TIA: LIVE OR MEMOREX?
DISTINGUISHING TRANSIENT NEUROLOGIC DEFICITS

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Distinguish between TIA, seizure, and migraine as the cause of a transient spell
TRANSIENT NEUROLOGIC DEFICIT (TND) DIFFERENTIAL DIAGNOSIS

- Transient ischemic attack (TIA)
- Seizure
- Migraine

All 3 phenomena can present with symptoms referable to the brain lasting seconds to hours—

Think TND before TIA!
DIAGNOSTIC CRITERIA FOR TIA & MIGRAINE: THE LITERATURE

- Diagnostic criteria for TIA and stroke mimics (e.g., ABCD2 Score for TIA and TM Score for stroke mimics) are primarily based on presence of concurrent vascular risk factors and motor findings, yet hypertension is common during migraine attacks and hemiplegic migraine is under recognized.

- Diagnostic criteria for migraine (International Classification of Headache Disorders, 3rd ed. = ICHD-3) are based on clinical presentation; however, the ICHD-3 criteria are:
  - Based on opinions (since there are no objective diagnostic tests for migraine) & therefore filled with both truths & untruths
  - Designed for scientific studies with a focus on headache, not the many nonheadache manifestations of migraine (though they include the category “typical aura without headache,” acknowledging one can have a migraine without headache)
  - Too restrictive & impractical for daily use
ABCD2 SCORE FOR TIA
Widely used, but misleading & not useful

- Age ≥ 60 1
- BP ≥ 140/90 mm Hg at initial evaluation 1
- Clinical features of the TIA:
  - Unilateral weakness 2
  - Speech disturbance without weakness 1
- Duration of symptoms
  - 10-59 minutes 1
  - ≥ 60 minutes 2
- Diabetes mellitus in patient's history 1

0-3 low stroke risk; hospital observation unnecessary
4-5 high stroke risk; hospital observation justified
6-7 very high stroke risk; hospital observation worthwhile

However,
1. Migraine attacks can occur at any age.
2. High BP is common during migraine attacks.
3. Hemiplegic & aphasic migraines are not rare.
4. Migraine commonly lasts minutes to hours.

Johnston SC et al. Lancet. 2007;369;283
### THE TELE-STROKE MIMIC (TM) SCORE

<table>
<thead>
<tr>
<th>Factor</th>
<th>Score</th>
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<tbody>
<tr>
<td>Age</td>
<td>+ 0.2/Y</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>+ 6</td>
</tr>
<tr>
<td>Hypertension</td>
<td>+ 3</td>
</tr>
<tr>
<td>Seizure</td>
<td>- 6</td>
</tr>
<tr>
<td>Facial weakness</td>
<td>+ 9</td>
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<tr>
<td>NIHSS score &gt; 14</td>
<td>+ 5</td>
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TRANSIENT ISCHEMIC ATTACK (TIA)
DEFINITION & DESCRIPTION

- Transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischemia, without infarction
- Typically 5-20 min—but time duration is not part of definition
- Risk of stroke = 5% w/in 2 d, 10% w/in 3 m
- Challenges:
  - Not all transient neurologic deficits are due to TIA—differential is TIA, seizure, migraine
  - TIAs have many possible causes (find source of embolus!)
    - Evaluate brain, arteries, and heart (e.g., MRI w/ DWI/ADC, intracranial MRA, carotid duplex, echocardiogram)
    - Prevent stroke by finding cause of TIA to determine correct 2° prevention strategy, including correct antithrombotic agent
    - Admit to “observation status” to facilitate rapid evaluation
TRANSIENT ISCHEMIC ATTACK
FEATURES MOST CONSISTENT WITH ISCHEMIA

- Neurologic symptoms (sxs)
  - No stereotypical pattern (no previous similar spells)
  - Sudden onset (possibly w/ Valsalva or neck manipulation)
  - Static (not migratory or traveling)
  - Confluent onset (no progression from 1 type to another)
  - Negative visual (black) & sensory (▼ sensation) sxs
  - Duration 5-20 minutes

- Associated features
  - Stroke risk factors (HTN, DM, hyperlipidemia, cigarette smoking)
  - Clotting history (including miscarriages)
  - Abnormal exam
  - Abnormal MRI (DWI/ADC), esp. if symptoms ≥ 1 hour
  - Identifiable high-risk stroke cause (atrial fibrillation, high-grade carotid stenosis, etc.)
Ischemia to focal area of CNS, esp. brain

- Usually due to **thromboembolus**
  - Thrombus = blood clot
  - Embolus = floating plug
  - Blood clot forms in vascular system (arteries or heart), travels downstream, plugs a brain artery

- Blood clots form for 1 of 2 reasons:
  - Platelets (Velcro) – stick to bumpy pipes (white clot)
  - Clotting factors (Jello) – clump when blood stagnant (red clot)

