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CHAPTER 31

THE WOMAN WITH ACUTE SEVERE HEADACHE

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Case History

A 25-year-old woman presented with a 3-day history of uncharacteristic, severe, and unremitting headache. The headache initially was present upon awakening, was moderate in intensity at that time, and subsequently worsened. The pain was largely nonpulsatile but became "throbbing" and more severe when she attempted to walk. The pain was nonlateralized and centered at the vertex. There was no significant positional component. She described associated photophobia and some sonophobia but no nausea, vomiting, or aura. She described eye pain with eye movement in all directions of gaze. She denied fever, neck stiffness, recent trauma, or symptoms consistent with recent systemic illness.

Her past medical history was unremarkable, and she specifically denied any prior history of headaches sufficiently severe to inhibit or prohibit daily activity. She took no medication chronically, and she specifically denied recent use of an antibiotic.

Her physical examination was normal except for an oral temperature of 37.8°C. There was no evidence of neck pain or stiffness with anterior flexion.

She was treated with sumatriptan 6 mg subcutaneously, and within 30 minutes her headache declined in intensity from severe to mild. Lumbar puncture was performed, and the opening pressure was normal; cerebrospinal fluid (CSF) analysis yielded 257 white blood cells per cubic mm (98% lymphocytes), no red blood cells, protein concentration 58 mg/dL and glucose 62 mg/dL; Gram's stain was negative for organisms.

Questions about This Case

- Given the patient's history, what diagnoses should have been considered prior to lumbar puncture?
- What do the cerebrospinal findings suggest, and what do they rule out?
- How should this patient be managed?

Case Discussion

This previously healthy and headache-free woman presented with a severe headache. The most common stimulus for this clinical presentation is new onset migraine, but that diagnosis must be considered suspect for three reasons. First, the International Headache Society (IHS) diagnostic criteria for migraine headache stipulate that an individual must have experienced at least five attacks of characteristic headache in order for that diagnosis to be made with a reasonable degree of certainty. Second, and regardless of whether or not the patient has an established history of migraine, the "worst headache of my life" invariably requires careful diagnostic intervention and exclusion of conditions which may mimic migraine. Lastly, the patient is febrile, and when fever accompanies headache as the primary presenting complaint, infection involving the central nervous system must be excluded.

The most important condition to consider here is subarachnoid hemorrhage from a ruptured berry aneurysm. Clinically devastating aneurysmal rupture often is heralded by a low volume, "sentinel" leak, and it is imperative that the correct diagnosis be made at this earlier point. The incidence of mortality or major neurologic morbidity from high volume aneurysmal hemorrhage is distressingly high, and little satisfaction can be taken from establishing the diagnosis after this cataclysmic event has occurred. On the other hand, if the sentinel bleed is diagnosed without delay, and if the aneurysm is then secured surgically, disaster can be averted.

Many other conditions may mimic new onset migraine, and a number of these are potentially danger-

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ous. Patients with infectious meningitis may present with acute, severe headache, and fever and neck stiffness are not always present. Although tuberculous meningitis typically is more subacute in onset, patients with bacterial or viral meningitis become ill quickly, and it is virtually impossible to distinguish between the two without CSF analysis. Patients with viral encephalitis often complain of headache; if there is alteration of consciousness, focal neurologic deficit, seizure activity, or some combination thereof, this diagnosis should be considered. [*Editors' note: Lyme disease from* Borrelia burgdorferi *should be considered in some parts of the world. A history of tick bite, bull's-eye rash, or residence in an area with a large deer population is usually present.*]

There are noninfectious conditions which may mimic new onset migraine. Patients with primary intracerebral hemorrhage from hypertensive arteriopathy, recreational drug abuse, or other causes frequently complain of headache which may possess migrainous features, but parenchymal hemorrhage is with few exceptions accompanied by focal neurologic signs. Patients with extra-axial (subdural or epidural) hematoma from recent head injury may present with headache as the chief complaint, and focal neurologic signs may be subtle or absent. Patients with low intracranial pressure from a dural tear and associated CSF leak may present with acute headache, but during the first few days to weeks that headache typically has a strong positional component (much worse while the individual is upright and relieved by lying flat); a history of an inciting traumatic event is not always elicited.

