Chapter 15

The Patient with Another Sudden Headache

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Case History

A 32-year-old woman goes to her local hospital's emergency department because of the sudden onset of a very severe headache. Pain is bioccipital and is so severe as to make her assume a fetal position on the examination table.

She is a long-time migraine sufferer, but this headache is different because of much higher pain intensity and location. Most of her migraines are unilateral and temporal, and most of these occur perimenstrually. She does have some nausea with this headache, which is typical for her migraines.

Recent medical history is remarkable for a viral illness the previous month. The patient's husband relates that she has been complaining of some "hazy vision" recently. Past medical history is remarkable for two pregnancies, during which headaches were very infrequent. She is otherwise healthy, with no history of diabetes, cardiac disease, or hypertension.

Vital signs are normal, with blood pressure (BP) 130/88, and a regular pulse of 82 bpm. She is afebrile. Fundi appear benign. Neck is supple. Head and neck examination is normal. Lungs and heart sound normal.

Neurologic examination is remarkable for anisocoria, with the right pupil at 4 mm and left at 3 mm, both reactive to light and accommodation. Extraocular movements are full, and the remainder of the neurologic examination is normal.

The emergency room physician recommended a noncontrast computed tomography (CT) scan of the head, which was done quickly and was normal. A lumbar puncture was then done with the following cell count results: Tube 1 had 560 red blood cells (RBCs), 4 white blood cells (WBCs); Tube 3 had 288 RBCs, 2 WBCs. Cerebral spinal fluid (CSF) protein was 38 mg/dL and glucose was 82 mg/dL. Opening pressure was 190 mm H_2O. Gram stain was negative. The CSF picture was felt to be consistent with a traumatic tap and the patient was treated with ketorolac 30 mg intramuscularly. This was only minimally helpful, and she was then treated with sumatriptan 6 mg subcutaneously, which in 30 minutes produced dramatic reduction in pain.

Twelve days later, the patient is brought to a tertiary medical center's emergency department by ambulance after complaining of another sudden severe headache which began several hours earlier. She is mildly somnolent and cannot give much more history. Vital signs are as follows: BP 150/102, pulse 66 bpm, respirations 14/min, temperature 37°C. Fundoscopic examination is grossly normal, but photophobia makes this difficult. Her neck is slightly stiff, and moving her neck or legs seems to make her very uncomfortable. There are no obvious signs of trauma. Cranial nerve examination again reveals some anisocoria as before. She is able to move all her limbs well, and sensation seems intact in her extremities and trunk. Reflexes are slightly hyperreflexic. Plantar reflexes are equivocal. Gait is not testable.

Questions on the Case

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

- What are your diagnostic considerations in this case?
- What diagnostic testing is indicated at this point?
- What is the most likely explanation for this patient's presentation 12 days earlier?
- What treatment will be necessary?
- What can you tell the family of this patient about prognosis?

Case Discussion

The differential diagnosis now includes subarachnoid hemorrhage due to ruptured aneurysm or arteriovenous malformation (AVM); intracerebral hemorrhage due to vascular malformation, bleeding diathesis, or hemorrhagic mass or stroke; spontaneous arterial dissection; cerebral venous thrombosis; and primary headache.

C. Miller Fisher in 1984 coined the term "crash migraine" to describe patients who experienced rather sudden severe migraine headaches. These may occur in migraineurs, but do not really fulfill the International Headache Society criteria for migraine, and have been termed by Dodick and others as "benign thunderclap headache." This entity is particularly interesting in that it has been associated with segmental intracerebral vasospasm, clinically presenting with fluctuating neurologic deficits and seizures. However there are a number of features to this case suggestive of more ominous causes of headache.

Neck stiffness can occur with migraine, but this patient seems to demonstrate true meningismus. Based on her discomfort with leg and neck movements, one suspects that if tested, Kernig's sign (straight leg raising leads to neck pain) and Brudzinski's sign (flexion of the neck results in knee and hip flexion) would both have been positive. The anisocoria is perhaps chronic and benign, but raises concern about dysfunction in autonomic pupillary control (perhaps related to third nerve involvement). Somnolence is of major concern. It raises the possibility of increased intracranial pressure, which might also explain the increased BP and decreased pulse rate (Cushing's triad: hypertension, bradycardia, and slowing of respiration). The "equivocal" plantar reflexes should also raise concern, although a Babinski's sign should really only be noted if clearly positive, as there are many patients in whom toe withdrawal can be confounding.