- Blood clots come from 1 of 3 locations:
  - Artery – esp. hardening of artery wall (atherosclerosis)
  - Heart – esp. irregular heart rhythm (atrial fibrillation)
  - Blood – blood too sticky (hypercoagulable state)
TIA & ISCHEMIC STROKE 2º PREVENTION

Therapy varies based on cause of TIA/AIS

TIA/AIS 2º Prevention—
Three Distinct Components

- Vascular risk factor modification—all pts
- Antithrombotic therapy—varies based on:
  - Clot source (artery, heart, or blood)
  - Clot type (white or red)
- Carotid revascularization—if carotid stenosis is the cause of TIA/AIS
  - Carotid endarterectomy (CEA)
  - Carotid angioplasty & stenting (CAS)
# TIA & ISCHEMIC STROKE

**Etiologic evaluation—where’d the clot come from?**

<table>
<thead>
<tr>
<th></th>
<th>NONINVASIVE Day 1</th>
<th>INVASIVE Day 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BRAIN</strong></td>
<td>MRI (w/ DWI &amp; ADC)</td>
<td></td>
</tr>
<tr>
<td><strong>ARTERIES</strong></td>
<td>MRA +/- carotid duplex or CTA head &amp; neck</td>
<td>*Catheter angiogram</td>
</tr>
<tr>
<td><strong>HEART</strong></td>
<td>ECG &amp; monitor Cardiac biomarkers Transthoracic echo (TTE)</td>
<td>*Trans-esophageal echo (TEE)</td>
</tr>
<tr>
<td><strong>BLOOD</strong></td>
<td>*Hypercoagulable profile</td>
<td>*in select patients</td>
</tr>
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</table>
HYPERCOAGULABILITY (= THROMBOPHILIA)
Possible cause of TIA & ischemic stroke

Excessive blood clotting, even in normal arteries or veins. Symptomatic thrombophilia is usually a 2-hit phenomenon. Obtain complete profile in any patient w/ no other identifiable cause.

- Excessive clotting factors
  - Fibrinogen
  - Factor VII
  - Factor VIII
  - Factor XI

- Deficient natural anticoagulants
  - Antithrombin III
  - Protein C
  - Protein S (total & free)

- Genetic mutations
  - Leiden factor V (activated protein C resistance = APCR)
  - Prothrombin G20210A
  - Methyltetrahydrofolate reductase (MTHFR) C677T & A1298C

- Autoimmune phenomena (antiphospholipid antibodies)
  - Lupus anticoagulant
  - Anticardiolipin Abs
  - Anti-β-2-glycoprotein I Abs
  - Antiphosphatidylserine Abs

- Other
  - Lipoprotein (a)
  - Sickle cell screen
  - Dehydration
  - Acute infection/inflammation
  - Nephrotic syndrome
  - Inflammatory bowel disease
  - Paraneoplastic syndrome
TIA/AIS 2º STROKE PREVENTION
EXTRACRANIAL CAROTID STENOSIS

No difference between procedures (CEA & CAS) in CREST

- **Indication**
  - Symptomatic pts ≥ 50% stenosis by angio
    (> 70 % duplex, CTA, or MRA)

- **Outcomes**
  - No overall difference in stroke, MI, death between carotid endarterectomy (CEA) & carotid angioplasty with stenting (CAS)
  - CEA less strokes, esp. in pts ≥ 70
  - CAS less MIs (but pts w/ MI reported better quality of life than those w/ strokes)

- **Timing** – 2 d (TIA/minor AIS) to 2 wk

- **Post-procedure antiplatelet therapy**
  - CEA – ASA only
  - CAS – ASA + clopidogrel x 2-4 mo, then only ASA

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**No difference between procedures (CEA & CAS) in CREST**

*Brott et al. NEJM 2010;363:11  CREST*
PARTIAL (FOCAL) SEIZURE

DEFINITION & DESCRIPTION

- Abnormal \( \uparrow \) activity in a focal area of the brain, usually lasting secs to mins
- Following \( \uparrow \) activity, there is often a time of \( \downarrow \) activity in the same brain focus (postictal state) lasting mins to hours
- Symptoms vary based on location of brain focus (e.g., motor, sensory, visual, psychic)
- Simple-partial seizure \( \rightarrow \) no change in LOC
- Complex-partial seizure \( \rightarrow \) change in LOC
- Implies a focal brain lesion is present (e.g., stroke, tumor, abscess, gliotic scar) – look for one on MRI
PARTIAL (FOCAL) SEIZURE
FEATURES MOST CONSISTENT WITH SEIZURE

NEUROLOGIC SYMPTOMS
- Often stereotypical (previous similar spells)
- May be preceded by epigastric or psychic aura (e.g., déjà vu)
- Migratory (traveling) over secs
- Usually positive
  - Visual – flashing lights
  - Sensory – tingling
  - Motor – tonic (stiff), then clonic (shaking)
- ↓ consciousness w/ postictal confusion (complex partial)

ASSOCIATED FEATURES
- Amnesia for the event (complex partial)
- Possible abnormal exam
- Possible abnormal tests, esp. MRI, EEG, glucose, other chemistries
MIGRAINE: WHAT IT IS NOT
MIGRAINE DOES NOT MEAN HEADACHE

“Headache is never the sole symptom of migraine, nor indeed is it a necessary feature of migraine attacks.”

