CHAPTER 27

THE MAN WITH EVOLVING HEADACHE

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Case History

A 54-year-old, right-handed, white male came to the office complaining of daily headaches. He was the president of the local hospital. He had a history of "migraine" for over 10 years. The headaches were usually left hemicranial pounding headaches. They were severe enough to make him curtail his customary activities and lay down. He experienced nausea, vomiting, and photophobia. There was no phonophobia. Sleep typically brought resolution of the headache.

Over the years, he had found ergotamine tartrate to be helpful and was using about 30 or more tablets per month. In fact, for the 2 months or so prior to his visit to the office, his headaches had evolved into a chronic daily pattern. His migraines never had an accompanying aura, and his headaches were still relieved with ergotamine tartrate and/or sleep.

In the past, he had been treated preventively with propranolol, which made him feel fatigued, so it was stopped. A computed tomography (CT) scan of the brain done 10 years before presentation was reportedly normal (with the films being no longer available for review). There was a family history of migraine in his father. His mother had a history of hypertension and apparently had suffered from a brain tumor, although he did not know which type. Perfume and certain brands of beer seemed to be triggers for his headaches. A complete neurologic examination was entirely normal.

The patient was placed on metoprolol with the dosage titrated up to 100 mg twice a day, and his ergotamine tartrate was stopped. There was significant improvement in his headaches (they became milder and intermittent), but over a period of some weeks he became slightly lethargic, and so the dosage of this drug was tapered off.

Diltiazem was substituted which controlled his headaches but also gave him a sensation of fatigue, so this was discontinued. His headaches recurred, so a lower dose of metoprolol (50 mg twice a day) was initiated. He felt much better with occasional headaches he could control, but a confounding variable of stresses at work lead to a referral for behavioral medicine measures.

His headache pattern continued to wax and wane with intermittent headaches over the next few months. Eight months after his initial office visit, he complained of difficulty concentrating. He was using injectable sumatriptan to control his severe headaches, with good response. He was complaining again, however, of a low-grade constant headache and therefore his metoprolol was stopped and sertraline was begun. Five days later his wife called saying that he seemed even more depressed and was behaving oddly.

A CT scan of the brain was obtained which was abnormal. A magnetic resonance imaging (MRI) scan confirmed the existence of a large mass appearing to arise from the right frontal lobe and extending well into the right parietal lobe. Examination of the patient by neurology resident physicians after they had seen this scan still revealed only "possible papilledema" and a "possible" left pronator drift.

The patient was taken to the operating room. Stereotaxic biopsy revealed glioblastoma multiforme. Despite surgical debulking, radiotherapy, and chemotherapy, he had a progressive downhill course, and expired approximately 1 year later.

Questions about This Case

- How many types of headache did this patient have?
- Why did this patient have episodes of both intermittent and chronic daily headache?

- When does a patient with a headache need a scan?
- What are the causes of daily headache?

Case Discussion

This case represents every physician's and patient's worst fear—having a secondary (threatening) rather than a primary (benign) headache syndrome. Actually, this patient had both; first a long history of migraine without aura, then a new headache (ergotamine-dependency) which resolved with the discontinuation of the offending medication, then yet another worsening presumably due to the intracranial tumor.

There is no doubt that the patient had migraine without aura. He had a long history of intermittent hemicranial severe pounding headaches, with nausea and vomiting, and photophobia. There was a family history of migraine, and the patient had triggers for his headaches. Between attacks, his health was normal. He had undergone a normal CT scan of his brain. He met the IHS criteria for migraine without aura.

Along the way, he developed a pattern of chronic daily headaches, in the setting of daily use of ergotamine. The ergotamine-dependency headaches are in many ways analogous to analgesic-rebound headaches. Increasing use of symptomatic medication results in a vicious cycle of more frequent refractory headaches and the consumption of increasing amounts of medication attempting to achieve relief. Abrupt cessation of the offending medication may result in a transient worsening of the headaches, but cessation generally leads to improvement over a period of weeks to even months. This patient did return to an intermittent headache pattern after stopping ergotamine.

Medications can be a problem not only in that symptomatic remedies may worsen headache if overused, but also because prophylactic options are limited both with regard to efficacy and side effects. Both beta-blockers and even a calcium channel drug provoked fatigue in this patient, although he achieved adequate relief of headache and amelioration of the side effects with a reduction of the dosage.

The recurrence of daily headache without the overuse of symptomatic medications was worrisome. There was the confounding variable of stress in his professional life—he had just had a very trying few months and a particularly difficult interaction with a staff physician who subsequently quit. The patient attributed the worsening headache pattern to his stress. Notably, his headaches (at least the severe ones) responded to sumatriptan. It is known that response to sumatriptan or other antimigraine drugs *is not* diagnostic of migraine.

Neuroimaging studies were carried out, because of the patient's progressive headache pattern and the development of abulia. The presence of a malignant tumor was confirmed. The frontal lobe is notoriously a relatively "silent area" of the brain which may harbor lesions for a period of time before they are discovered, especially if the lesions are unilateral. Glioblastoma multiforme is an aggressive, infiltrative tumor, which is generally only diagnosed when incurable. These tumors cause progressive deterioration in most cases despite vigorous efforts at treatment, with the demise of the patient generally within 1 year.