This patient's positive response to treatment with sumatriptan did not assist in establishing a diagnosis. Sumatriptan is nonspecific therapy and has been reported to be effective in patients with postictal headache or headaches from aneurysmal subarachnoid hemorrhage. The same can be said for any medication used to treat acute migraine headache. A variety of stimuli will activate the peripheral trigeminovascular system and central pathways which generate and modulate head pain, and any agent which exerts its pharmacologic effect within those areas may work to oppose pain, regardless of the stimulus involved.

Taken along with her clinical presentation, the results of this patient's CSF analysis indicate that the correct diagnosis is viral meningitis. The normal glucose level, lymphocytic pleocytosis, and elevated protein concentration are characteristic of aseptic meningitis of viral origin. There was no evidence of recent subarachnoid hemorrhage; no fresh red cells were present, and the protein concentration was not elevated to the level one would expect from recent crenation of a high volume of red cells. Results of the Gram's stain and the lack of history of recent antibiotic use exclude untreated or partially treated bacterial meningitis. The CSF profile is consistent with viral encephalitis, but the patient did not express symptoms or exhibit signs referable to the brain itself.

Management Strategies

Management of this patient should hinge primarily on the question: is hospitalization for general support required? If the patient is able to maintain oral hydration, her head pain can be managed with oral or subcutaneous medication, and there can be someone at home who will observe her and confirm that her course is consistent with resolving viral meningitis, then hospitalization makes little sense. On the other hand, dehydration will aggravate and prolong the symptoms of meningitis, and intravenous fluids may be required to avoid this.

To the author's embarrassment, this patient was admitted by his department's service despite near total resolution of her headache following administration of sumatriptan, her ability to maintain oral hydration, and the availability of concerned and informed family members at home. She was placed in an isolation room, and antibacterial and antiviral medications were administered intravenously. A brain imaging study was performed and was normal. An electroencephalogram was requested.

None of this makes very good sense. Medical resources needlessly were utilized, and worse, the patient suffered unnecessary discomfort and some risk exposure. Such aggressive diagnostic and therapeutic intervention should be reserved for patients with presumed viral meningitis whose presentations are more atypical (examples include antibiotic treatment prior to lumbar puncture, atypical CSF profile, or depression of consciousness). Straightforward viral meningitis should be managed in a straightforward fashion.

Case Summary

- Patients presenting with uncharacteristically severe acute head pain require meticulous diagnostic evaluation.
- In such circumstances, aneurysmal subarachnoid hemorrhage must be excluded.
- Viral meningitis is a common, temporarily disabling but typically benign condition which most often can be managed with simple supportive therapy only.

Overview of Aseptic Meningitis

"Aseptic meningitis" implies inflammation of the meninges in the absence of bacterial or fungal infection and without symptoms or signs referable to the brain, brain stem, or spinal cord. Afflicted patients present with

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fever, headache, signs of meningeal irritation, and characteristic CSF findings. Many have come to regard aseptic meningitis and viral meningitis as being synonymous, and although it is true that viral infection is the leading cause of this syndrome, the CSF profile associated with aseptic meningitis may be produced by conditions as widely varied as treponemal infection, Behçet's disease, and exposure to certain medications or contrast agents (e.g., nonsteroidal anti-inflammatory drugs, gamma globulin, iohexol). Aside from viruses, infections which may produce aseptic meningitis include leptospirosis, Lyme disease, syphilis, mycoplasma, and chlamydia. Parainfectious causes include partially treated bacterial meningitis, parameningeal infection, and endocarditis. Among the noninfectious causes not already mentioned are sarcoidosis, collagen vascular diseases, and migraine. If the term is employed in its broadest sense, encompassing both acute and more chronic processes, the list of causative conditions expands significantly, and there can be said to be no single characteristic clinical presentation. For example, a patient with acute aseptic meningitis of viral origin or from exposure to contrast material used in myelography may present rapidly and with prominent symptoms, in contrast to a patient with human immunodeficiency virus (HIV)-related syphilitic meningitis who may express no symptoms whatsoever.