Oliver Sacks, Migraine, Revised & Expanded, 1992

A book intended for laypersons with multiple descriptions of the varied symptoms (“phenomenology”) of migraine. Heavy reading, but very informative.

Oliver Sacks also wrote the book Awakenings, later turned into a movie in which Robin Williams played the role of Oliver Sacks.
HEADACHE VS. MIGRAINE: SYMPTOM VS. SYNDROME

■ Headache
  ➢ Pain in the head

■ Migraine
  ➢ A syndrome of episodic brain dysfunction with systemic manifestations (that may include headache)

Migraine—a “primary headache” disorder—is by far the most common cause of recurrent, episodic headache without sequelae, but actually may present with no headache at all and migraine with NO headache is very common.
THE PARALLELS BETWEEN SEIZURE & MIGRAINE

Seizure
- Episode of abnormal electrical activity in the brain
- ↑ activity (seizure) followed by ↓ activity (postictal state)

Epilepsy
- Condition in which a person has a predisposition to seizures

Migraine attack
- Episode of abnormal chemical activity in the brain
- ↑ activity (cortical spreading excitation) followed by ↓ activity (cortical spreading depression)

Migraine
- Condition in which a person has a predisposition to migraine attacks

Like many other neurologic conditions, it is likely that epilepsy & migraine are channelopathies, i.e., due to dysfunction of neuronal ion channels with resultant hyperexcitable neurons.

Think of migraine as a slow-motion seizure.
Genetic condition in which a person has a predisposition to suffering recurrent transient episodes (attacks) of brain dysfunction with systemic manifestations that may include:

- **headache/neck pain** – from mild to severe, variable location
- **focal neurologic symptoms** – mimics stroke/TIA
- **GI symptoms (upper or lower)** – equals IBS, mimics gallstones
- **chest pain** – mimics heart attack, equals atypical noncardiac CP
- **autonomic dysfunction** – BP, pulse, sinus congestion, etc.

“triggered” by environmental, hormonal, or other physiologic changes, and consisting of **4 possible phases** (prodrome, aura, pain, postdrome).
TRIGGERING A MIGRAINE ATTACK: MIGRAINEURS HAVE LOWER THRESHOLD

ATTACK THRESHOLD

WITHOUT MIGRAINE GENE

WITH MIGRAINE GENE

MINOR TRIGGER

MAJOR TRIGGER
CLINICAL PHASES OF A MIGRAINE ATTACK – OVERVIEW

- **Entire Migraine** – Dysautonomia with GI & vascular changes
  - GI – Nausea, vomiting, diarrhea, constipation, dyspepsia
  - Vascular – BP ↑ or ↓, arrhythmias, vasoconstriction/vasodilatation
- **Prodrome** – Changes in mood, cognition, appetite
- **Aura** – Focal neurologic symptoms (migratory & progressive)
- **Pain** – Headache, sensory phobias, sinus congestion (vasodilatation)
- **Postdrome** – Migraine hangover

After Blau JN. Lancet. 1992
MIGRAINE PATHOPHYSIOLOGY
A JIGSAW PUZZLE WITH MISSING PIECES

Trigger ➔ Hypothalamic dysfunction & hyperexcitable cortex (esp. occiput) ➔ Prodrome

“Cortical spreading depression” (excitation/depression w/ hyperemia/oligemia, esp. occiput) ➔ Aura

Spreading depression in insula or brainstem serotonergic & noradrenergic dysfunction ➔ Dysautonomia

CN V/cervical root sensitization with pain receptor stimulation & release of neuropeptides (e.g., CGRP) ➔ Head & neck pain (+ sensory phobias & cranial arterial changes, e.g., sinus congestion)

Platelet & serum serotonin levels decrease during attacks of migraine, tension headache, IBS, & PMS.
Cerebral serotonin & magnesium decrease during a migraine attack.
MIGRAINE TRIGGERS: EXTERNAL & INTERNAL CHANGES

- Environmental changes
  - Barometric pressure (weather, altitude), motion
  - Scents, smoke, fumes

