
<td>• Or</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arm weakness</td>
<td>★ ★</td>
<td>STROKE</td>
<td>3.99</td>
</tr>
<tr>
<td><strong>Diagnostic formulation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Signs can be laterised to the right/left brain</td>
<td>★</td>
<td>STROKE</td>
<td>2.03</td>
</tr>
<tr>
<td>• Signs can be placed in an OCSP category</td>
<td>★ ★</td>
<td>STROKE</td>
<td>5.09</td>
</tr>
</tbody>
</table>
How to improve accuracy: brain imaging

• Positive findings on the CT confirm the diagnosis of an ischaemic stroke
• Look for early CT signs of infarction
  – Loss of tissue density
  – Tissue swelling
• Pathology:
  – Influx of water into ischaemic cells
  – grey matter affected before white matter
Hyperdense MCA

- Occlusion of the MCA by fresh clot
- May be seen in other main vessels, distally or in lenticulostriate arteries
- Frequency varies
- 50% with proven MCA occlusion don’t have the sign
Basal ganglia changes

- Loss of definition of grey matter - best seen at edges of internal capsule
- Swelling compresses the adjacent lateral ventricle
Cortical surface changes

- ‘Insular ribbon sign’
  - loss of distinction between external capsule and insular cortex
- Also look for swelling of cortical sulci - effacement (loss of visibility)
Investigations: Imaging

• Rationale:
  – to exclude (rare) stroke mimics eg SDH
  – to distinguish between haemorrhage and infarct

• Plain CT is the imaging technique of choice
  – available, rapid
  – reliably differentiates haemorrhage: 
    
    *blood is white*
PICH on CT

- Is always seen
- Apparent immediately
- Lasts 1 week
- Then disappears and looks like an infarct
Ischaemic stroke on CT

- Infarcts seen as areas of hypodensity
- Become more obvious as time progresses
- Small infarcts appear later than large ones - 75% TACI vs 45% LACI
- Overall, 40% strokes have normal CT
- Posterior fossa difficult
MRI in acute stroke

• Advantages:
  – much better at defining the anatomy
  – shows ischaemic changes earlier, and in a greater proportion of patients
  – diffusion weighted imaging can show ischaemia within minutes-hours, and differentiate between old and new lesions
  – MRA allows imaging of blood vessels non-invasively

• Disadvantages:
  – expense, time, lack of access to the patient
A 42 year old man with headache and left hemiparesis

CT brain (3 hours) ? R MCA hypodensity

DWI (24 hrs) obvious R MCA infarct

MRA (24 hrs) dissection R ICA with distal occlusion
Take home messages:

1. Watch out for timing of symptom onset

2. Early ischaemic changes on CT confirm the diagnosis

3. Be aware of red flags for mimics
Interobserver Agreement for the Bedside Clinical Assessment of Suspected Stroke

Peter J. Hand, Janneke A. Haisma, Joseph Kwan, Richard I. Lindley, Bart Lamont, Martin S. Dennis and Joanna M. Wardlaw

Stroke 2006;37;776-780; originally published online Feb 16, 2006;

DOI: 10.1161/01.STR.0000204042.41695.a1

http://stroke.ahajournals.org/cgi/content/full/37/3/776