Chapter 45

Diagnosis and Differential Diagnosis of Migraines

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The diagnosis of migraine is made clinically; there are no blood tests, imaging studies, or electrophysiologic tests to confirm the diagnosis. Investigations may be needed to exclude structural, biochemical, and other causes of headache that can mimic migraine.

Migraine is easy to diagnose when it is episodic, is associated with an aura, or is accompanied by gastrointestinal symptoms and associated symptoms such as photophobia, phonophobia, and pallor (4). Relief with sleep, aggravation of the pain by a Valsalva maneuver or routine physical activities, pain involving half of the head, and attacks triggered by such factors as the menstrual cycle, fasting, oversleeping, or indulgence in alcohol are all helpful in the diagnosis. Recurrent headaches of this type, especially if there is a family history of similar headaches, over a period of years separated by periods of freedom make the diagnosis of migraine so likely that investigations are rarely necessary (2). When the history is less typical, when the subject is seen with or shortly after the initial headache, or when anxiety is such that more than reassurance is needed, neuroimaging may be necessary. Computed tomography (CT) or, preferably, magnetic resonance imaging (MRI), are the investigations of choice to exclude structural abnormalities mimicking migraine.

Migraine can simulate or be simulated by most of the primary and secondary headaches; as a consequence, the differential diagnosis is essentially that of almost all conditions that can present with headache. Table 45-1 lists many disorders that must be considered.

HEADACHE ATTRIBUTED TO CRANIAL OR CERVICAL VASCULAR DISORDER

Transient Ischemic Attack

Headache as a manifestation of transient cerebral ischemia is relatively common (7,10), but the focal neurologic symptoms of the attack need to be differentiated from an aura of migraine. The motor or sensory symptoms contralateral to hemispheric ischemia, like the weakness or subjective sense of heaviness and the paresthesias of a migraine aura, can involve the face, limbs, or trunk. A motor or sensory march of symptoms may occur but tends to be much quicker in a transient ischemic attack (TIA) than in migraine. The motor or sensory spread of a TIA is rapid, taking at most only seconds to a minute to move from the face to the hand, then marching up the arm to the trunk. Progression down the trunk to the lower limb can occur in both conditions. The march of motor and sensory changes in migraine is slow, taking a number of minutes to reach to its maximum distribution. The sensory symptoms in migraine are commonly a positive phenomenon, that is, a tingling sensation rather than a sense of numbness or sensory loss. Although the former can occur in a TIA, a sense of numbness or deadness is more often described. In both conditions, although more common in migraine, the sensory disturbances still can be spreading to new areas of involvement while simultaneously clearing from previously involved areas.

The weakness of a TIA is usually far greater than in a migrainous aura, but in the case of hemiplegic migraine, the difference can be minor and not diagnostic. Recovery can be over a similar period in both TIAs and migraine, but most TIAs are very short lived, and recovery is within minutes. A long history of similar attacks, onset in youth or early adult life, a personal or family history of migraine, and a normal clinical and noninvasive neurovascular examination all point to a migraine aura as the cause of the transient symptoms. Even in later life, when TIAs are more common, migraine can be the cause of such events (8,9).

Hemianopia is a relatively rare manifestation of a TIA and does not generally have the scintillating and spreading features of the visual aura of migraine. The visual loss of a TIA is usually a negative scotoma (black) rather than the

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TABLE 45-1 Causes of Headache in the Differential Diagnosis of Migraine

Cerebrovascular disorders
Transient ischemic attacks
Cerebral infarction
Cerebral hemorrhage
Subarachnoid hemorrhage, especially sentinel leaks
Intracranial hematoma
Intracranial aneurysm and AVM
Arterial dissection, carotid or vertebral
Venous thrombosis
Arterial hypertension
Cranial vasculitis
Nonvascular intracranial disorders
Benign intracranial hypertension (pseudotumor)
Low CSF pressure
Intracranial neoplasm
HaNDL
Chemical, metabolic, endocrine and abnormalities
Nitrites, nitrates, other vasodilators
Hypoxia, hypoglycemia, dialysis, hypercarbia
Cranium, neck, eyes, and nose
Arnold-Chiari malformation
Cervical spine abnormalities
Purulent sinusitis
Sinus and base of skull neoplasms
Acute angle closure glaucoma, refractive errors (children)
Tolosa-Hunt syndrome
Raeder's syndrome
Others
Epilepsy
Trauma
Other primary headaches
Fever, systemic disease

Abbreviations: AVM, arteriovenous malformation; CSF, cerebrospinal fluid; HaNDL, headache and neurologic deficits with cerebrospinal fluid lymphocytosis.

positive scotoma (bright) of migraine. *Amaurosis fugax* is a sudden onset of monocular blindness followed by gradual clearing of vision in 5 to 10 minutes. This pattern of visual disturbance is contrasted with an initial small area of scintillating scotoma that spreads gradually in the visual field in migraine.