Sinusitis, cervical spine disease, or other causes of head and neck inflammation can lead to severe head and neck pain, at times occurring rather acutely. Again, the somnolence and suggestion of focal neurologic deficits do not fit these scenarios. Temporal arteritis is a cause of sudden headache, which can be repetitive, but the young age of this patient essentially excludes this.

Hypertensive encephalopathy, pituitary apoplexy (due to hemorrhage), and spontaneous intracranial hypotension have all been reported in selected cases presenting with sudden severe headache, but these were all essentially excluded by work-up in the present case. Idiopathic intracranial hypertension can rarely present with acute-onset headache, but is highly unlikely here because of the normal opening pressure on previous lumbar puncture.

Cerebral venous sinus thrombosis (CVT) frequently presents with new head pain, and there are reports of sudden headaches in some cases. Typical findings include papilledema, and later, seizures and focal neurologic deficits due to venous infarctions and subcortical hemorrhages. CVT can be difficult to diagnose, since CT and even magnetic resonance (MR) imaging can be negative. Lumbar puncture usually reveals increased opening pressure, and MR venography usually allows the definitive diagnosis.

Spontaneous carotid or vertebral dissection can present with acute severe headache, and while there are often focal neurologic deficits associated with these, there may be a delay before transient ischemic attack-like symptoms develop. MR angiography can be very helpful in most of these cases.

Parenchymal intracranial hemorrhage (ICH), whether due to AVM, stroke, neoplasm, or aneurysm, generally produces neurologic deficits (hemiparesis, sensation loss, visual field deficit, aphasia, etc), not present in this case. Noncontrast head CT is virtually 100% sensitive in ICH.

Meningeal infection can produce the clinical picture in the present case, but the sudden headache is somewhat unusual, particularly with the prodromal headache 12 days earlier. Bacterial meningitis, of course, usually presents with a rapidly worsening clinical picture, but in this case, the prodromal headache could represent an unusual migraine, with the more dramatic headache on the second emergency room visit resulting from meningeal irritation. A more indolent meningitis, such as fungal meningitis, tuberculosis, or meningeal carcinomatosis is a likelier possibility, with the possible third nerve palsy resulting from meningeal cranial nerve involvement.

Subarachnoid hemorrhage (SAH) is the most likely diagnosis here, with headache and meningismus on the basis of hemorrhagic irritation of the meninges. The anisocoria could be explained by a posterior communicating artery aneurysm with pressure on the third nerve (and the "hazy vision" may actually result from mild extraocular movement dysfunction, since many patients with diplopia may perceive it as "blurring" of images). Somnolence may be due to increased intracranial pressure, which may in fact be leading to elements of Cushing's triad. Early corticospinal tract involvement may explain the possible Babinski's reflexes.

The severe headache 12 days previously is suggestive of the so-called "sentinel headache" preceding some SAH events. The pathophysiology of this is still not clear, but supposedly represents undetected low-level leakage of an aneurysm. Another possibility is the proposed expansion of an unruptured aneurysm, with pain resulting from stretching of nociceptive fibers in its wall. This concept was first introduced by Day and Raskin when they reported a 42-year-old woman with several sudden severe headaches in the absence of any evidence of SAH. This was the case for whom they coined the term "thunderclap headache."

Raps, in a 1993 study of a series of patients with unruptured intracerebral aneurysms, found that 5 to 6% had reported thunderclap headaches at some point.

The prodromal headache may of course have been a migraine, explaining its dramatic response to sumatriptan. However the literature is now replete with cases of non-migrainous headache responsive to triptan medication. In addition, the similarity and temporal relationship between the two headache presentations suggest that they are causally related.

