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Neuroscience Journal

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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

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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 angio (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

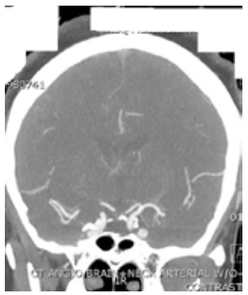


FIGURE A. | CTA showing left M2 clot (black arrow)

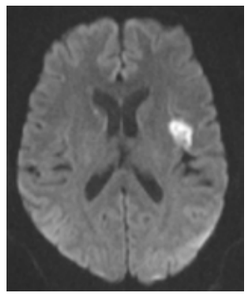


FIGURE B. | CTA showing left M2 clot (black arrow)

(TICI3). MRI done post thrombectomy showed focal acute cortical infarct in the left insula with associated lacunar infarct in the inferior right cerebellum. Continuous cardiac monitoring and Holter ECG did not detect atrial fibrillation (Afib) at any time during the course of the disease. A loop recorder was implanted and did not detect evidence of Afib as of the patient's last clinic follow up.

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. ◄

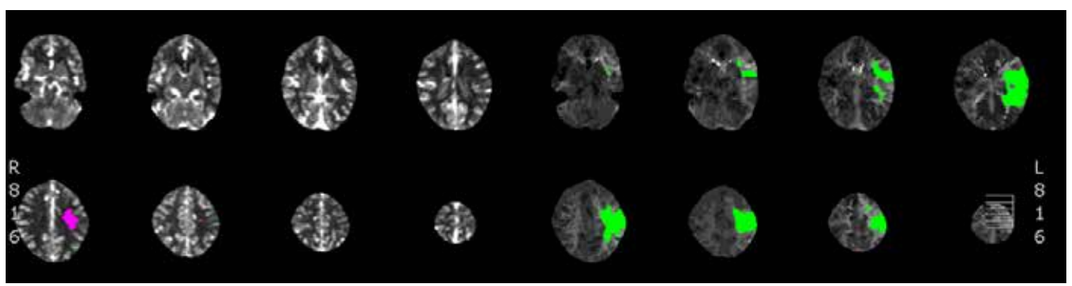


FIGURE C. | CT perfusion scan showing mismatch

References

1. Apical ballooning syndrome: an important differential diagnosis of acute myocardial infarction. Prasad A; Circulation. 2007 Feb 6; 115(5):e56-9.Yoshimura S, Toyoda K, Ohara T, Nagasawa H, Ohtani N, Kuwashiro T, Naritomi H, Minematsu K

2. Takotsubo cardiomyopathy in acute ischemic stroke. Yoshimura S, Toyoda K, Ohara T, Nagasawa H, Ohtani N, Kuwashiro T, Naritomi H, Minematsu K

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.

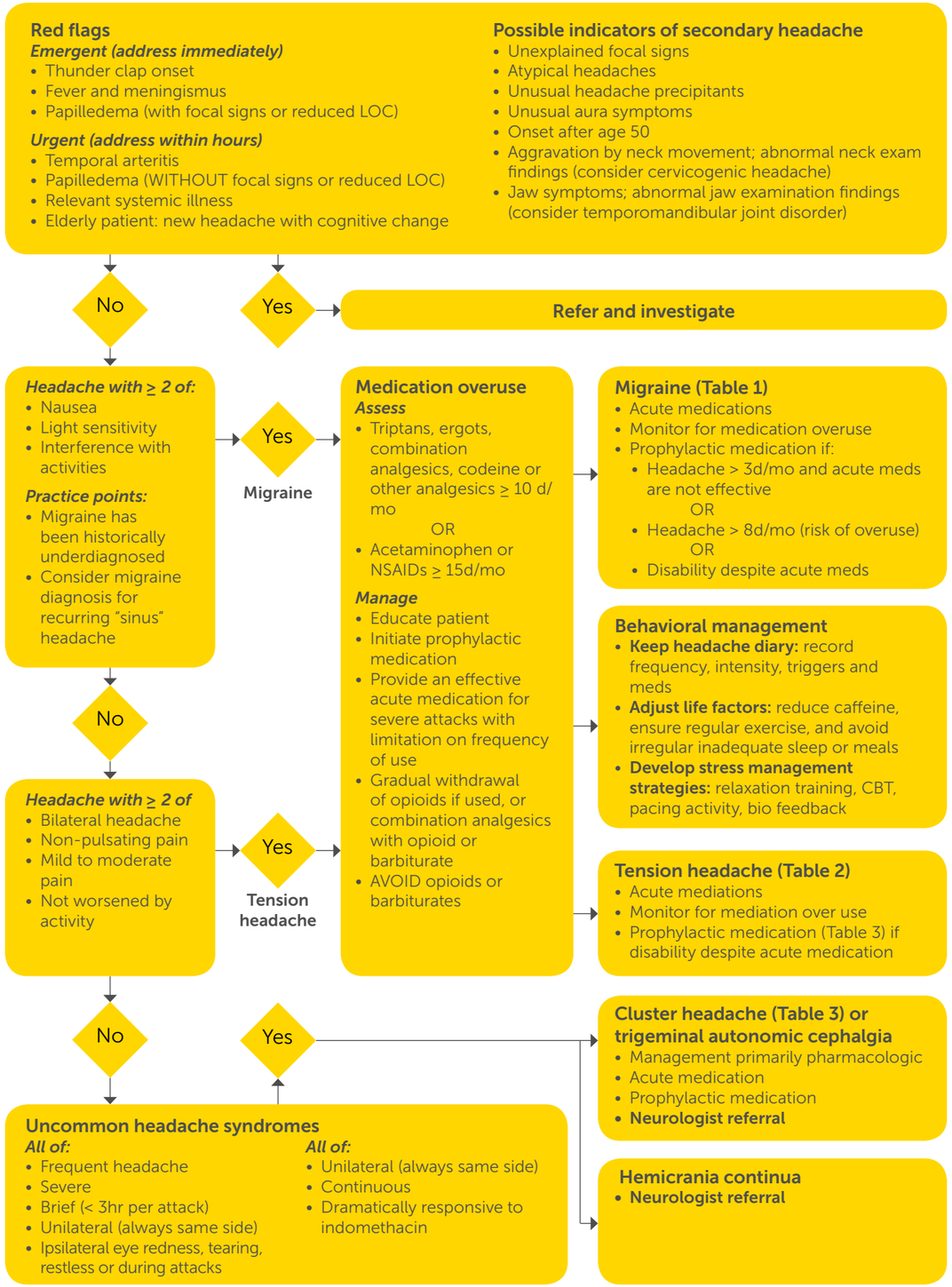
This article outlines information on management tips and indications for neurologist referral, based on the Guideline for Primary Care Management of Headache in Adults developed by a consortium of organizations and clinicians from Alberta, Canada. The initial algorithmic approach flow chart is depicted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