Transient ischemic events can result in brainstem and temporooccipital dysfunction, leading to vertigo, tinnitus, bilateral visual disturbances, weakness of both sides of the body, and brainstem symptoms such as dysarthria, dysphagia, and diplopia. A similar constellation of symptoms occurs in basilar artery migraine (2). Headache can occur in both conditions, but in basilar migraine the headache is severe and almost always presents as the neurologic symptoms subside. Basilar migraine is most common in teenagers or in early adult life, whereas vertebrobasilar TIAs usually occur later in life. An overlap does occur; therefore, age alone is not an arbiter. Arteriography (MR or conventional) may be required for clarification.

Thromboembolic Stroke

Cerebral infarction, particularly cerebral embolism, often is associated with headache (7,19) and sometimes with positive visual symptoms, such as phosphenes or other visual hallucinations, when the vertebrobasilar arterial system is involved. It is rarely confused with migraine, because the resulting neurologic deficit generally suggests the presence of the structural lesion. Arteriography or noninvasive vascular studies, echocardiography, and coagulation studies may be required for final diagnosis. The dominantly inherited arteriopathy associated with recurrent subcortical infarction (CADASIL) can, in its course, be manifested by migraine attacks. The family history, the progressive course, and the characteristic subcortical infarcts shown on MRI make the diagnosis clear.

Intracranial Hematoma

In most instances, an intracranial hematoma, if it gives rise to headache, also produces other neurologic symptoms. Impaired consciousness, focal neurologic deficits, and a progressive course are characteristic. A hematoma in the head of the caudate nucleus or periventricular area may cause severe headache without obvious neurologic symptoms. A subcortical hematoma in a nonsymptomatic area may cause only dull headache, and careful neurologic examination of mental and higher cortical function may suggest the diagnosis. Confusion with migraine could occur in a patient with a prior history of the primary headache disorder. The recent and sudden onset of a headache, a history of head trauma, or the development of neurologic signs, especially if progressive, should lead to examination by CT or MRI, which then reveals the hematoma.

Subarachnoid Hemorrhage and Intracranial Aneurysms

Many patients who eventually have a subarachnoid hemorrhage (SAH) report a history of headaches that were not recognized as warnings of an impending catastrophic hemorrhage (15). Such sentinel or warning headaches are caused by small, self-limited hemorrhages from the aneurysm or (more rarely), arteriovenous malformation (AVM), which eventually gives rise to the major hemorrhage. Many sentinel headaches are ignored or dismissed as migraine, tension-type headache, or as caused by other benign causes. Reported misdiagnosis of SAH ranges from 12 to 51% (13). The patients with the greatest probability of benefiting from surgery (those with the least neurologic deficit) are the ones that most commonly receive an

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incorrect diagnosis and complications develop in patients with a wrong diagnosis more commonly than those with an accurate diagnosis and, thereby, prompt surgical intervention (6). Neck stiffness may be absent, and the pain may have subsided by the time the patient is examined. An unenhanced CT scan to look for blood in the basal subarachnoid cisterns should be obtained. If the CT is normal, a cerebrospinal fluid (CSF) examination should be performed. Unfortunately, a normal CT and CSF examination does not completely exclude a small SAH or help to distinguish between a migraine and the potentially far more serious headache. MR or conventional angiography should be obtained when there is any doubt about the nature of the headache.

Thunderclap headache applies to a sudden, explosive headache with maximal intensity at onset. The sudden onset of pain is atypical for migraine headache. The diagnosis of primary thunderclap headache is one of exclusion (11). The most common secondary cause of thunderclap headache is SAH, but other causes to be considered include intracerebral hemorrhage, cerebral venous thrombosis, arterial dissection, central nervous system (CNS) angiitis, reversible benign CNS angiopathy, pituitary apoplexy, colloid cyst of the third ventricle, hypertensive encephalopathy, and spontaneous CSF leak (11). Whether an unruptured intracranial aneurysm can produce a thunderclap headache is of considerable controversy (6).

Unruptured Intracranial Vascular Malformations

A headache indistinguishable from migraine with or without aura can occur ipsilateral to a vascular malformation. The unlikely presence of an AVM is but one of the reasons a CT or MRI scan should be considered in the evaluation of any patient with a migrainous history. The coexistence of migraine and seizures should especially prompt investigation, because an AVM is even more likely to produce epilepsy than headache.

