Transient and Persistent Neurological Manifestations of Migraine

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The clinical syndrome of migraine is estimated to affect 23 to 29% of women and 15 to 20% of men. This very common condition is characterized by recurrent attacks of headache associated with photophobia, anorexia, nausea, vomiting, and other autonomic disturbances and frequently by striking focal neurological manifestations. The episodes are distinctly varied in frequency, severity, and duration and separated by symptom-free intervals. A family history of vascular headaches is obtained in about 75% of cases. While agreed upon diagnostic criteria are lacking, migraine is subdivided as follows: common type if there are no associated neurological signs or symptoms; classic migraine if characteristic visual or other sensory or motor disturbances precede or accompany the headache; cluster headaches; lower half (facial) headaches; and hemiplegic and ophthalmoplegic migraine in which the neurological deficits outlast the headache phase.

The cause of migraine is unknown. Decreased and increased cerebral and extracerebral blood flow, increased platelet aggregation, and increased platelet release of serotonin have been demonstrated in migraine. Current theories of pathogenesis have recently been reviewed and include primary cerebral cortical depression, primary cardiovascular hyperreactivity, altered neural control of cerebral blood flow, and disordered central monoamine transmission affecting autonomic function or pain perception. The several varieties of migraine may represent more than one closely related entity. This report will focus on the transient and persistent neurological manifestations of migraine.

Transient Neurological Manifestations

A variety of mood alterations, both positive and negative, can occur for hours before or after both common and classic migraine attacks. During the headache despair is typical, and irritability and lack of concentration may be prominent. Classic migraine is differentiated from the common type by transient neurological symptoms, termed the aura or prodrome, which precede, overlap, or sometimes accompany the headache. Approximately 12% of patients with migraine regularly experience stereotyped classic attacks, and about two-thirds have occasional classic episodes with common migraine at other times. Vasoconstriction or vasospasm is the presumed mechanism for the focal neurological symptoms, which have a characteristic, gradual onset and slow progression, typically building over 5 to 30 minutes and lasting 15 to 60 minutes with a gradual offset. However, in up to 25%, the onset may be fairly abrupt.

Visual Symptoms

A spectrum of visual disturbances accounts for well over half of the transient neurological manifestations. They usually affect both eyes simultaneously but can affect one eye alone. The patient may experience negative phenomena only and describe hemi- or quadrantanopias, complete blindness, tunnel vision, asymmetrical field deficits, monocular blindness, altitudinal defects, or one or more scotomata. More frequently, positive phenomena occur and consist of stars, sparks, uniformed flashes of light (photopsia), simple and complex geometrical patterns, or jagged zig-zags of lights (teichopsis or fortification spectra). These visual hallucinations are usually white but can be any color. They are typically present with eyes open or closed. The slowly evolving images have a shimmering, flickering quality. The positive and negative visual phenomena are frequently combined, and the term scintillating scotoma is used. The patient may report wavy lines like heat off of pavement or as though looking through rain covered glass. Visual distortion or misperception, such as micropsia, is uncommon and implies temporal or parietal lobe dysfunction.

The most common sequence is the slow onset of bilateral central scotomata or luminous phenomena which move slowly in an arc to the periphery of one visual field. The leading edge is a zig-zag of light followed by moving geometrical patterns which in turn leave behind expanding homonymous scotomata.

The occipital lobe cortex is responsible for visual disturbances occurring in homonymous fields and the more complex hallucinations. The less common monocular symptoms are attributed to retinal migraine and are less apt to be associated with headache. There may be difficulty differentiating between occipital and retinal localization because some patients confuse homonymous symptoms for monocular involvement.

