Transient Ischemic Attack

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"The vision in my right eye went fuzzy for over an hour yesterday. My arm also felt a little weak. What's wrong with my eye?"

What is the diagnosis?

"The vision in my right eye went dark for over an hour yesterday. My arm also felt a little weak. What's wrong with my eye?"

The real question: How would you manage this patient?
Normal Eye Examination
- RTC 1 month, sooner if recurrent?
- PCP within 1 week?
- Neuro-op/neurologist within 1 week?
- Emergency room today?

The United States in 2005:
- Strokes 700,000
- Stroke Related Deaths 160,000
- Stroke Fatality Rate 23%

TIA precedes stroke in ~ 15% of cases

The outcome of 105,000 strokes may be altered by our intervention!

The Cost of Stroke in the United States in 2006:
- Total cost 57 billion
- Percentage of Direct Cost:
  - Initial hospitalization 43%
  - Rehabilitation 16%
  - Physician cost 14%
  - Hospital readmission 14%
  - Medications 13%

Proper management of TIA has significant effect on mortality/morbidity/cost

National Stroke Association, Englewood, CO

Goals For This Evening:
- Review definition, symptoms, signs, and prevalence of TIA
- Determine short-term risk of stroke after TIA
- Determine what patients are at highest risk
- Review the basic pathophysiology of TIA/stroke
- Outline current strategies in management of TIA
**Transient Ischemic Attack (TIA)**

**Classic Definition:**
A transient neurological disturbance lasting less than 24 hours that is confined to an area of the brain or eye perfused by a specific artery that upon resolution results in no permanent structural/functional damage.

**New Proposed Definition:**
A brief episode of neurologic dysfunction, caused by brain or retinal ischemia, with clinical symptoms typically lasting less than one hour, without evidence of cerebral infarction.

*New Eng J Med 2002;347:1713-1716*

**What are “neurologic disturbances?”**

- Amaurosis fugax
- Hemispheric partial paralysis or numbness
- Altered speech
- Intermittent amnesia
- Dizziness
- Confusion or altered personality

You have to ask your patient about these symptoms!!!

**What Actually is a TIA?**

An embolus, thrombus, or other cause of decreased blood flow that resolves in a short period of time (< 24 hours) and without causing permanent damage to brain tissues.
The prevalence of at least one TIA symptom in a national sample of over 18,400 individuals was 17.8%.

Who thinks this is high?

Prevalence of TIA?
Amaurosis Fugax

Unilateral "Graying-Out" of all/partial vision
Duration of minutes to hours
May be associated with other neurologic symptoms

You have to ask about other neurologic symptoms!

Amaurosis Fugax: What's Happening?

Temporary reduction in retinal, ophthalmic, or ciliary artery blood flow

Embolic
Carotid
Cardiac
Any vessel

Hypoperfusion
Decreased flow or increased metabolic demand in stenosed arteries or hyperviscosity

Vasospastic

Migraine
Cold
Emotion/Stress
Autoimmune
Infectious

Atherosclerosis
Giant Cell Arteritis
Hyperviscosity Syndromes

The Problem: TIA Not Easy to Diagnose

Bilateral
Flashing lights, not graying out
Involves right/left hemifield
Often moves across the field
Usually lasts 10-20 minutes
Rarely completely occludes
Headache may/may not follow

Migraine Aura
Ocular Surface Disease

Intermittent blurring of vision
Not complete graying out
Changing character with blink
Environmental triggers
Characteristic ocular signs
Contact Lens Dryness/Fit
Sudden drop in blood pressure may be associated with a drop in heart rate and typically associated with a trigger:
- Unpleasant stimuli
- Extreme emotions
- Prolonged heat exposure

The Problem: TIA Not Easy to Diagnose

- Postural Hypotension
  Occurs after change in body position
  May have low systemic blood pressure

- Syncope
  Sudden drop in blood pressure
  May be associated with a drop in heart rate
  Typically associated with a trigger:
  - Unpleasant stimuli
  - Extreme emotions
  - Prolonged heat exposure

The Problem: TIA Not Easy to Diagnose

- Hypoglycemia?
- Seizure?
- Medication Side Effects?
- CNS Tumor?