The diagnosis of SAH is usually obvious on CT of the head, with a relatively low false-negative rate of around 10% at most. One potential cause of missing SAH on CT is low hematocrit (< 30), which tends to make blood isodense. When CT is negative, however, lumbar puncture usually provides the answer. In our case, the lumbar puncture results were confounded by the presumed "traumatic tap." Here, RBC count is supposed to drop in successive samples, as it did in our case. Unfortunately, this method for determining a traumatic lumbar puncture is not entirely reliable. An added clue is the presence of lack of xanthochromia, detected by spectrophotometry of the spun CSF sample. If present, it is fairly clear evidence for subarachnoid blood. Unfortunately, the lack of xanthochromia is not reliable evidence to the contrary, particularly if CSF is collected early, since it takes several hours for RBC to hemolyze and liberate oxyhemoglobin and bilirubin which cause the yellowish tinge. For this reason, some authors have suggested delaying lumbar puncture for several hours in cases of suspected SAH, which would be risky if meningitis is also a possible diagnosis.

Management at this point must be simultaneously directed at 1) making sure this patient's cardiac, respiratory, and neurologic functions are stable, and 2) arriving at the correct diagnosis. First steps must include airway and respiration assessment, perhaps with bedside spirometry, since there is the possibility of intracranial hypertension. Electrocardiogram should be obtained since SAH can lead to cardiac conduction abnormalities including ST segment elevation or depression, T wave changes, lengthening of the QT interval, and the presence of U waves. Complete blood count, electrolytes, glucose, prothrombin time, partial thromboplastin time, and arterial blood gases (or at least pulse oximetry) should be done. CT of the head should be obtained immediately to rule out parenchymal hemorrhage, subarachnoid hemorrhage or mass, and if normal, lumbar puncture should be the next step.

In this case, with the confounding features described above, cerebral angiography may not be avoidable, even with normal CT and CSF, so one could make a case for proceeding directly to cerebral arteriography even if the CT shows no obvious subarachnoid and parenchymal blood.

Further Data from History and Diagnostic Testing

CT scan was remarkable for high signal changes in the subarachnoid space diffusely, with prominent perimesencephalic cistern blood and mild hydrocephalus. When this was compared with the previous CT from the outside hospital, it seemed as though there may have been some subtle blood signal in the cistern of the velum interpositum on that first set of images. Cerebral arteriography was done next and revealed a posterior communicating artery aneurysm with no other findings.

This patient was admitted to the intensive care unit for close monitoring. She became more somnolent and was intubated, but did not require ventilatory assistance. On day 3, she underwent craniotomy for aneurysm clipping. She had a fairly stormy course, with hydrocephalus requiring a ventriculostomy and drain. This was eventually removed, and she recovered with only some mild cognitive and balance difficulties. Headaches also persisted for several weeks, but gradually resolved, with reemergence of menstrual and occasionally sporadic migraine headaches.

Management Strategies

Management of Thunderclap Headache

Given the dire consequences of missing an aneurysmal rupture, careful evaluation of the sudden acute headache is essential. The case presented here raises the controversial question of whether angiography is indicated when both CSF examination and CT of the head are both unrevealing of hemorrhage. Many authors suggest MR angiography, and more recently, as it has become more widely available, CT angiography has also been promoted as an alternative.

An added factor in the decision about traditional cerebral arteriography is the observation that "benign thunderclap headache" (a real diagnostic possibility in these cases) has been associated with segmental intracerebral vasospasm, which could presumably be exacerbated by intra-arterial dye infusion, raising the usual 0.5% risk of permanent neurologic deficits to unacceptably higher levels.

The good news is that high quality CT scanning coupled with CSF analysis has a very high sensitivity for detecting SAH. Some authors have suggested that the false-negative rate for CT plus lumbar puncture analysis is unacceptably high, but an encouraging study done by Wijdicks and colleagues prospectively followed 71 patients with thunderclap headache and normal CT and CSF for several years, and found that none later experienced SAH.