- Hormonal changes
  - Stress (esp. stress “letdown”), exercise, thyroid
  - Estrogen > progesterone—menarche, pregnancy, hormonal contraceptives, menopause, ovulation/menstruation

- Sleep changes
  - Deficiency or excess, change in shift

- Diet changes
  - Hunger, dehydration
  - Alcohol (all types, but esp. red wine)
  - Artificial foods (nitrates/nitrites, MSG, sulfites, aspartame, sucralose)

- Other physiologic changes / medical conditions
  - Head trauma, fever
  - Cerebral blood flow changes (AVM, endarterectomy/angioplasty, ischemia—e.g., paradoxical embolism via PFO)

Triggers can be additive, i.e., having multiple triggers at one time makes a migraine attack more likely than having one trigger alone.
MIGRAINE PHASES: PRODROME/PREMONITORY*

1. Prodrome
2. Aura
3. Pain
4. Postdrome

- Mood changes
  - Irritability, depression/hypoactivity, euphoria/hyperactivity
- Difficulty concentrating
- Stiff neck
- Fatigue, malaise, yawning
- Autonomic/GI symptoms
  - constipation, diarrhea, urinary frequency
- Anorexia or food cravings
  - esp. foods that increase serum serotonin and/or magnesium, e.g., chocolate, bananas, nuts, peanut butter, sweets, fatty foods

May begin hours to days before attack, persist through all 4 phases—likely related to serotonin, magnesium, hypothalamic changes

*ICHD-3 suggests elimination of the term “prodrome” & substituting “premonitory” instead
MIGRAINE PHASES:
AURA (1 of 2)

- Transient neurologic symptoms
  - Due to cortical spreading excitation/depression
  - Symptoms referable to location of transient chemical changes in cerebral cortex

- Pattern of symptoms
  - Recurrent & stereotypical (previous similar spells)
  - Gradual onset
  - Migratory (1 part of body to another) over mins to hrs
  - Progressive (1 type of symptom to another)
  - Duration minutes to hours

Chemical chain reaction in the brain leads to focal symptoms that change—in location & type—during an attack
MIGRAINE PHASES:
AURA (2 of 3)

Types of focal neurologic symptoms

- Visual—Usually positive (scintillation) followed by negative (scotoma)
  - Shimmering, scintillating, flashing lights
  - Spots, dots, bubbles, lines (zigzag, wavy, heat off pavement)
  - Any color, but often silver, gray, or clear
  - Usually associated w/ motion, e.g., moving, vibrating, coalescing
- Sensory—Usually positive (tingling) followed by negative (numbness)
- Motor—Hemiparesis (= “hemiplegic migraine”)
- Cognitive—Aphasia, confusion, amnesia, olfactory hallucinations
- Brainstem/temporal lobe—
  - Vertigo, ataxia, diplopia, tinnitus, dysarthria, ↓ consciousness
MIGRAINE PHASES:
AURA (3 of 3)

More types of neurologic symptoms

- Autonomic nervous system/insula/brainstem
  - GI symptoms – Nausea/vomiting, anorexia, dyspepsia, abdominal cramping, flatulence, diarrhea, constipation
  - Cranial dysautonomia – Horner syndrome, sinus congestion/epistaxis, facial/scalp flushing (e.g., red ear)
  - Temperature changes – Hypothermia, mild fever
  - Cardiovascular changes – Hypertension, hypotension, syncope, palpitations, arrhythmias

*Migraine causes headache & transient hypertension, but hypertension does not cause headache*
MIGRAINE PHASES: PAIN

- Headache characteristics—No specific pattern
  - Location variable
    - Unilateral, bilateral
    - Anterior (frontal, periorbital, etc.), posterior (occipital, neck)
    - Diffuse, focal (e.g., nummular = coin-shaped)
  - Throbbing, pulsating, pounding, pressure, squeezing, dull, aching
  - Severe, moderate, mild, absent
  - Onset usually gradual; duration hours, days, weeks

- Associated symptoms
  - Sensory phobias – photo, phono, kinesio, thermo, osmo
  - Allodynia – pain due to light touch, breeze, hair moving, etc.
  - “Lightheadedness” – vibratory or buzzing paresthesia in head

Trigeminal nerve (CN5) & cervical nerve root sensitization in the meninges results in headache, sensory phobias, neuropathic symptoms
MIGRAINE PHASES: POSTDROME

- Fatigue, malaise
- Difficulty concentrating
- Mood changes
- Muscle aches
- Scalp tenderness
- Food cravings or anorexia

The migraine hangover
MIGRAINE WITH AURA
“OFFICIAL” DEFINITION PER ICHD-3

“Recurrent attacks, usually lasting minutes, of unilateral fully reversible visual, sensory, or other central nervous system symptoms that usually develop gradually and are usually followed by headache and associated migraine symptoms.”