Other Cerebral Symptoms

The second most common symptom is somatosensory: a numbness or tingling (or both) frequently af-
fecting the hand and lower face (a cheiro-oral distribution), a more circumscribed distribution, or one-half of the body. In decreasing order dysarthria, various forms of aphasia, hemiparesis, or clumsiness of one side are encountered alone or in combination. Exceptional cases with auditory or olfactory hallucinations or distorted perception of body parts are described. These nonvisual manifestations are estimated to occur as the only neurological accompaniment of migraine in 4% of migraineurs. More frequently, they occur in combination with visual disturbance. The individual nonvisual symptoms also have a leisurely onset and slowly spread from one body part to another. When combined, there is generally a delay of some minutes between onsets.

**Basilar Artery Migraine**

A separate, distinct entity is basilar artery migraine which is usually seen in young women or children and consists of brainstem and cerebellar complaints in addition to occipital lobe visual manifestations and headache. Vertigo, ataxia, dysarthria, diplopia, numbness and tingling, disturbed consciousness, weakness, and tinnitus occur in variable combination and order. The frequently associated visual symptoms are typical of migraine but may affect both visual fields. The episodes are usually followed by vascular headache. There is often a history of other forms of migraine in the past or subsequently. Basilar artery migraine can be viewed as a subtype of classic migraine and is estimated to affect 10 to 24% of migraineurs at some time.

**Changes in Sensorium**

Alteration of consciousness can occur in migraine. In a series of 500 patients, 7.6, 4.6, and 6.8% experienced a faint sensation, actual syncope, and confusion with some migraine attacks. Syncope and presyncope were usually but not always associated with other vertebrobasilar distribution symptoms. The loss of consciousness is gradual in onset as a rule. Confusion lasting hours can occur as the only neurological manifestation of migraine, especially in children and adolescents. Transient global amnesia is possibly related to migraine. Transient global amnesia is possibly related to migraine. Very rarely, overt seizures have been reported in association with migraine attacks which included focal neurological symptoms. Despite these rare cases and long-standing controversy, the consensus is that there is no direct relationship between migraine and epilepsy.

**Vertigo**

Especially prominent in basilar artery migraine, vertigo can occur as the only transient neurological accompaniment of a migraine attack. In addition, benign recurrent vertigo without cochlear symptoms or headache has been reported as a possible migraine equivalent in women with a strong personal or family history of migraine.

**Migraine Without Headache**

The headache which usually follows but may accompany the neurological dysfunction can be ipsilateral or contralateral to the involved cerebral hemisphere or bilateral. Attributed to vasodilation, the headache is often throbbing but can be steady in character. The headache of classic migraine is generally milder and briefer than that of common migraine, but this apparent observation may be a reflection of the patient's reason for seeking care. When present, the headache outlasts the neurological manifestations of classic migraine. However, virtually any of the above described neurological symptoms can occur entirely without headache. Such isolated auras can be termed migraine equivalents. Sometimes the sole expression of migraine, isolated auras typically occur in patients who experience headache at other times.

**Late-Life Migraine**

Although 90% start before the age of 40, migraine can begin at any age. In the young patient with a positive family history, diagnosis is straightforward. In the middle-aged or older individual makes diagnosis more difficult, especially when there is no associated headache. Fisher points out that the presence of typically migrainous visual phenomena, the slow onset and spread of symptoms within type or from one type to another, the presence of multiple attacks over a course of years, the presence of headache, and a duration consistent with migraine all favor a diagnosis of late-life migraine accompaniments. Cerebral angiography may be required to exclude symptomatic atherosclerotic occlusive disease when migraine begins after the age of 40. However, patients with migraine have an increased incidence of complications of angiography, and this procedure should be avoided when possible, especially during or soon after a migraine attack. Digital subtraction angiography should prove quite helpful in this situation.

**Horner’s Syndrome**

Finally, although not everyone agrees that cluster headaches are a variant of migraine, 60 to 69% of patients develop an ipsilateral Horner’s syndrome with their acute cluster attacks which becomes permanent in 0.5 to 6.7%.

