Broken heart, broken brain: A case report of Takotsubo syndrome leading to stroke
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Primary care headache management: tips and advances
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As physician co-leaders of Prisma Health–Midlands neuroscience service,
we share a vision to provide the most advanced neurology and neurological surgery treatments available to the residents of South Carolina. We are excited to share this latest edition of our neuroscience journal featuring a case report of Takotsubo syndrome leading to stroke plus tips for primary care headache management.

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Broken heart, broken brain:
A case report of Takotsubo syndrome leading to stroke

By Ketan Jhunjhunwala MD, PhD1,2, Tushar Trivedi, MD, MPH1,2, Souvik Sen MD, MS, MPH1,2
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Takotsubo means octopus trap in Japanese. Takotsubo syndrome (TS) is an acute cardiomyopathy, characterized by transient left-ventricular apical ballooning. TS is a new diagnostic entity, which mimics an acute myocardial infarction (MI), but is characterized by the absence of obstructive coronary artery disease[1]. It occurs exclusively in postmenopausal women and is frequently triggered by emotional stress. This condition favors formation of an intracardiac mural thrombus, although this seems to be an exceptional finding since thromboembolic complications occur in 0.8% of cases[2]. We report the case of patient who had an acute brain infarction (BI) with a fully documented TS.

Case Description:
A 58-year-old African American woman, with a past medical history of hypertension, presented with an acute chest pain in the context of a stressful situation. At the Emergency Department (ED), the clinical examination was normal, but the ECG showed diffuse T-wave inversion in V3-V6. There was a three-fold increase in troponin levels, but myoglobin was normal. Transthoracic echocardiogram (TTE) showed an extensive large apical akinetic area, an ejection fraction of 60%, and no apical thrombus. Coronary angiography was normal, but ventriculography confirmed an apical ballooning.

The association of an acute coronary syndrome (ACS) with apical ballooning at the TTE along with a normal coronary angiogram led to the diagnosis of TS. Four days later, the patient suddenly had a sudden onset right-sided hemiplegia which resolved initially when she came to the ED. About three hours later, the patient again had sudden onset expressive aphasia with NIH Stroke Scale (NIHSS) score of 5. ECG was in sinus rhythm. Patient was further evaluated with computed tomography angiography (CTA) head and neck (with and without contrast) and computed tomography brain perfusion (CTP). Patient’s CTA showed left middle cerebral artery (MCA) M2 occlusion and CTP showed a mismatch of 50 cc.

The patient was taken for thrombectomy after consent from her family. Thrombectomy was successful with thrombolysis in cerebral infarction
References
Yoshimura S, Toyoda K, Ohara T, Nagasawa H, Ohtani N, Kuwashiro T, Naritomi H, Minematsu K

Discussion
Yoshimura et al.[2] reported seven patients with TS discovered after a BI. TS occurred between 10 hours and 12 days after stroke. All patients were women, and six were age 75 years or older. Here, TS was thought to be a consequence of subarachnoid hemorrhage or BI including the insular cortex. In our case, the patient was also a postmenopausal woman, but TS preceded BI. The cardio embolic mechanism is self-evident as the wall motion abnormality of the apical region represents a condition for mural thrombus formation due to low blood flow in the apex of the left ventricle[1]. Patients with TS do not typically have coronary artery disease. Left ventriculogram shows characteristic regional ballooning involving the apical segments. TS is an uncommon cardiomyopathy, and a potential cause of mural thrombus formation in the left ventricle. Although the prognosis of TS is usually benign, it represents a risk of embolic BI, and stroke physicians need to maintain awareness of this fact.

Primary care headache management: tips and advances
By Nishanth Kodumuri, MD, PGY-3, Neurology; Souvik Sen, MD, Chair, Neurology

Headache is one of the most common reasons patients seek help from primary care physicians. The prevalence of headache is 66%; approximately 15% for migraine, 50% for tension headache, and <1% for cluster headache. South Carolina, like several other states in the US, has an acute shortage of neurologists and headache specialists, which often puts the responsibility of initial management on primary care physicians.

This article outlines information on management tips and indications for neurologist referral, based on the Guideline for Primary Care Management of Headache in Adults developed by a consortium of organizations and clinicians from Alberta, Canada. The initial algorithmic approach flow chart is depicted on page 8.

