



## PALLIATIVE CARE CASE OF THE MONTH

### “Diagnosis and Medication Management of Post-operative and Migraine Headache”

by

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#### Case Part 1:

Ms. JA is a 49-year-old woman who presented to the ER with headache and nausea. She was two weeks post-op from resection of a low-grade glioma. In the ER, she received magnesium 2gm IV x 1 and ketorolac 15mg IV x 2, without reduction in the intensity of her headache. She was admitted and started on cyclobenzaprine 10mg every 8-hours orally and diphenhydramine 25mg IV every 8-hours scheduled, along with oxycodone 5mg every 4-hours as needed, as there was concern for tension-type headache. She was also started on ondansetron for nausea associated with her headache. Palliative care was consulted to assist with pain management for her persistent headache. Limited history was initially able to be obtained given her extremis from pain.

This case posed the following questions: (1) What is the etiology of the headache? (2) Which acute/abortive treatment options are available? (3) Which long-term prophylactic treatment options are available?

#### Determination of the type of headache:

The first step in acutely managing headache is to determine which type of headache the patient has—is the headache primary or secondary? Primary headaches are disorders by themselves and are caused by independent pathologic mechanisms; examples include migraine, tension-type, and cluster headaches.<sup>1</sup> Secondary headaches develop as a symptom secondary to another disorder; examples include tumor, post-craniotomy, trauma, meningitis, and medication overuse.<sup>1</sup> The International Headache Society (IHS) (<https://ichd-3.org>) provides an open-source listing of criteria for the diagnosis of specific headache types.

#### Case Part 2:

Initial concern was for a secondary headache mechanism given her recent surgery and known brain tumor. Potential secondary headache types included headache due to increased intracranial pressure secondary to tumor or edema and post-craniotomy headache. Initial imaging showed no evidence of residual tumor or edema. Therefore, it was felt that her headache was a post-craniotomy headache. She reported significant improvement in her headache following initiation of dexamethasone and promethazine. Additionally, opioids and ondansetron, which can cause headache, were discontinued.

Once her acute pain improved, a more thorough headache history was obtained. She reported onset of headache at age 16 coinciding with her menses. She described them as unilateral and throbbing, associated with photophobia, phonophobia, and nausea.

She denied aura. Given this description of her headaches, it was felt that she had underlying migraine headaches. She was taking Migralieve, an OTC treatment from England containing acetaminophen and codeine, which she reported provided effective relief. She reported throat swelling with previous sumatriptan use.

#### Emergency room and inpatient management of intractable headache:

A combination approach of targeting multiple mechanisms achieves synergy in the acute management of intractable migraine headache.<sup>2</sup> Medication classes include IV fluids, IV magnesium, dopamine agonists, NSAIDs, anti-epileptic medications, and steroids.<sup>2</sup> In addition to decreasing the headache itself, dopamine agonists, such as metoclopramide, prochlorperazine, promethazine, chlorpromazine, and haloperidol, have the added effects of aiding in the control of headache-associated nausea and of providing sedation, which can be beneficial as sleep also aids in the management of acute headache.<sup>2</sup> Vasoconstrictors, such as dihydroergotamine, and anti-seizure medications, such as valproic acid, can be considered, though these are recommended for use only by practitioners with experience, such as neurologists.<sup>2</sup> Opioids should be avoided in the acute management of headache as they have low efficacy.<sup>2</sup>

#### Abortive management of headache with migraine features:

In the setting of brain tumors, patients whose oncologic disease is controlled and demonstrates stable imaging may be treated similarly to patients with a primary headache type that is chronic.<sup>3</sup>

When a migraine headache occurs acutely, the best approach to treatment is to take abortive medication as soon as the headache onsets rather than waiting until the pain becomes severe. Some patients find relief with non-specific analgesic medications, including NSAIDs, aspirin, and acetaminophen. The triptan class of medications is effective in aborting acute migraine headache. The triptans come in multiple formulations, including oral tablet, ODT, subcutaneous, and intranasal. However, the triptans affect multiple serotonergic receptors, thus causing vasoconstriction; subsequently, triptans should be avoided in patients with known or risk-factors for cardiovascular disease.<sup>4,5</sup>

If nausea is a significant part of the headache semiology, metoclopramide, prochlorperazine, promethazine, and olanzapine are effective for the nausea as well as help augment the efficacy of the triptans and NSAIDs.