- Use prophylactic pharmacologic therapy, when indicated, to reduce attack frequency
- Use non-pharmacologic therapies
- Evaluate and treat coexistent medical and psychiatric disorders
- Encourage patients to participate actively in their treatment and to employ self-management principles:
  - -self-monitoring to identify factors influencing migraine
  - -managing migraine triggers effectively
  - -pacing activity to avoid triggering or exacerbating migraine
  - -maintaining a lifestyle that does not worsen migraine
  - -practicing relaxation techniques
  - -maintaining good sleep hygiene
  - -developing stress management skills
  - -using cognitive restructuring to avoid catastrophic or negative thinking
  - -improving communication skills to talk effectively about pain with family and others
  - -using acute and prophylactic medication appropriately

Monoclonal antibodies acting on the calcitonin gene-related peptide or on its receptor are new drugs to prevent migraine. Four monoclonal antibodies have been developed, one targeting the calcitonin gene-related peptide (CGRP) receptor (erenumab) and three targeting the CGRP molecule itself (eptinezumab, fremanezumab, and galcanezumab). Apart from the proven effectiveness, these antibodies are well-tolerated and could improve patient compliance due to the drugs' long half-lives allowing less frequent administrations. The status for these medications, dose/administration, supporting evidence and FDA approval status is listed in Table 4. ◄

Table 1a. Acute migraine medications

Type	Acute medications
First line	Ibuprofen 400 mg, naproxen sodium 500-550 mg, acetaminophen 1000 mg, aspirin 1000 mg
Second line	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 • Subcutaneous sumatriptan 6 mg if the patient is vomiting early in the attack. Consider for attacks resistant to oral triptans • Oral wafer: rizatriptan 10 mg or zolmitriptan 2.5 mg if fluid ingestion worsens nausea • Nasal spray: zolmitriptan 5 mg or sumatriptan 20 mg if patient is nauseated Antiemetics: metoclopramide 10 mg for nause
Third line	Naproxen sodium 500–550 mg in combination with a triptan
Fourth line	Fixed-dose combination analgesics (with codeine if necessary; not recommended for routine use)

Table 1b. Prophylactic migraine medications

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

Table 2. Tension headache medications

Medication	Dose
Acute	
Ibuprofen	400 mg
Aspirin	1000 mg
Naproxen sodium	500–550 mg
Acetaminophen	1000 mg
Prophylactic First line	
Amitriptyline	10–100 mg/d
Nortriptyline	10–100 mg/d
Second line	
Mirtazapine	30 mg/d
Venlafaxine	150 mg/d

Table 3. Cluster headache medications

Consider referral to neurologist)

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

*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

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

* Cardio and cerebrovascular disease

References
1) Becker WJ, Findlay T, Moga C, Scott NA, Harstall C, Taenzer P. Guidelines for primary care management of headache in adults. Canadian Family Physician. 2015; 61:670-79.
2) Sacco S, Bendtsen L, Ashina M, Reuter U, Terwindt G, Mitsikostas D-D, Martelletti P. European headache federation guideline on the use of monoclonal antibodies acting on the calcitonin gene related peptide or its receptor for migraine prevention. The Journal of Headache and Pain. 2019;20(6):1-33.

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