Physical examination of headache patient typically include the following elements:

• Screening neurologic examination
  - general assessment of mental status
  - cranial nerve examination
  - ophthalmoscopy, pupils, eye movements, visual fields, evaluation of facial movements for asymmetry and weakness
  - assessment for unilateral limb weakness, reflex asymmetry, and coordination in the arms
  - assessment of gait, including heel-toe walking (tandem gait)

• Neck examination
  - posture, range of motion, and palpation for muscle tender points

• Blood pressure measurement

• If indicated by other neurologic symptoms or signs on screening examination, a focused neurologic examination (e.g., lower cranial nerve examination in a patient with dysarthria, or plantar responses in a patient with reflex asymmetry)

• If indicated by associated jaw complaints, an examination for temporomandibular disorders
  - assessment of jaw opening
  - palpation of muscles of mastication for tender points

Consider the following when managing patients with migraine:

• Pay attention to lifestyle and specific migraine triggers in order to reduce the frequency of attacks. Lifestyle factors to avoid include the following:
  - irregular or skipped meals
  - irregular or too little sleep
  - a stressful lifestyle
  - excessive caffeine consumption
  - lack of exercise
  - obesity

• Use acute pharmacologic therapy for individual attacks
Red flags (address immediately)
- Thunder clap onset
- Fever and meningismus
- Papilledema (with focal signs or reduced LOC)

Urgent (address within hours)
- Temporal arteritis
- Papilledema (WITHOUT focal signs or reduced LOC)
- Relevant systemic illness
- Elderly patient: new headache with cognitive change

Possible indicators of secondary headache
- Unexplained focal signs
- Atypical headaches
- Unusual headache precipitants
- Unusual aura symptoms
- Onset after age 50
- Aggravation by neck movement; abnormal neck exam findings (consider cervicogenic headache)
- Jaw symptoms; abnormal jaw examination findings (consider temporomandibular joint disorder)

Table 1a. Acute migraine medications

<table>
<thead>
<tr>
<th>Type</th>
<th>Acute medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>First line</td>
<td>Ibuprofen 400 mg, naproxen sodium 500–550 mg, acetaminophen 1000 mg, aspirin 1000 mg</td>
</tr>
<tr>
<td>Second line</td>
<td>Triptans: oral sumatriptan 100 mg, rizatriptan 10 mg, almotriptan 12.5 mg, zolmitriptan 2.5 mg, eletriptan 40 mg, frovatriptan 2.5 mg, naratriptan 2.5 mg</td>
</tr>
<tr>
<td></td>
<td>Subcutaneous sumatriptan 6 mg if the patient is vomiting early in the attack. Consider for attacks resistant to oral triptans</td>
</tr>
<tr>
<td></td>
<td>Oral wafer: rizatriptan 10 mg or zolmitriptan 2.5 mg if fluid ingestion worsens nausea</td>
</tr>
<tr>
<td></td>
<td>Nasal spray: zolmitriptan 5 mg or sumatriptan 20 mg if patient is nauseated</td>
</tr>
<tr>
<td></td>
<td>Antiemetics: metoclopramide 10 mg for nausea</td>
</tr>
<tr>
<td>Third line</td>
<td>Naproxen sodium 500–550 mg in combination with a triptan</td>
</tr>
<tr>
<td>Fourth line</td>
<td>Fixed-dose combination analgesics (with codeine if necessary: not recommended for routine use)</td>
</tr>
</tbody>
</table>

Migraine (Table 1)
- Acute medications
- Monitor for medication overuse
- Prophylactic medication if:
  - Headache ≥ 3/d/mo and acute meds are not effective
  - Headache ≥ 8/d/mo (risk of overuse)
- Disability despite acute meds

Medication overuse
- Triptans, ergots, combination analgesics, codeine or other analgesics > 10 d/mo
- Acetaminophen or NSAIDs > 15 d/mo

Manage
- Educate patient
- Initiate prophylactic medication
- Provide an effective acute medication for severe attacks with limitation on frequency of use
- Gradual withdrawal of opioids if used, or combination analgesics with opioid or barbiturate
- AVOID opioids or barbiturates