Dural AVMs of the sigmoid or cavernous sinus region can produce episodic headache with the features of migraine. They also can cause raised intracranial pressure and a variety of visual symptoms. Neurovascular imaging is required for definitive diagnosis.

Arteritis

Giant cell arteritis (temporal arteritis) is characteristically a cause of headache in patients aged over 65 years (5). The headache tends to be constant, progressive, and associated with tenderness of the scalp, jaw claudication, and often systemic symptoms such as fatigue, myalgias, and low-grade fever. The headaches are often worse at night and on exposure to cold. The progressive nature of the headache and the associated features help to distinguish it from migraine. The elevated sedimentation rate and abnormal temporal artery biopsy confirm the diagnosis.

Carotid or Vertebral Artery Dissection

Dissection of one of the great cervical vessels usually results in unilateral pain of sudden onset. Carotid dissection causes local neck pain and pain behind the ipsilateral eye (17). The pain is persistent for some days to several weeks. An ipsilateral Horner syndrome is commonly noted. Migraine usually is excluded easily by the history, although the pain may wax and wane and may be made worse by coughing, sneezing, and bending. Angiography is the definitive investigation, although MR angiography and carotid ultrasound also may be diagnostic. Vertebral artery dissection produces neck and occipital pain. The abrupt onset and occasional association of brainstem ischemic symptoms should prevent confusion with migraine.

HEADACHE ATTRIBUTED TO NONVASCULAR INTRACRANIAL DISORDER

Elevated Cerebrospinal Fluid Pressure

Pseudotumor cerebri can result in episodic headache and vomiting (3), but it is unlikely to be confused with migraine for long, because the development of visual blurring, visual obscurations, and persistent headache prompts the subject to seek medical help. The association of headache, obesity, menstrual irregularity, and papilledema in a young woman is likely due to idiopathic intracranial hypertension. An MRI, to rule out an intracranial mass, particularly in the posterior fossa, is essential. An MRV is necessary if venous sinus thrombosis is suspected.

Low Cerebrospinal Fluid Pressure/Volume

This type of headache occurs after a lumbar puncture or may be caused by loss of fluid through the nose, ears, or operative site (18). The headache is usually characteristic. Standing typically increases the pain and recumbency gives almost immediate relief. This orthostatic pattern is quite unlike migraine; MRI of the head with gadolinium usually shows characteristic changes. Although the opening CSF pressure is usually low, this is not universal. Traumatic or spontaneous rupture of the thecal sac in the spine is the usual cause of orthostatic headache (18). Unilateral or bilateral subdural hematoma sometimes occurs as a consequence of low CSF pressure and may add a different type of headache. Radionuclide cisternography or CT myelography may be required in the investigation of a spontaneous low CSF pressure headache.

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Intracranial Tumors

Headache caused by an intracranial tumor initially may be episodic and mimic migraine or tension-type headaches. With time, the headache may change to that of raised intracranial pressure, wakening the subject during the night and becoming associated with nausea and vomiting. The temporal profile depends on whether the lesion obstructs the CSF pathways early or late in its development. Posterior fossa lesions have a much shorter time course.

Colloid cysts and other ventricular tumors, such as ependymomas, can present with episodic headache, nausea, and vomiting, and hence are the most likely of intracranial masses to mimic migraine. Examination by CT or preferably MRI reveals the cause.

Syndrome of Transient Headache and Neurologic Deficits With Cerebrospinal Fluid Lymphocytosis

The clinical picture of this syndrome is 1 to more than 20 discrete episodes of transient neurologic deficits lasting hours, accompanied or followed by moderate to severe headache. The neurologic manifestations can reflect hemisphere, brainstem, or cerebellar dysfunction. The episodes may recur for several weeks, and patients are asymptomatic between the episodes of neurologic dysfunction and headache. Some patients report a "march" of symptoms similar to that of migraine aura. CSF shows CSF lymphocytosis and elevation of CSF protein—findings not present in migraine. CT and MRI scans are normal (1). Microbiological studies are normal. The syndrome is self-limited.

HEADACHE ATTRIBUTED TO INFECTION

Although infections can produce episodic headaches of a throbbing type that worsen with coughing, they are usually progressive and may be associated with fever, cranial nerve deficits, and neck stiffness. After noninvasive imaging with CT or MRI, a CSF examination confirms the presence of a meningeal process.

HEADACHE ATTRIBUTED TO A SUBSTANCE OR ITS WITHDRAWAL

Many substances responsible for the headache are, ironically, used for relief of headaches. Ergotamine preparations, triptans, and combination analgesics have been identified as causing headaches when taken more than 2 to 3 days per week. Alcohol, nitrites and nitrates, monosodium glutamate, indomethacin, nifedipine, and many other substances can induce headache resembling migraine or trigger migraine. Removal or avoidance of the offending substances with relief of the headache confirms their role as migraine triggers or the cause of the headache.