Management of Subarachnoid Hemorrhage

Most cases of SAH are due to ruptured berry aneurysm of one of the vessels in the region of the Circle of Willis. AVM rupture and mycotic aneurysm rupture make up a small fraction. Although risk factors including hypertension, ethanol abuse, and cigarette smoking are known, the specific mechanisms leading to rupture are unclear. Approximately 2 to 6% of the population have intracranial aneurysms (findings vary in autopsy studies). Aneurysms have a predicted rate of hemorrhage of approximately 1 to 2% per year, and the annual incidence of SAH is approximately 6 to 10 people per 100,000.

Approximately 1% of patients presenting to the emergency room for treatment of headache have SAH. Interestingly, as shown in two studies, about 12% of patients presenting with sudden headache and normal neurologic examinations had SAH.

The presentation of SAH is typically an explosive headache, along with mental status and other neurologic symptoms and signs, such as occurred in this case. Prompt diagnosis is essential, and is usually fairly straightforward. Unfortunately, approximately 20% of clear cases will have negative arteriograms. In these cases, repeat angiography should be done.

On presentation, SAH is classified using the Hunt and Hess Grading scale below:

Grade 1: asymptomatic (may have mild headache)
Grade 2: moderate to severe headache or third nerve palsy
Grade 3: confusion, drowsiness, or mild focal signs
Grade 4: stupor
Grade 5: coma

Prognosis tends to depend on grade, and Grade 3 (this case) carries about 20% mortality and high morbidity. Other measures and grading systems have been devised in an attempt to predict outcome, based on estimated volume of blood, exam features, etc. Investigators have also attempted to use these data to determine timing of neurosurgical intervention (craniotomy and aneurysm clipping). A multicenter international study suggested poorest outcome when surgery was done between days 7 and 10, and that early surgery produced the best outcomes. Low-grade SAH (Grades 1 and 2) are generally operated on within the first 36 hours. Grade 3 is controversial, but is often treated similarly to lower grade cases if stable. Higher grade SAHs have such poor prognoses that timing of intervention is still not clear.

Complications of SAH include rebleeding, vasospasm, hydrocephalus, seizures, and cardiac conduction abnormalities (ST and T wave changes, QT interval abnormalities, etc, as above). Thus, initial treatment is aimed at stabilization of vital functions, avoidance of vasospasm, reversal of hydrocephalus if it occurs, and resection of the aneurysm as soon as is deemed safe. If seizures occur or if cardiac complications arise, then these should be dealt with promptly.

Control of BP is a delicate matter, as high pressure may lead to rebleeding and low pressure can exacerbate vasospasm. If there is hydrocephalus, increased intracranial pressure can be controlled with ventricular shunting. Nimodipine 60 mg q4h is helpful to reduce vasospasm. Seizures can be prevented with phenytoin at a 15 to 20 mg/kg loading dose, followed by maintenance therapy titrated to appropriate blood levels.

Another option for treatment of intracranial aneurysms is endovascular coil embolization. This approach is being studied at a number of radiologic centers, and holds promise.

Selected Readings

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Editorial Comments

This masterful summary by Dr. Levin addresses the major issues in diagnosing and treating SAH, including the nature of thunderclap and sentinel headaches, and the controversies over MRA and CT arteriography versus conventional angiography. He also explores what to do with high clinical suspicion and a normal lumbar puncture and CT. It is worth remembering the utility of a lumbar puncture even later after a normal CT, if clinical suspicion is high. Within 24 hours of an event, CT scans yield a 92 to 95% probability in detecting acute SAH. The sensitivity of CT then decreases to 80% at 3 days, 58 to 85% at 5 days, 50% at 1 week, and 30% at 2 weeks, and is zero at 3 weeks. However, lumbar puncture remains positive for xanthochromia by spectrophotometry, 100% positive at 12 hours, 1 week, and 2 weeks, and > 70% positive at 3 and 4 weeks (Vermeulen M, Hasan D, Blijenberg BG, et al. Xanthochromia after subarachnoid haemorrhage needs no revisitation. J Neurol Neurosurg Psychiatry 1989;52:862–8). Therefore, one could do the lumbar puncture if the patient shows up later with a thunderclap of magnitude several weeks ago! Or possibly give consideration to doing an MRA or CT angiogram.

Final diagnoses:

Posterior communicating artery aneurysm and subarachnoid hemorrhage