Tension headache (Table 2)
- Acute medications
- Monitor for medication overuse
- Prophylactic medication (Table 3) if disability despite acute medication

Cluster headache (Table 3) or trigeminal autonomic cephalgia
- Management primarily pharmacologic
- Acute medication
- Prophylactic medication
- Neurologist referral

Hemicrania continua
- Neurologist referral

Behavioral management
- Keep headache diary: record frequency, intensity, triggers and meds
- Adjust life factors: reduce caffeine, ensure regular exercise, and avoid irregular inadequate sleep or meals
- Develop stress management strategies: relaxation training, CBT, pacing activity, bio feedback

Uncommon headache syndromes
- Frequent headache
- Severe
- Brief (< 3 hr per attack)
- Unilateral (always same side)
- Ipsilateral eye redness, tearing, restless or during attacks

Abbreviations
- NSAID: non-steroidal anti-inflammatory drug
- CBT: cognitive behavioral therapy
- LOC: level of consciousness
### Table 1. Prophylactic migraine medications

<table>
<thead>
<tr>
<th>Prophylactic medications</th>
<th>Starting dose</th>
<th>Titration,* daily dose increase</th>
<th>Target dose or therapeutic range†</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First line</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propranolol</td>
<td>20 mg twice daily</td>
<td>40 mg/wk</td>
<td>40–120 mg twice daily</td>
<td>Avoid in asthma</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>50 mg twice daily</td>
<td>50 mg/wk</td>
<td>50–100 mg twice daily</td>
<td>Avoid in asthma</td>
</tr>
<tr>
<td>Nadolol</td>
<td>40 mg/d</td>
<td>20 mg/wk</td>
<td>80–160 mg/d</td>
<td>Avoid in asthma</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>10 mg at bedtime</td>
<td>10 mg/wk</td>
<td>10–100 mg at bedtime</td>
<td>Consider if patient has depression, anxiety, insomnia, or tension headache</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>10 mg at bedtime</td>
<td>10 mg/wk</td>
<td>10–100 mg at bedtime</td>
<td>Consider if patient has depression, anxiety, insomnia, or tension headache</td>
</tr>
<tr>
<td><strong>Second line</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topiramate</td>
<td>25 mg/d</td>
<td>25 mg/wk</td>
<td>50 mg twice daily</td>
<td>Consider as a first-line option if the patient is overweight</td>
</tr>
<tr>
<td>Candesartan</td>
<td>8 mg</td>
<td>8 mg/wk</td>
<td>16 mg</td>
<td>Few side effects; limited experience in prophylaxis</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>300 mg/d</td>
<td>300 mg every 3–7 d</td>
<td>1200–1800 mg/d divided into 3 doses</td>
<td>Few drug interactions</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Divalproex</td>
<td>250 mg/d</td>
<td>250 mg/wk divided into 2 doses</td>
<td>750–1500 mg/d divided is possible</td>
<td>Avoid in pregnancy or when pregnant</td>
</tr>
<tr>
<td>Pizotifen</td>
<td>0.5 mg/d</td>
<td>0.5 mg/wk</td>
<td>1–2 mg twice daily</td>
<td>Monitor for somnolence and weight gain</td>
</tr>
<tr>
<td>Onabotulinum-toxinat</td>
<td>155–195 units</td>
<td>No titration needed</td>
<td>155–195 units every 3 mo</td>
<td>For chronic migraine only (headache on ≥ 15 d/mo)</td>
</tr>
<tr>
<td>Flunarizine</td>
<td>5–10 mg at bedtime</td>
<td>No titration needed</td>
<td>10 mg at bedtime</td>
<td>Avoid in patients with depression</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>37.5 mg/d</td>
<td>37.5 mg/wk</td>
<td>150 mg/d</td>
<td>Consider for migraine in patients with depression</td>
</tr>
<tr>
<td><strong>Over the counter</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnesium citrate</td>
<td>300 mg twice daily</td>
<td>No titration needed</td>
<td>300 mg twice daily</td>
<td>Effectiveness might be limited; few side effects</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>400 mg/d</td>
<td>No titration needed</td>
<td>400 mg/d</td>
<td>Effectiveness might be limited; few side effects</td>
</tr>
<tr>
<td>Butterbur</td>
<td>75 mg twice daily</td>
<td>No titration needed</td>
<td>75 mg twice daily</td>
<td>Effectiveness might be limited; few side effects</td>
</tr>
<tr>
<td>Coenzyme Q10</td>
<td>100 mg 3 times daily</td>
<td>No titration needed</td>
<td>100 mg 3 times daily</td>
<td>Effectiveness might be limited; few side effects</td>
</tr>
</tbody>
</table>