56 patients examined by 8 neurologists in pairs:
- Agreed TIA present: 36 patients
- Agreed TIA absent: 12 patients
- Disagreed: 14% of patients


The Problem: TIA Not Easy to Diagnose

A Clinical Pearl From a Very Good Neuroophthalmologist:

Giant Cell Arteritis Can Present Like TIA!

Ask the Questions!
- Weight loss
- Temporal Headache
- Jaw claudication
- Next pain
- Malaise

Is there really 13-16% TIA prevalence in the population?
Age | Prevalence of CVA on MRI
---|---
55-59 years | 7.9%
60-64 years | 13.7%
65-72 years | 22.9%

Overall prevalence of 15.3% in the population

The prevalence of TIA and Stroke are High

So if TIA is diagnosed, when should we refer the patient?

You have to understand the short-term risk of stroke!
Greater Cincinnati/Northern Kentucky Stroke Study

Incidence and Short-Term Prognosis of Transient Ischemic Attack in a Population-Based Study


<table>
<thead>
<tr>
<th>Time</th>
<th>Recurrence</th>
<th>Infarct</th>
<th>Combined (Infarct/Death)</th>
<th>Combined (Infarct/TIA/Death)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 d</td>
<td>2.4</td>
<td>3.9</td>
<td>3.0</td>
<td>0.0</td>
</tr>
<tr>
<td>7 d</td>
<td>3.7</td>
<td>7.0</td>
<td>3.9</td>
<td>0.6</td>
</tr>
<tr>
<td>1 mo</td>
<td>6.9</td>
<td>11.2</td>
<td>5.3</td>
<td>3.2</td>
</tr>
<tr>
<td>2 mo</td>
<td>7.8</td>
<td>13.3</td>
<td>5.5</td>
<td>4.4</td>
</tr>
<tr>
<td>3 mo</td>
<td>8.6</td>
<td>14.6</td>
<td>22.5</td>
<td>5.2</td>
</tr>
<tr>
<td>6 mo</td>
<td>9.9</td>
<td>17.3</td>
<td>25.0</td>
<td>8.2</td>
</tr>
</tbody>
</table>


English population of 1.3 million with 63 general practitioners and nine health centers

In 87 TIA patients: Risk of Stroke

At 7 days: 8.0%
At 30 days: 11.5%
At 90 days: 17.3%

Coull et al. BMJ 2004;328:326-328

Population based study of early risk of stroke after transient ischemic attack or minor stroke: implications for public education and organisation of services


1707 patients identified by emergency room physicians as having had a TIA

Within 2 days: 91 (5.3%) had strokes
Within 90 days: 180 (10.5%) had strokes
44 (2.6%) had cardiovascular events
45 (2.6%) died
216 (12.7%) had recurrent TIA

Mortality and Cause of Death after Hospital Discharge in 10,981 Patients with Ischemic Stroke and Transient Ischemic Attack
Kazumi Kimura, Kazuo Minematsu, Seiji Kazui, Takenori Yamaguchi, for the Japan Multicenter Stroke Investigators’ Collaboration (J-MUSIC)
Cerebrovascular Division, Department of Medicine, National Cardiovascular Center, Osaka City, Japan

Mortality after TIA?

16,922 consecutive patients discharged after TIA
One year cumulative mortality rate was 6.8%:
- CVA 24.1%
- Heart disease 18.1%


Have I gotten your attention?

TIA is one of the most important diagnoses we can make in our practices

So to review:

Symptoms of TIA in population ~13-18%
Stroke within 2 days of TIA 3.9 – 5.3%
Stroke within 7 days of TIA 7.0 – 8.0%
Stroke Related Death within 90 days 2.6 – 5.2%

Coull et al. BMJ 2004;328:326-328
So to review:

Symptoms of TIA in population ~13-18%

Stroke within 2 days of TIA 3.9 – 5.3%
Stroke within 7 days of TIA 7.0 – 8.0%

Stroke Related Death 2.6 – 5.2%
within 90 days

The incidence of TIA and Stroke is High!

