

THE WOMAN WITH DAILY WORSENING HEADACHE

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Case History

A 35-year-old woman presented with a 22-year history of headaches. Currently, the patient reports increasingly severe, daily, and persistent headache associated with persistent sensitivity to light, sound, and smell. On a daily basis, her headaches and neck pain are rated at 4 of 5 in severity with a holocephalic pattern and accompanying neck pain with stiffness. Periodically (3 to 4 times per week), she experiences more intense and throbbing headache, associated with nausea and vomiting.

The patient reports increasing headache intensity over the past several weeks. Anxiety with muscle twitching and cramps, periodic confusion, and depression have been noticeably worse during this time as well.

The patient has been treated by many physicians and clinics. Current medications include amitriptyline 150 mg at bedtime, fluoxetine 80 mg daily, 5 days per week use of butalbital/acetaminophen (up to 8 capsules per day), hydromorphone 12 mg (2 mg six times per day), and fentanyl 50 µg in the form of a fentanyl dermal patch every 72 hours. In the past several weeks, the dose of hydromorphone was raised, and zolmitriptan was introduced, which she now takes 3 to 4 days per week.

Her past medical history includes headache onset at age 13 years, characterized as episodic, throbbing, bilateral discomfort occurring 2 days prior to the onset of her menstrual periods. The headaches were associated with sensitivity to light and sound, nausea, and occasional vomiting. During her adolescent years, these headaches increased in frequency, and she began to use over-the-counter (OTC) analgesics. Over time, she was prescribed barbiturate-containing analgesics along with the OTC medications. By age 30 years, the patient was using mixed hydrocodone or oxycodone analgesics.

At age 31 years, the patient was involved in a motor vehicle accident. She experienced a flexion-extension neck injury, with aggravation of her headache and persistent neck pain since. At that time, her medications were changed, and she was administered hydromorphone in place of the other opioids. She also underwent physical therapy. Despite these efforts, as well as the addition of fentanyl to the hydromorphone, her symptoms worsened, including her depression. Numerous preventive medications for chronic headache were tried over the years without success. These included beta-adrenergic blockers, tricyclic antidepressants, valproic acid, topiramate, lamotrigine, methysergide, phenelzine, and COX-2 inhibitor nonsteroidal anti-inflammatory drugs.

Aside from the above, the patient is in generally good health. She reports that a physician recently diagnosed her as having “fibromyalgia” because her pain, which appeared to be spreading, now includes her shoulders and back.

Questions on the Case

Please read the questions, try to answer them, and reflect on your answers before reading the author’s discussion.

- What is the differential diagnosis of beginning episodically and transforming into daily headache?
- What studies are appropriate to help establish the diagnosis in this patient?
- What are the treatment options for this patient?
- Which of her symptoms are iatrogenic?

More Case History

Past diagnostic testing included blood studies, a magnetic resonance imaging scan of the brain and C-spine, and sinus images. These were all reported to be normal.

Upon examination, her blood pressure was 158/92 in both arms. Her pulse rate was 100 bpm and regular. She appeared anxious and slightly tremulous. She looked older than her stated age. Her mental status examination was normal, although her responses were slow and halting. Periodic myoclonic jerking was noted in her fingers and facial musculature. A mild distal postural tremor was noted. There was no evidence of neck bruit or cardiac murmur. Examination of her neck demonstrated limitation of motion in all directions with evidence of bilateral C2-3 facet tenderness. Short duration nystagmus was present in lateral gaze bilaterally. The remainder of her neurologic examination was normal.

Blood tests ordered included a urinary drug screening, liver function studies, electrolytes, blood urea nitrogen and creatinine, thyroid, hematologic studies, a high sensitivity C-reactive protein (CRP), erythrocyte sedimentation rate, and urinalysis. Results of these tests demonstrated normal findings, except for an elevated high sensitivity CRP at 6 and the presence of opioids and prescribed agents in her urine.

Physical assessment was undertaken and indicated depression with anxiety features.

Diagnoses

The patient was given a tentative diagnosis of transformed migraine, medication-overuse headache (rebound), post-traumatic (C2-3) cervical facet syndrome, and possible early serotonin syndrome. Opioid and barbiturate dependency was also present. Opioid-enhanced hyperalgesia, the result of chronic use of opioids, was considered likely.

Hospital Course

The patient was hospitalized on a specialty head pain unit. Her blood pressure was 140/90 with a pulse of 120 bpm and regular. She was administered intravenous fluids as well as chlorpromazine 5 mg tid and diphenhydramine 25 mg tid, both administered intravenously. Her amitriptyline dose was reduced by 50% and then discontinued soon thereafter, and the fluoxetine was discontinued on the day of admission. The butalbital/acetaminophen and zolmitriptan were discontinued abruptly. Clonazepam was administered orally at a dose of 0.5 to 1 mg tid and nadolol was administered orally at a dose of 20 mg bid. Opioids were titrated downward with discontinuance planned over 10 days.

Within 24 hours of admission, the patient's myoclonic jerking and sense of anxiety lessened, as did her tremor. Her head pain was reported as severe. The chlorpromazine and diphenhydramine doses were adjusted upward temporarily, which was moderately helpful. Intravenous fluids

were continued. On the fourth day of hospitalization, the patient began to experience symptoms of abdominal pain, increasing headache, and increasing irritability. Clonidine, via skin patch, was administered at a dose of 0.2 mg. The opioid downward titration was slowed. On the seventh day of hospitalization and after her blood pressure had normalized, dihydroergotamine was administered intravenously at a dose of 1 mg, 3 times per day. The chlorpromazine and diphenhydramine were discontinued, as was the intravenous fluid administration. Modest additional benefit was reported.