Abortive therapies should be limited in use to decrease the risk for development of medication overuse headache. Medication overuse headache typically does not occur if triptans are limited to fewer than 10 days per month and if NSAIDs are taken fewer than 10-15 days per month.

*Personal details in the case published have been altered to protect patient privacy.*

For palliative care consultations please contact the Supportive and Palliative Care programs at PUH/MUH, 412-647-7243, pager # 8511, Shadyside, 412-647-7243, pager # 8513, Perioperative/ Trauma Pain, 412-647-7243, pager # 7246, UPCI Cancer Pain Service, pager 412-644-1724, Magee Women's Hospital, pager 412-647-7243 pager # 8510, VA Palliative Care Program, 412-688-6178, pager # 296. Hillman Outpatient: 412-692-4724. For ethics consultations at UPMC Presbyterian-Montefiore and Children's pager 412-456-1518

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### Discussion Continued

Additionally, opioids and butalbital-containing medications (e.g. Fioricet) should be avoided, as they increase the risk of developing medication overuse headache in fewer than 10 days.<sup>6</sup>

The pathophysiology and treatment of headache is an active field of research. Within the past 1-2 years, multiple new migraine-targeted medications in the calcitonin gene-related peptide (CGRP) antagonist class have obtained FDA approval. For the acute treatment of headache, new CGRP-antagonist oral medications include two “gepant” medications (ubrogepant, rimegepant), and one “ditan” medication (lasmiditan). One advantage of the CGRP-antagonists is that they do not cause vasoconstriction.

### Prophylactic management of headache with migraine features:

For patients who have 3 or more functionally disabling headaches or 6-8 headache-days per month requiring acute treatment, prophylactic treatment should be considered.<sup>6</sup> Until recently, no targeted migraine prophylactic medications existed, and treatments were from other medication classes, including anti-seizure (topiramate, gabapentin), anti-depressant (tricyclic antidepressant, venlafaxine), and anti-hypertensive (calcium channel blocker, beta-blocker). Comorbid conditions such as insomnia, mood disorders, and seizure disorder should be considered when choosing a prophylactic medication. Botulinum toxin, an every-3-month injection, is an effective medication in the treatment of chronic migraine headache (more than 15 headache days per month, at least 8 of which are migraine).

The CGRP-antagonist class also has four monoclonal antibody medications available for migraine prophylaxis—erenumab, fremanezumab, galcanezumab, and eptinezumab. All are monthly subcutaneous injections except eptinezumab, which is an every-3-month IV infusion. Insurances typically require failure of an oral prophylactic medication prior to approval.

Non-pharmacologic measures form a cornerstone of migraine therapy, including behavioral interventions (biofeedback, CBT, and relaxation therapy), nutritional counseling, and sleep medicine (treatment of obstructive sleep apnea, insomnia).<sup>4</sup> Lifestyle management is a key aspect of headache management, including limiting caffeine intake to 8-12 oz daily and avoiding caffeine-containing abortive medications such as Excedrin, hydrating with 60-80 oz of water daily, eating regular meals and snacks, getting 6-8 hours of sleep per night, getting regular exercise (30-40 minutes/week, including yoga), keeping a regular routine, and avoiding artificial sweeteners. If medications have failed or are not tolerated, alternative options incorporate neuromodulation, including Cephaly and Nerivo devices.

### **Case Resolution:**

Ms. JA declined changing abortive medication or initiation of a prophylactic medication, citing that her baseline headaches were monthly and well-controlled with her current regimen. Given concern that her baseline migraine frequency and severity may increase in the post-operative setting as well as in the setting of increased stress, she was given a follow-up appointment in the palliative care clinic the following week. During that visit she reported continued efficacy of promethazine in aborting her headaches.

### **References:**

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