- Frequency: ≥ 2 attacks
- Aura: ≥ 1 of the following fully reversible aura sxss
  - visual
  - sensory
  - speech &/or language
  - motor
  - brainstem
  - retinal

- Characteristics: ≥ 2 of 4 following
  - ≥ 1 aura sx spreads gradually over ≥ 5 min &/or ≥ 2 sxss occur in succession
  - each individual aura sx lasts 5-60 min (though motor sxss may last 72 h & “persistent aura without infarction” may last ≥ 1 wk)
  - ≥ 1 aura sx is unilateral (incl. aphasia)
  - aura accompanied, or followed w/in 60 min, by HA

- No other cause of sxss

Cephalalgia 2013;33(9):629-808
MIGRAINE WITH AURA
PREVIOUS TERMS & TYPES PER ICHD-3

**PREVIOUS TERMS**
- Classic or classical migraine
- Ophthalmic migraine
- Hemiparesthetic migraine
- Hemiplegic migraine
- Aphasic migraine
- Migraine accompagnée
- Complicated migraine

**TYPES**
- Migraine w/ typical aura
  - Visual or sensory aura
  - With or without headache
- Migraine w/ brainstem aura
  - Dysarthria
  - Vertigo
  - Tinnitus
  - Hypacusis
  - Diplopia
  - Ataxia
  - ↓ level of consciousness
- Retinal migraine (monocular)
- Hemiplegic migraine
MIGRAINE WITH “TYPICAL” AURA DESCRIPTIONS PER ICHD-3

- Migraine w/ visual aura
  - Most common (> 90%) aura
  - Fortification spectrum – zigzag figure that may gradually spread & assume laterally convex shape w/ angulated scintillating edge, leaving absolute or relative scotoma in its wake
  - Scotoma without positive phenomenon may occur
  - May occur with or without headache

- Migraine w/ sensory aura
  - 2nd most frequent aura
  - Pins & needles moving slowly from point of origin affecting 1 side of body, face, &/or tongue
  - Numbness may occur in its wake
  - Numbness may also be the only symptom
  - May occur with or without headache
HEMIPLEGIC MIGRAINE (HM) ASSOCIATED SXS & TYPES PER ICHD-3

- Often associated w/ “typical aura” & “brainstem” symptoms
- May be associated with change in consciousness (incl. coma), confusion, coma, fever, CSF pleocytosis
- Familial HM type 1 (CACNA1A)
  - Mutation in calcium channel gene on chromosome 19
- Familial HM type 2 (ATP1A2)
  - Mutation in K/Na-ATPase gene on chromosome 1
- Familial HM type 3 (SCN1A)
  - Mutation in sodium channel gene on chromosome 2
- Familial HM other loci
- Sporadic hemiplegic migraine
  - Same prevalence as familial HM
COMPLICATIONS OF MIGRAINE PER ICHD-3

- Status migrainosus
  - Debilitating attack lasting > 72, often caused by medication overuse
- Persistent aura without infarction
  - Aura symptoms ≥ 1 week with normal neuroimaging
- Migrainous infarction
  - Cerebral infarction occurring during course of typical migraine with aura attack
  - Does NOT include cerebral infarction coexisting with or presenting with symptoms resembling migraine with aura
- Migraine aura-triggered seizure
  - Seizure triggered by an attack of migraine with aura (= migralepsy)
  - Does NOT include common phenomenon of migraine-like headache in epileptic postictal period

Per DLG: 1. Migrainous infarction nearly always occurs in the setting of an underlying hypercoagulable state.
2. Cerebral ischemia (infarction or TIA) can trigger migraine
**MEDICATION-OVERUSE SYNDROME/ ANALGESIC REBOUND HEADACHE**

*Near-daily use of certain drugs—esp. migraine abortive agents—causes migraine symptoms to be constant*

- **Caused by:**
  - Analgesic*, triptan, decongestant, or muscle relaxant use > 2 days/week (*except for prescription naproxen)
  - Any use of ondansetron, PPI, or dipyridamole

- **Relationship to migraine:**
  - More common in migraineurs
  - Changes migraine symptoms from intermittent to chronic (incl. headache, GI, chest pain, visual, tingling, vertigo, hemiplegia, etc.)
  - Common cause of chronic migraine & status migrainosus
  - Renders all migraine therapies ineffective

- **Treatment:** Avoid all analgesics, triptans, muscle relaxants, decongestants, etc. x > 4 weeks
MIGRAINE AURA
FEATURES MOST CONSISTENT WITH MIGRAINE

**Neurologic sx$s**
- Stereotypical (previous similar spells)
- Gradual onset
- Migratory (traveling) x mins to hrs
- Progressive (1 to another)
- Classic, often positive, visual sx$s
  - Flashing lights
  - Spots, dots, zigzag lines (usually moving, often silver, gray, clear, or shimmering)
- Positive sensory sx$s
  - Tingling
  - Limb or chest pain
- Vertigo
- Confusion, amnesia, syncope
- Duration hours (or longer with medication overuse syndrome)