The CSF profile in aseptic meningitis generally demonstrates a white cell pleocytosis which numbers in the tens to hundreds, and the cells are chiefly lymphocytes. The glucose concentration is normal, and the protein concentration is moderately elevated. The degree of abnormality present in the CSF tends to parallel the severity of the patient's symptoms. In a minority of cases, and especially when the meningeal inflammatory response is intense and lumbar puncture is performed early in the course, the white cell count may be higher, a greater proportion of neutrophils may be present, and the glucose concentration may be decreased. In that event, bacterial or tuberculous meningitis becomes of greater concern, and it may be safer to initiate appropriate antibiotic therapy and to continue such treatment until cultures initially obtained return as negative and repeat lumbar puncture demonstrates findings consistent with evolving aseptic meningitis.

As indicated previously, most acute aseptic meningitis is viral in origin, and patients presenting with viral meningitis may appear quite ill, exhibiting fever, headache, lethargy, irritability, and varying degrees of neck stiffness; the last is variable and may be absent. Photophobia may be prominent, and patients often complain of pain with eye movement. On rare occasions the examiner will find evidence of early papilledema, but alteration of consciousness, focal neurologic signs, or seizure activity are typically inconsistent with the diagnosis of aseptic meningitis and demand that encephalitis or other conditions which involve the brain itself be considered.

Viral meningitis is evanescent; the patient rapidly becomes sick and miserable and almost as rapidly improves to his or her normal state of health. Long term sequelae are very rare. The viral agents incriminated most commonly in cases of aseptic meningitis are enteroviruses (echovirus and coxsackievirus), but the mumps virus, herpesviruses (notably, type 2), lymphocytic choriomeningitis virus, and Epstein-Barr virus may be culpable as well. Benign recurrent aseptic meningitis (Mollaret's meningitis) may result from reactivation of a herpesvirus. Human immunodeficiency virus may cause aseptic meningitis early in its course, and the meningitis may coincide with or predate seroconversion.

The peculiar intersection of migraine and aseptic meningitis deserves a brief mention. Both are common clinical conditions, and it is inevitable that a certain percentage of individuals with established migraine will contract viral meningitis. Beyond the coincidental relationship, however, there is some evidence to suggest that migraine itself may induce a meningeal response similar to that observed with aseptic meningitis and that in this situation efforts to establish an infectious or other noninfectious source for the meningitis will be fruitless. Compounding the potential for diagnostic confusion, patients with migraine-associated aseptic meningitis may exhibit progressive obtundation or express sensorimotor symptoms. Suffice it to say that the incidence and biogenesis of "migraine meningitis" remain obscure and that the diagnosis of this condition should be considered tenuous at best.

Selected Readings

Beghi E, Nicolosi A, Kurland LT, et al. Encephalitis and aseptic meningitis, Olmstead County, Minnesota, 1950–1981: epidemiology. Ann Neurol 1984;16:283–94.

Ratzan KR. Viral meningitis. Med Clin North Am 1985;69: 399–413.

Editorial Comments

Aseptic meningitis is usually a self-limiting disorder without sequelae. However, the diagnosis is not always easy or straightforward, and the differential diagnoses include several serious and life threatening disorders. Dr. Rothrock leads us through an erudite overview and discussion of this entity. He points out the pitfalls in diagnosis and provides sensible management strategies. He even mentions the entity of "migraine meningitis," an obscure disorder, somewhat familiar to neurologists and physicians dealing with acute headache.