TIA may predict stroke

Stroke 2 days of TIA 3.9 – 5.3%
Stroke 7 days of TIA 7.0 – 8.0%

Why not just urgently refer all TIA patients for a full work-up even if it might be TIA?

TIA Work-Up = $$$$$

CT Scan ~$800
MRI ~$1200
Carotid Doppler ~$250
Cerebral Angiography ~$3000
MRA/ CTA ~$2000
Echocardiogram ~$300
Physician and Hospitalization Cost ~$1200
Lab Costs ~$800
The incidence of TIA and Stroke is High!

So whom do we need to refer and when?

How do we decide the level of risk?

Identified Risk Factors:
- Age > 60 years
- Symptom > 10 min
- Motor weakness
- Speech impairment
- Diabetes

With 5 risk factors: 34% risk of stroke at 90 days
With no risk factors: 0% risk

A simple score (A8CD) to identify individuals at high early risk of stroke after transient ischaemic attack

Point system derived from Oxfordshire Community Stroke Project
N = 105,000

Validated in two large cohort studies:
- Oxford Vascular Study: N = 378 TIA
- Hospital Based TIA Clinic: N = 210 TIA

A = Age
B = Blood Pressure
C = Clinical Features
D = Duration
**ABCD² Score: Risk Factor Assessment of Stroke After TIA**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Score</th>
<th>2-Day Stroke Risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 60 years</td>
<td>1 point</td>
<td>1.0</td>
</tr>
<tr>
<td>BP &gt; 140/90</td>
<td>1 point</td>
<td>2 points</td>
</tr>
<tr>
<td>Unilateral weakness</td>
<td>2 points</td>
<td>1 point</td>
</tr>
<tr>
<td>Speech disturbance</td>
<td>1 point</td>
<td>0 points</td>
</tr>
</tbody>
</table>

**Stroke Risk**

<table>
<thead>
<tr>
<th>Risk</th>
<th>ABCD² Score</th>
<th>2-Day Stroke Risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Risk</td>
<td>&lt; 4</td>
<td>1.0</td>
</tr>
<tr>
<td>Moderate Risk</td>
<td>4-5</td>
<td>4.1</td>
</tr>
<tr>
<td>High Risk</td>
<td>&gt; 5</td>
<td>8.1</td>
</tr>
</tbody>
</table>

**California Study**

90-Day Risk of CVA


**ABCD Study**

7-Day Risk of CVA


**Based on Rothwell. Lancet 2005;366:29-36**

**2-Day Risk of Stroke After TIA**

**Completely Misses Time of Greatest Risk**

"It was really weird. Three weeks ago, my vision blacked out in one eye for about 15 minutes. Everything else seemed normal."

- **56 years old**
- **Blood Pressure: 135/80**
- **Duration: 59 – 10 min**
- **No speech/neurologic**
- **No diabetes**
- **Total: 1 pt**

**Risk of Stroke within 2 days:** Low (1%)

Johnston. Lancet 2007;369;283-292

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**Risk Assessment of Theoretical Patient**

Discuss case with PCP

**Outpatient Follow-up**

- **Risk of Stroke within 7 days:** Low (0%)


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**Risk Assessment of Our Earlier Patient?**:

"The vision in my right eye went fuzzy for over an hour yesterday. My arm also felt a little weak. What’s wrong with my eye?"

- **82 years old**
- **Blood Pressure 145/85**
- **Unilateral Weakness**
- **Duration of time > 60 min.**
- **Not Diabetic**
- **Total: 6 pts**

**Risk of Stroke within 2 days:** High (8.1%)


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**Risk Assessment of Our Earlier Patient?:**

Immediate Referral to place that can manage the TIA to prevent CVA


**National Stroke Association Guidelines for the Management of Transient Ischemic Attacks**


Same-day access to imaging:
- CT/CTA
- MRI/MRA
- Ultrasonography
- Echocardiogram

Hospitalization:
- First TIA within 24-48 hours
  - "Crescendo TIA"
  - High risk ABCD² Scores

Refer to places with these capabilities!!!!