**Associated features**
- Past/family hx of migraine (?)
- Identifiable triggers
  - $\Delta$ stress, exercise
  - $\Delta$ estrogen, thyroid
  - $\Delta$ weather, sleep, diet
  - $\Delta$ cerebral blood flow
  - EtOH, scents, artificial foods
  - Head trauma, motion, fever

**Associated features**
- Sensory phobias (photo, phono, kinesio, thermo, osmo)
- Nausea, vomiting
- Diarrhea, abdominal cramping
- Sinus congestion/epistaxis
- Hypertension or hypotension
- Normal exam
- Normal tests (DWI/ADC)
LATE-LIFE MIGRAINE ACCOMPANIMENTS
OF C. MILLER FISHER

- Mid-life (age 50-60) flurry of symptoms
- Scintillating scotomata
- Buildup of scintillations
- March of paresthesias
- Progression from 1 symptom to another
- 2 or more identical spells
- Concurrent headache in 40-50% of pts
- Episodes last 15-25 min
- Generally benign course
- Normal angiography
- Exclusion of stroke or epilepsy

Now, normal DW MRI—though not necessary if history is clear

Can J Neurol Sci 1980;7:9
Stroke 1986;17:1033
GIVING IV TPA TO THE WRONG PATIENT: DON’T WORRY, IT’S MIGRAINE

- Many pts receive IV tPA for a presumed stroke don’t actually have stroke—range 4-24%
- Migraine is the most common diagnosis among these pts*
- “Normal” people who receive IV tPA nearly always have good outcomes

*Both acute ischemic stroke & migraine cause sudden-onset focal neurologic deficits with normal CT & labs (& migraine is MUCH more common than conversion reaction).

When in doubt, give tPA!
HOWEVER, NOT DIAGNOISING MIGRAINE LEADS TO WASTED DOLLARS & LIVES

- Imaging studies (CT, MRI, endoscopy, colonoscopy, etc.)
- Medications
  - Antibiotics (bacterial resistance)
  - Decongestants (chronic nasal congestion, HTN, chronic symptoms)
  - Anxiolytics, antidepressants (social consequences of false diagnosis)
  - Antithrombotic agents (hemorrhage)
  - Narcotics (chronic symptoms, drug-seeking behavior caused by docs)
- Surgeries
  - Gallbladder
  - Uterus and ovaries
  - Sinus and ear
- Disability, retirement, divorce
- Iatrogenic functional overlay (psychiatric symptoms superimposed on “organic” symptoms)
MRI BRAIN ISCHEMIC STROKE: HYPERACUTE FINDINGS

- **DWI & ADC**: Early infarction visible (within first few mins)
- **FLAIR**: No signal changes; possible sulcal effacement in area of infarction

*DWI = diffusion-weighted imaging; ADC = apparent diffusion coefficient
FLAIR = T2-weighted image w/ black standing water (e.g., CSF)*
MRI BRAIN ISCHEMIC STROKE: ACUTE-TO-SUBACUTE FINDINGS

- **DWI & ADC**
  - Signal changes persist for ~ 14 days

- **FLAIR**
  - Shows signal changes that persist indefinitely
TRANSIENT NEUROLOGIC DEFICIT > 1 H: MRI BRAIN DISTINGUISHES “TIA” & MIGRAINE

- Pts w/ cerebral ischemia significantly more likely to have abnormal DWI MR if Sxs last > 1 hour

**DWI MR scans of two patients showing acute ischemia (within minutes to 14 d)**

Patients who have migraine aura will have normal DWI even if symptoms last hours to days

Crisostomo RA et al. Stroke 2003;34:932
MRI BRAIN PARTIAL SEIZURE: MAY MIMIC TIA/STROKE ON DWI

- Pts w/ prolonged seizure may have abnormal DWI MR during postictal state, mimicking stroke—but FLAIR will never turn positive

*DWI MRI of a 39-year-old man w/ AIDS, cryptococcal meningitis, & prolonged partial seizure w/ right hemibody shaking, showing increased signal in left medial frontal area*
MRI BRAIN MIGRAINE WITH AURA: CHRONIC CHANGES ON T2 & FLAIR

- Deep-white matter “UBOs” common in migraine w/ aura
  - White on T2 & FLAIR
  - Not seen on DWI & ADC
  - Located at gray-white junction
  - Small, round, indistinct borders
  - Often confused with:
    - Multiple sclerosis plaques
    - Strokes (“small-vessel disease,” “arteritis,” “vasculitis”)
  - Significance & cause unknown
  - Further evaluation not necessary
  - Reassure patient