HEADACHE ATTRIBUTED TO DISORDER OF HOMEOSTASIS

Hypoxia

High altitude, hypoxia caused by pulmonary disease, or sleep apnea can result in a pounding headache resembling migraine without aura. Migraneurs are particularly susceptible to the headaches of high altitude.

Carbon dioxide retention secondary to emphysema, often associated with hypoxia, also results in a vascular headache. Hypoglycemia and renal dialysis are both capable of producing a throbbing headache with migrainous features.

In each instance, the history should provide the clue to the cause of the headache. Pulmonary function studies, overnight polysomnography, arterial blood gas analysis, and determination of the plasma glucose may be required. In some instances, CT or MRI examination of the head is necessary to exclude an intracranial cause, especially when severe carbon dioxide retention results in papilledema.

Arterial Hypertension

Rapid elevation of blood pressure from any cause can result in headache. Pheochromocytoma or certain vasoactive drugs such as amphetamines, phenylpropanolamine, or a monoamine oxidase inhibitor in the presence of an amine can produce severe episodic headaches. When headache is a manifestation of sustained severe hypertension, it may be associated with papilledema. The early morning headache of hypertension can mimic migraine. Blood pressure measurement leads to the diagnosis. A CT or MRI scan of the head is necessary to rule out an intracranial mass or hydrocephalus causing the papilledema.

HEADACHE OR FACIAL PAIN ATTRIBUTED TO DISORDER OF THE CRANIUM, NECK, EYES, EARS, NOSE, SINUSES, TEETH, MOUTH, OR OTHER FACIAL OR CRANIAL STRUCTURES

Cervical Spine

The role of the neck in the pathogenesis of headache is controversial. It has been stated that a cervicogenic headache radiates from the neck, often unilaterally to the orbital

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or retroorbital region ipsilaterally (21). Associated autonomic features can include ipsilateral overflow of tears and conjunctival injection. More generally accepted is an occipital-cervical pain secondary to cervical muscle tension triggered by bony and postural abnormalities of the cervical spine. The headache is not accompanied by autonomic features and should be readily distinguished from migraine. The history, pain, and limitations of movement of the cervical spine and cervical spine radiographic findings are helpful in the diagnosis.

Eyes

In children, refractive errors can give rise to episodic frontal headaches resembling migraine without aura. This rarely occurs in adults.

Acute glaucoma in adults can result in severe eye and supraorbital pain. Attacks may occur at night and resemble migraine. The affected globe may be hard and the cornea steamy. Ophthalmologic examination confirms the diagnosis.

Sinuses

Contrary to common lay opinion, sinus abnormalities other than acute purulent sinusitis are rarely the cause of headache. Many individuals who receive a diagnosis of sinus headache have migraine headaches (14).

Teeth, Jaws, and Temporomandibular Joint Disease

Referred pain from these structures can cause headache, but rarely with the characteristics of migraine. Pain on chewing or pain on exposure of the teeth to hot and cold stimuli should help to pinpoint the source of the pain.

HEADACHE ATTRIBUTED TO HEAD OR NECK TRAUMA

Acute attacks of migraine, especially migraine with aura, can be triggered by recurrent minor head trauma, for example, footballer's (soccer player's) migraine from "heading" the ball (16). Acute posttraumatic headache is not likely to be confused with migraine if the history is ascertained. Chronic posttraumatic headaches, although they tend to be persistent, can be episodic and may have features of migraine (22). Neuroimaging is necessary to exclude such conditions as a chronic subdural hematoma.

MISCELLANEOUS HEADACHES OCCASIONALLY CONFUSED WITH MIGRAINE

Primary cough headache, primary exertional headache, and the primary headache associated with sexual activity can occur in migraineurs or independently. The history of a sudden onset of headache during exertion, during sexual activity, or in relation to a cough or sneeze differentiates the headache from that of migraine.

Epilepsy can result in recurrent headaches, but the seizure prior to the headache indicates the nature of the disorder. Headache as an ictal manifestation of seizures has been rarely noted.

Recurrent migrainelike episodes have been described in persons infected with HIV in the absence of intracranial infection. In many patients who have been studied, anticardiolipin antibodies have been detected (20).

Migraine can be a feature of the mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome and other mitochondrial disorders. Recurrent strokes in the MELAS syndrome and myoclonic epilepsy in association with a mitochondrial myopathy help distinguish these rare disorders from migraine (12).

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