**Primary Stroke Centers in Anaheim Area**

- University of California Irvine Medical Center
  - 181 The City Drive
  - Orange, CA 92868
  - 714-456-5878

- Cedars - Sinai Medical Center
  - 8700 Beverly Boulevard
  - Los Angeles, CA 90048
  - 310-423-5191

- Mission Hospital Regional Medical Center
  - 27700 Medical Center Road
  - Mission Viejo, CA 92691
  - 949-365-2248

- Glendale Adventist Medical Center
  - 1509 Wilson Terrace
  - Glendale, CA 91206
  - 818-409-8000

- Long Beach Memorial Medical Center
  - 3881 Atlantic Avenue
  - Long Beach, CA 90801
  - 562-933-2000

- Cedars - Sinai Medical Center
  - 8700 Beverly Boulevard
  - Los Angeles, CA 90048
  - 310-423-5191

- University of California Irvine Medical Center
  - 181 The City Drive
  - Orange, CA 92868
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1278 patients with acute diagnosis of TIA

607 referred directly to hospital
620 referred for outpatient assessment
51 not referred for secondary assessment

Express Study

Does Urgent Referral and Work-Up Work?

Group | Median time to assessment | To first treatment
----- | ------------------------- | -------------------
Urgent | < 1 day                   | 1 day
Outpatient Assessment | 3 days                   | 20 days

Missed Greatest Risk!

90-Day Risk of Stroke

Express Study

Represents a 80% reduction in risk of early recurrent stroke
Independent of age and sex
Did not increase the risk of intracerebral hemorrhage or other bleeding event

701 patients with confirmed acute diagnosis of TIA
Work-up and appropriate treatment within 4 hours

SOS – TIA Study

Observed 90-Day Risk of Stroke in SOS Study

90 Day Stroke Risk based on ABCD² Score
Standard Outpatient Treatment

ABCD² Scores Predict True TIA

Higher ABCD² Score Predicts Patients Most Likely to Have True Transient Ischemic Attack

713 TIA diagnosed by PCP/ER Doctors
Confirmed by neurologist (90% agreement)

ABCD² scores significantly higher in true TIA group

True TIA diagnosis associated with 24% 90-day stroke risk compared to 1.4% in non-true

Josephson et al. Stroke 2008;49: Epublication Before Print
Stroke Basics:
Cessation of blood flow to the brain by occlusion or vessel rupture with neurologic symptoms lasting greater than 24 hours or resulting in structural damage.

Only difference between stroke and TIA is duration and detectable damage!

National Institute of Neurologic Disease and Stroke Data Base

“What is going to happen to me when I get to the hospital?”
First Line Medical Therapy for Small Vessel Disease and All TIA Causes

Blood pressure control:
- Diuretics
- Diuretics + ACE-inhibitor
- Beta-blockers

Diuretics
Diuretics + ACE-inhibitor

Blood pressure control: Reduction ~10/5 mmHg or Below 120/80 mmHg

Diabetic control:
- Blood Sugar: <126 mg/dl
- HbA1c: <7%

Lowering lipids:
- Simvastatin
- Pravastatin


Risk Factor Modification for Small Vessel Disease and All TIA Causes

Avoidance of excessive alcohol
- 1 drink/day for women Protective
- ≤ 2 drinks/day for men Protective
- > 5 drinks/day Increased risk

Weight reduction
- BMI 18.5 - 24.9 kg/m²
- Waist < 35 in. for women
- < 40 in. for men