Kruit MC et al. JAMA 2004;291:427
MIGRAINE WITH AURA & VASCULAR RISK

- Women’s Health Study; mean 10-y f/u
- Prospective cohort study, 27,840 US women ≥ 45 y, free of cardiovasc. disease (CVD) or angina at entry
- 1° outcome—first nonfatal IS, MI, or isch vasc death
- Migraine without aura—no ↑ CVD risk
- Active migraine w aura—2x ↑ CVD risk
  - Major CVD—HR 2.15, p < .001
  - Ischemic stroke (IS)—HR 1.91, p=.01
  - Myocardial infarction (MI)—HR 2.08, p=.002
  - Coronary revascularization—HR 1.74, p=.002
  - Angina—HR 1.71, p=.007
  - Ischemic vascular death—HR 2.33, p=.01

Kurth T et al. JAMA 2006;296:283
Both lisinopril (ACE-I) and candesartan (ARB) have been shown to be effective migraine prophylactic agents.

Schrader H et al. BMJ 2001;322:1
Tronvik E et al. JAMA 2003;289;65

Migraine w/ aura pts ≥ 45 y have ↑ CVD risk
ACE-Is & ARBs ↓ CVD risk beyond effect on BP
Thus, Rx all migraine w/ aura pts (esp. those ≥ 45 y) w/ lisinopril or candesartan?
TRANSENT NEUROLOGIC DEFICIT MANAGEMENT WHEN DX UNCERTAIN

- TIA vs. Migraine
  - Lisinopril or **candesartan**
  - ECASA 81 mg daily

- Seizure vs. Migraine (or both)
  - Topiramate or divalproex first line
  - Gabapentin, lamotrigine, or levetiracetam second line
CASE 1: APHASIA
Presentation—Diagnosed as Stroke by Referring Hospital

- 58-year-old woman transferred from outside hospital (by a primary-care physician) for “acute stroke”
- Found to have psychiatric aphasia on exam
- History of “pseudoseizures,” “gastroparesis,” and “anxiety with noncardiac chest pain”
- Admitted 18 times to 3 different hospitals in last 6 months with normal EEGs, video EEGs, cardiac catheterizations, upper endoscopy, & colonoscopy
- Has had 1 year of constant headache and lower abdominal cramping pain and daily diarrhea for which she takes daily Lortab & Reglan
- Current episode occurred after one of her typical “pseudoseizures”
CASE 1: APHASIA

Clarification & Outcome

Clarification of “pseudoseizure” episodes:
- First lightheadedness, then loss of consciousness and tone
- Rapid awakening w/ vertigo, nausea, vomiting, headache, confusion

Final diagnoses:
- Syncopal migraine
- Migraine with vertigo aura
- Abdominal migraine
- Precordial migraine
- Medication overuse syndrome
- Functional overlay (aphasia)

Outcome:
- On topiramate, all symptoms markedly improved & patient went to the ED only 4 times in next 4 years

The patient does NOT have stroke, pseudoseizures, gastroparesis, or anxiety-induced chest pain.

REAL DIAGNOSIS: MIGRAINE
CASE 2: LEFT HEMIBODY PAIN & BLINDNESS

Presentation—Diagnosed as MS by Resident

- 28-year-old tearful woman with “pain all over,” unable to move L side due to pain and with bilateral blurred vision
- Six weeks ago, had difficulty holding objects in L hand, then noted “waves of pain” in both shoulders radiating over minutes into both hands, L > R, followed by a lightning sensation into L thigh, radiating into L toes
- Lyrica caused intolerable lethargy, Cymbalta ineffective after 1 month
- One month ago, symptoms became constant without relief from daily Fentanyl patch, Tylenol, ibuprofen, Lortab, and Dilaudid
- Lost nursing job 3 weeks ago when she became bedbound with daily vertigo and occipital headache radiating to R temple & eye
- For last week, severe R chest pain (R anterior axilla to upper back)
- For last few days, blurred vision in both eyes, initially intermittent, then constant
- For one day, nausea and vomiting
CASE 2: LEFT HEMIBODY PAIN & BLINDNESS
Clarification & Outcome

- Blurred vision = whitish-tan wavy lines or “heat-off-the-pavement” throughout her vision in both eyes
- Since early childhood
  - Intermittent headaches, bioccipital, radiating to right temple and eye with nausea, vomiting, sensory phobias, photopsia (star bursts), tingling (head, neck, both hands), & vertigo (saw multiple doctors for vertigo)
- For last few years, episodes of intermittent, severe R abdominal pain with bloating, nausea, vomiting, & diarrhea daily for 1 week, followed by constipation for days, then recurrent abdominal pain; no gallstones; cholecystectomy did not help
- Diagnoses: Status migrainosus due to medication overuse syndrome, migraine with aura (visual, sensory, vertigo), abdominal migraine, precordial migraine, depression with anxiety
- Management: All analgesics discontinued except prescription naproxen; topiramate & venlafaxine begun; 3 weeks later, patient markedly improved, started new RN job, &, after 3 days promoted to manager