Management Strategies

- Establish the correct diagnoses in this case. This requires a complete history and examination.
- Follow the patient serially in the office, to assess their response to therapy, and make appropriate adjustments.
- Re-evaluate the patient by history and/or examination at the time of any significant negative change.
- Neuroimaging would generally be recommended for a patient with an abnormal examination, a persistent refractory daily headache, or a worsening or changing headache pattern despite appropriate treatment. Laboratory work, and lumbar puncture (assuming neuroimaging shows no contraindication such as a mass lesion) may also be appropriate in some cases.

Case Summary

- The patient did have migraine without aura.
- The patient also had chronic daily headaches due to ergotamine overuse (ergotamine-dependency headaches).
- A brain tumor also occurred, presumably after the initial office visit (these tumors grow rapidly), and caused the reoccurrence of chronic daily headache.
- Patients may have multiple causes of headaches, and previous diagnoses of benign (primary) headaches do not mean that the patient cannot develop a threatening (secondary) headache.
- Flexibility in diagnosis and management implies assessing the patient's response to therapy and their changing symptoms over time.

Approach to the Patient with Frequent (Daily) Headaches

The assessment of the patient with daily, or near-daily headaches can be difficult. Many patients who present with such headaches fear they harbor a brain tumor; fortunately, most do not. A thorough history and complete examination serve as the basis for deciding whether or not further testing is necessary and/or appropriate.

Guidelines regarding neuroimaging procedures have been published (see *Selected Readings*).

In patients with a history of migraine and chronic daily headache, the inappropriate consumption of either analgesics or ergotamine is often the cause of the problem. The cessation of this overuse (either gradually as an outpatient under medical supervision or more rapidly in the hospital) usually leads to improvement over a number of weeks. Failure to improve should lead to further diagnostic considerations. Also, it is always possible that a chronic daily headache leads to the overuse of medications in an attempt to obtain relief.

Unrecognized medical conditions may lead to frequent headaches. Examples include thyroid disorders, polycythemia, malignant hyperthermia, and Lyme disease. In patients over 50 years of age (and occasionally younger), giant cell arteritis may be the cause of daily headaches. Appropriate physical examination (and an eye examination) plus laboratory evaluation is required.

Unrecognized psychiatric conditions may be associated with frequent headaches. Depressed patients frequently complain of unremitting headaches. There is a strong correlation, especially among women, between a history of abuse and refractory pain states, including headaches.

Unrecognized neurosurgical conditions may also be the source of refractory headache. Some patients with Chiari malformations (herniation of cerebellar tonsils below the level of the foramen magnum) will have headaches. These headaches are typically occipital/upper cervical and may be constant and/or worsened by Valsalva's maneuvers such as coughing. Surgical decompression may be curative.

Conditions that are being recognized with increasing frequency include various "cervicogenic headaches." Trapping of the dorsal C_2 nerve root may occur, for example, after trauma such as whiplash. There is typically a delay of a number of weeks, or months, between the injury and the development of head pain. Again, there may be unilateral (rarely bilateral) occipital/upper cervical aching with a tender occipital nerve, and pain which may radiate forward to above the ipsilateral eye. Pain sensation may be decreased on that side in the C_2 dermatome. A CT-guided anesthetic block of the C_2 ganglion may transiently relieve symptoms and suggest a response to surgery.

An intracranial neoplasm may present with headache although, surprisingly, about a half of patients with a brain tumor do not complain of headache. Headache is more likely to be present if there is raised intracranial pressure, shift/distortion of structures on neuroimaging, or if the patient had a previous history of headaches. In that case, the headaches associated with the brain tumor are always either more frequent or severe than their previous headaches *and* are accompanied by additional symptoms and/or physical signs.

The classic "brain tumor headache" written about so extensively (severe, awakening the patient at night with nausea/vomiting) turns out to be uncommon, reported only in 17% of brain tumor patients (as suggested by Forsyth). Patients with a long previous history of benign headache may develop a brain tumor and not even have a change in their headache pattern.

For intracranial masses above the tentorium cerebelli, a headache, when present, is usually bilateral, frontal, and somewhat worse ipsilateral to the mass. The headaches from intracranial mass lesions are nonspecific, may be mild (more like a tension-type headache in the majority unless the patient also has a history of migraine), and is usually detected by the presence of other signs or symptoms suggesting raised intracranial pressure or a focal lesion.

Patients with headaches should be considered for neuroimaging (I prefer MRI) when they develop new unexplained symptoms, abnormal signs on neurologic examination, or a different headache from their previous headache type. The lesson from this case is that a prior normal examination, a prior history of a benign (primary) headache such as migraine, the presence of other aggravating factors such as ergotamine-dependency headaches, and even previous normal neuroimaging, does *not* prevent a patient from developing a brain tumor or other ominous lesion, and continuous vigilance in the assessment of headache patients is essential.

Selected Readings

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Editorial Comments

Dr. Ward presents and discusses a fascinating yet ominous case of a patient with three types of headache. Intra-patient variability of headache types is very common, yet most remain primary benign disorders. The evolving nature and behavioral changes seen in this patient are always easy to recognize in retrospect but may be overlooked during clinical care, especially when a prior neuroimaging procedure was "normal." All physicians caring for headache patients have cases similar to Dr. Ward's. We can hope that treatable reversible causes can be found in some cases.

So beware the changing headache and do not hesitate to order a repeat scan if the clinical pattern has changed.