Exercise
30 minutes/day

Sacco et al. Stroke 2006; 37:577-617

Intervention Dependant of Cause of TIA

Large Artery Atherosclerosis
Cardioembolic

Extracranial
Extracranial

Small Vessel Disease
Intervention Dependant of Cause of TIA

Large Artery Atherosclerosis

Cardioembolic

Extracranial

Intracranial

Small Vessel Disease

Surgical Interventions for Large Artery Pathology

Endarterectomy

Carotid Shunting

Embolic Protection Devices

Angioplasty/Stenting

Extracranial carotids responsible for TIA

With TIA or Stroke within 6 months (Better within 2 weeks):

- > 70% stenosis: Endarterectomy (CEA)
- 50 - 69% stenosis: Consider CEA
- < 50% stenosis: Questionable value

North American Symptomatic Carotid Endarterectomy Trial
European Carotid Surgery Trial
Veterans Affairs Cooperative Study Group
Endarterectomy for asymptomatic carotid artery stenosis

The CEA Versus CAS Debate:

Stent-Supported Percutaneous Angioplasty of Carotids vs. Endarterectomy Study: SPACE
Endarterectomy vs Angioplasty in Patients with Severe Symptomatic Stenosis: EVA-3S
Carotid Revascularization Endarterectomy vs. Stenting Trial: CREST
International Carotid Stenting Study: ICSS

The CEA Versus CAS Debate:

Meta-analysis of Randomized Trials Comparing Carotid Endarterectomy and Endovascular Treatment
T. Luebbe, M. Alvesco, and J. Broeckx
Division of Vascular Surgery, University of Cologne, Cologne, Germany

Seven trials totaling 2972 patients randomized to CEA or CAS:

Results favored CEA over CAS in terms of:
- Death or stroke at 30 days
- Death or stroke at 6 months
- Risk of procedural failure

Eur J Vasc Endovas Surg 2007;34:470-479
Extracranial Vertebrobasilar Disease:
- Medications
- Endovascular interventions (Angioplasty/Stents)

Intracranial atherosclerosis:
- Medications
- Endovascular interventions

Warfarin Aspirin Symptomatic Intracranial Stenosis Trial (WASID) Stenting of Symptomatic Atherosclerotic Lesions of Vertebral and Intracranial Arteries Trial (SSYLVIA)

Intracranial Surgery for TIA/Stroke:
Merci Retriever
Recanalization occurred in 48% of patients compared to 18% of patients historically treated with tissue plasminogen activator

Medical Management of Vascular Pathology
Aspirin
Inhibits formation of the prostaglandin thromboxane that promotes platelet aggregation

Clopidogrel/Plavix
Affects platelet adenosine diphosphate (ADP)

Ticlopidine/Ticlid
Affects platelet adenosine diphosphate (ADP)

Dipyridamole/Aggrenox
Affects platelet adenosine diphosphate (ADP)
Role of Heart in TIA/Stroke

Inefficient cardiac functioning results in relative stagnation of blood and potential for thromboembolism.

Calcification of diseased valvular tissues can result in direct embolization.
Role of Heart in TIA/Stroke

Atrial Fibrillation:
- Most common cardiac arrhythmia
- Responsible for 75,000 CVA/year

Myocardial Infarction:
- Up to 12% of MI patients have stroke
- Greatest risk in first 1-3 months post MI
- Damage to muscle = stasis = thrombus

Cardiomyopathy:
- Primarily caused by CAD
- Stasis of blood = thrombus

Medical Management of Cardiac Pathology

Warfarin/Coumadin
- Interferes with formation of prothrombin and clotting factors
- Initial dose is 5-10 mg. Adjusted based on INR

INR (International Normalized Ratio)
- Standardization technique that takes into account the thromboplastin reagent used for the prothrombin time.

Some Thoughts About TIA

TIA is a short duration stroke without permanent damage.
- New definition of TIA emphasizes amaurosis fugax
- Significant risk of mortality/morbidity in short/long term
- Identifying TIA and prompt referral is essential
- If given the choice, Primary Stroke Centers are the best

Patients with transient blurred vision present to their eye doctors regularly!
If stroke is going to happen, first days after TIA are critical!

Final Thought About TIA

Know your ABCDs!!!!!

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UC Berkeley School of Optometry
UCSF Department of Ophthalmology

THANK YOU!