REAL DIAGNOSIS: MIGRAINE
CASE 3: INTRACTABLE VERTIGO EPISODES

Presentation—Conflicting Expert Diagnoses

- 80-year-old distraught man with intractable, intermittent, 12-hour episodes of vertigo, diplopia, ataxia, nausea, and vomiting occurring every 5-6 days that left him disabled and housebound
- MRI brain normal
- Symptoms became constant several months ago despite taking daily Voltaren, Protonix, and Zofran
- Famous quaternary referral center #1 – no diagnosis
- Famous quaternary referral center #2 – progressive, degenerative disease (multisystem atrophy)
- On exam, he had gait ataxia
CASE 3: INTRACTABLE VERTIGO EPISODES

Family History & Outcome

- His sister has similar episodes
- With candesartan and magnesium oxide, symptoms markedly improved—over next 6 months, patient had no vertigo, diplopia, nausea, or vomiting; he had persistent, mild, 1-hour episodes of gait ataxia upon awakening two days a week that resolved by late morning and did not interfere with his activities of daily living

REAL DIAGNOSIS: MIGRAINE
CASE 4: HEMIBODY TINGLING
Diagnosed as Stroke by Experts

53 yo postmenopausal, healthy woman w/ hypertension

- While participating in a tennis lesson, noted tingling in the left leg that gradually progressed to involve the left arm over minutes
- Later than evening, noted the tingling over her left neck and jaw
- MRI brain and carotid duplex normal (MRI only showed UBOs)
- For the last 23 years, has history of migraine visual aura with or without headache (left hemicranial throbbing) consisting of moving black spots in the right visual field, moving to the left visual field
- Headache specialist and neurologist diagnosed her with stroke and advised her to discontinue hormonal therapy and begin aspirin 81 mg daily

REAL DIAGNOSIS: MIGRAINE
CASE 5: RECURRENT HEMIPLEGIA W/ NORMAL MRI

Given IV TPA for All Four Episodes

- 74 yo woman w/ no vascular risk factors (other than age) has 4 episodes of hemiplegia (3 on right and 1 on left) over 6 years
  - Received IV tPA for all 4 episodes w/ complete resolution of symptoms
  - MRI brain repeatedly normal, including no evidence of acute ischemia on DWI or old ischemia on FLAIR
  - No potential cause of stroke found (normal ECG, cardiac monitor, echocardiogram, MR angiography)
  - Given aspirin, clopidogrel, metoprolol, and pravastatin for stroke prevention
  - On careful questioning, long history of “sinus headaches” w/ photophobia
  - On careful questioning, each episode had same sequence of events:
    - Strange feeling of something not right
    - Facial weakness, then arm weakness, then leg weakness
    - After weakness, face numbness (lack of sensation), then arm numbness, then leg numbness
    - After numbness, “soreness” in left occiput and “tension” in neck
    - Complete resolution within 90 minutes
    - Photophobia with at least one of the episodes

REAL DIAGNOSIS: MIGRAINE
63 yo tearful woman with acute aphasia and left hemiparesis for which she received IV tPA at our institution
She has a history of schizophrenia, DM type II, HTN, obesity, intractable headache, chest pain spells, and “TIAs”
She was recently discharged from another hospital w/admission diagnosis TIA and discharge diagnosis conversion disorder
MRI brain normal (including DWI)—symptoms did not resolve after IV tPA—but did resolve after IV Mg sulfate & IV Depacon
Daughter has identical spells of chest pain and left hemiparesis for which she has been to hospital emergency departments multiple times

REAL DIAGNOSIS: MIGRAINE
CASES 7 & 8: MIGRAINOUS INFarCTION
Both Found to Have Hypercoagulable State

- 50 yo woman w/ retinal infarction during migraine visual aura typical for her; admits to daily diarrhea for 15 years
  - Found to be positive for lupus anticoagulant (hypercoagulable state)
  - Treated with anticoagulation and candesartan with no recurrent retinal infarctions and resolution of diarrhea

- 28 yo woman w/ occipital infarction during migraine visual aura typical for her, occurring one month after starting oral contraceptive
  - Found to have MTHFR gene mutation (hypercoagulable state)
REFERENCES

- Josephson SA, Sidney S, Pham TN, Bernstein AL, Johnston SC. Higher ABCD2 score predicts patients most likely to have true transient ischemic attack. Stroke 2008; 39:3096-3098.
Distinguish between TIA, seizure, and migraine as the cause of a transient spell
THE END