Sixteen days into her hospitalization, the patient was totally free of opioid medication; however, diarrhea and sleeplessness were problematic. Urinary drug screen was negative for opioids. She was experiencing moderately severe headaches. Intravenous fluids were again administered for 24 hours. An antidiarrhea agent was provided. A lumbar puncture was performed. Opening and closing pressures following removal of 12 mL of cerebral spinal fluid (CSF) were 17 cm/H₂O and 12 cm/H₂O, respectively. CSF fluid assessment results were normal. A magnetic resonance venogram showed normal results.

On the eighteenth day of hospitalization, the patient was administered a cervical facet block under fluoroscopic guidance. She reported dramatic reduction in neck pain following the block. This reduction lasted 3 days.

A cervical facet radiofrequency rhizolysis at C2-3 bilaterally was carried out. The patient noted reduction in headache as well as an improvement in mood. By the twenty-third day of hospitalization the patient was reporting a 2-point intensity headache (scale 1 to 5) and a mild neck pain.

During her hospitalization, the patient was attended by staff physicians, psychologists, physician assistants, and nurses on a daily basis. Family interviews were held, previous persons who treated her were consulted, and family meetings were arranged. Plans for outpatient follow-up and psychotherapy were detailed.

On the twenty-fifth day, the patient was discharged on a treatment program consisting of nadolol 40 mg bid, nortriptyline 50 mg per day, and topiramate 50 mg bid. Pro re nata (prn) medication included zolmitriptan 2.5 mg bid prn for severe headache with a limit of 2 days per week usage, tizanidine 2 to 4 mg tid prn, and indomethacin suppositories 50 mg tid prn. Her physicians were contacted. It was recommended that opioids be avoided and that she maintain regular psychotherapy and headache center visits.

Discharge diagnoses included transformed migraine, medication-overuse headache with opioid and barbiturate dependency, posttraumatic cervical facet syndrome, early serotonin syndrome, and psychological illness associated with medical illness.

Case Discussion

This is a characteristic case in tertiary/quaternary headache centers. This woman underwent the progression of an episodic migraine syndrome associated with menstruation to eventually develop chronic migraine, with comorbid neuropsychiatric symptoms and medication-overuse phenomena. Her principal headache condition was confounded by the medication escalation. Cervical trauma in her early thirties contributed a cervicogenic component and perhaps threshold-lowering influence to her primary headache disorder through cervical/trigeminal dynamics.

The 2004 International Headache Society (IHS) classification reserves the term “chronic migraine” for headache meeting IHS criteria for migraine with at least 15 days per month in the absence of medication overuse. The classification reserves the term “medication-overuse headache” for patients who improve within 2 months of detoxification. Therefore, the Silberstein–Lipton criteria from 1996 are sometimes used to describe these patients as having transformed migraine with medication overuse.

Pre-referral administration of increasing doses of amitriptyline and fluoxetine and the most recent addition of zolmitriptan likely contributed to the development of an early “serotonin syndrome” manifested by hypertension and tachycardia, anxiety, and myoclonic jerking with cramping several days after zolmitriptan was added to her regimen for the first time. Discontinuation of these medications, along with the administration of clonazepam and a beta-blocker, helped reverse the syndrome. (The administration of cyproheptadine, a serotonin blocker, was considered, but her rapid improvement made it unnecessary.)

Prior to admission, the patient reported increasing headache, even with increasing doses of opioids. It was believed that “opioid-enhanced hyperalgesia” may have influenced the worsening headache course. Hospitalization focused on opioid detoxification, medical management for severe pain during the withdrawal period, and treatment of the chronic migraine and cervicogenic disorder. She responded well to cervical facet blockade, suggesting the importance of the cervical injury in the overall pain problem. The diarrhea and sleeplessness are predictable following opioid cessation. Behavioral management, involvement of the family, and discharge planning with her other physicians were important elements in the overall management of this case.

Management Strategies

- Avoid excessive numbers of serotonin-active medications at the same time (eg, tricyclic antidepressants, serotonin reuptake inhibitors, and triptans or ergots simultaneously).

- Opioid detoxification in patients with chronic headaches is usually critical.
- Addressing cervical injuries and cervical dysfunction can synergize with the benefits of detoxification and appropriate prophylaxis.
- Behavioral management, involvement of the family, and discharge planning with her other physicians are important elements in the overall management of severe chronic daily headache.

Case Summary

Episodic migraine can transform into daily headache, and this condition can be hastened or exacerbated by

- Cervical trauma
- Comorbid neuropsychiatric symptoms
- Medication-overuse phenomena
- Other organic and physiologic factors

For patients with severe daily headache, severe and multiple comorbidities, and high medication use, an inpatient multidisciplinary approach is often necessary that includes

- Detoxification
- Behavioral evaluation and therapy
- Intravenous and preventive medication to treat both withdrawal and the underlying primary headache disorder
- Careful consideration of the neck, with intervention when warranted

Selected Readings

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Editorial Comments

Dr. Joel Saper probably has more experience in the management of refractory chronic headache than almost

anyone in the world. His observations on treatment have been key in defining the basic parameters of the chronic daily headache syndromes and their clinical care. In this chapter, he succinctly outlines several of the most important features of refractory chronic daily headache: the patients often transform from episodic migraine, they usually have significant and complicating neuropsychiatric as well as medical comorbidities, they frequently have significant medication overuse, and they often also have unrecognized and untreated neck pathology. His inpatient facility is geared to evaluating and treating this constellation of problems, and all headache clinicians can learn from his experience and advice, as this case clearly demonstrates just how complicated chronic headache diagnosis and management can be, and usually requires a multidisciplinary approach.

FINAL DIAGNOSES:

Transformed migraine with medication overuse (Silberstein–Lipton criteria, 1996), posttraumatic cervical facet syndrome; early serotonin syndrome