*Titration: Increase dose weekly by the amount specified in the daily dose increase column.
†Target dose or therapeutic range: The range of doses at which the medication is effective for prophylaxis.

### Table 2. Tension headache medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>Ibuprofen 400 mg</td>
</tr>
<tr>
<td>Aspirin</td>
<td>3000 mg</td>
</tr>
<tr>
<td>Naproxen sodium</td>
<td>500–550 mg</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>3000 mg</td>
</tr>
<tr>
<td><strong>Prophylactic First line</strong></td>
<td>Amitriptyline 10–100 mg/d</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>10–100 mg/d</td>
</tr>
<tr>
<td><strong>Second line</strong></td>
<td>Mirtazapine 30 mg/d</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>130 mg/d</td>
</tr>
</tbody>
</table>

### Table 3. Cluster headache medications

**Consider referral to neurologist**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>Subcutaneous sumatriptan 6 mg</td>
</tr>
<tr>
<td>Intranasal zolmitriptan 5 mg</td>
<td></td>
</tr>
<tr>
<td>100% oxygen</td>
<td>12 L/min for 15 min through non-rebreathing mask</td>
</tr>
<tr>
<td><strong>Prophylactic First line</strong></td>
<td>Verapamil 240–480 mg/d (higher doses might be required)</td>
</tr>
<tr>
<td><strong>Second line</strong></td>
<td>Lithium 900–1200 mg/d</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Topiramate 100–200 mg/d</td>
</tr>
<tr>
<td>Melatonin</td>
<td>Up to 10 mg/d</td>
</tr>
<tr>
<td>Galcanezumab</td>
<td>300 mg SC monthly</td>
</tr>
</tbody>
</table>

*If the patient has more than two attacks daily, consider transitional therapy while verapamil is built up (eg, 60 mg of prednisone for 5 days, then reduced by 10 mg every two days until discontinued).

### Table 4. CGRP-inhibitors, dose/administration, supporting evidence and FDA approval status

<table>
<thead>
<tr>
<th>CGRP-inhibitor</th>
<th>Dose/administration</th>
<th>Supporting trial</th>
<th>Avoid/caution</th>
<th>FDA approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erenumab (Aimovig)</td>
<td>70 mg SC monthly</td>
<td>ARISE episodic migraine</td>
<td>Hypersensitivity</td>
<td>May 2018</td>
</tr>
<tr>
<td></td>
<td>140 mg SC monthly</td>
<td>STRIVE chronic Migraine</td>
<td>Pregnancy Nursing</td>
<td>CVD*</td>
</tr>
<tr>
<td>Fremanezumab (Ajovy)</td>
<td>225 mg SC monthly</td>
<td>HALO episodic migraine</td>
<td>Hypersensitivity</td>
<td>September 2018</td>
</tr>
<tr>
<td></td>
<td>675 mg SC quarterly</td>
<td></td>
<td>Pregnancy Nursing</td>
<td>CVD</td>
</tr>
<tr>
<td>Galcanezumab (Emgality)</td>
<td>240 mg loading dose 120 mg SC monthly</td>
<td>EVOLVE-2 episodic migraine</td>
<td>Hypersensitivity</td>
<td>September 2018</td>
</tr>
<tr>
<td></td>
<td></td>
<td>REGAIN chronic Migraine</td>
<td>Pregnancy Nursing</td>
<td>CVD</td>
</tr>
<tr>
<td>Eptinezumab (NOT AVAILABLE)</td>
<td>1000 mg IV quarterly</td>
<td>PROMISE 1 episodic migraine</td>
<td>n/a</td>
<td>Pending</td>
</tr>
</tbody>
</table>

*Cardio and cerebrovascular disease

References:
Contact us for more information or to refer a patient

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