**Persistent Neurological Manifestations**

Complicated migraine refers to attacks in which the neurological manifestations outlast the headache or its expected duration. This category includes ophthalmoplegic migraine, hemiplegic migraine, and other lasting stroke-like neurological sequelae.

**Ophthalmoplegic Migraine**

Ophthalmoplegic migraine affects the third cranial nerve more often than the sixth or fourth. This variety is very uncommon, accounting for only eight in a series of 5,000 cases of migraine. It occurs in children or young adults, usually with a prior history of common...
migraine. The oculomotor paresis often begins as the headache ends and takes days to weeks to resolve. Multiple attacks may leave a permanent residual. The mechanism may be compression by swollen arteries or delayed ischemic neuropathy. Ophthalmoplegic migraine must be differentiated from other causes of oculomotor dysfunction, especially intracranial aneurysm.

Hemiplegic Migraine
The term hemiplegic migraine has been used variably. It should be reserved for patients with recurrent episodes of severe paresis which outlast the headache. However, given the aforementioned prevalence of migraine, 15 to 30% of all stroke patients would be expected to have a past history of migraine. Therefore, other causes of stroke must be excluded before making a diagnosis of complicated migraine. In addition, the neurological deficits should mimic the prior migrainous symptoms and follow a typical attack. Despite these guidelines it is conceivable that a stroke from an alternative mechanism could provoke a simultaneous migraine attack in susceptible individuals.

The persistent neurological complications of migraine are presumed to be due to vasospasm-induced ischemia, which may be aggravated by small vessel occlusion resulting from increased platelet aggregation. Angiography is usually normal, but approximately 25% of cases show occlusion of the posterior cerebral or middle cerebral artery or one of their branches. Persistent neurological sequelae are much more apt to occur in patients with classic migraine and somewhat more likely in patients with frequent and severe attacks, but they have been reported in patients with a history of common migraine only. As a distinguishing feature, the complicated migraine patients are younger than the usual stroke population.

The deficits tend to follow the symptoms of classic migraine, and thus, two-thirds involve visual loss, usually in the form of a hemianopia or quadrantanopia. Motor weakness, somatosensory loss, dysphasia, and brainstem syndromes account for the remaining one-third. Mixed deficits are common. Retinal or optic nerve ischemia can produce monocular visual loss, and central serous retinopathy and retinal hemorrhage occur. Patients with persistent sequelae tend to improve with time, and as opposed to the ophthalmoplegic and hemiplegic varieties, only 10% sustain additional deficits with subsequent migraine attacks. While the outcome is generally good, extraordinary cases of life-threatening migraine and even death have been reported.

The best estimate of relative risk for stroke with migraine is from the Collaborative Group for the Study of Stroke in Young Women. The relative risk for thrombotic stroke was twofold for women with migraine when compared with neighbor controls, neither of whom were taking oral contraceptives. However, the data were judged inconclusive because hospital controls did not show similar results, and the apparently increased risk could be attributed to hypertension, reported to be 1.7 times higher in migraineurs. Use of oral contraceptives and a history of migraine are probably simple additive risk factors for thrombotic stroke. Since oral contraceptives have also been reported to provoke or increase the frequency and severity of migraine attacks, migraine is considered a relative contraindication to oral contraceptive use. The interaction between oral contraceptives and migraine may relate to the effect each has in increasing platelet aggregation. A recent review of the causes of cerebral infarction in young adults found that 5% were associated with migraine only, 2% with oral contraceptives only, and 7% with both together.

In the older literature there are occasional reports of hemorrhagic stroke in patients with migraine, but alternative causes were not always excluded. It is unlikely that migraine itself predisposes to intracranial hemorrhage. Several cases of retinal hemorrhage with migraine have been reported, but the mechanism was most likely related to prolonged Valsalva efforts (vomiting). Although the yield is low, patients with complicated migraine require thorough evaluation to exclude underlying cerebrovascular occlusive disease, vasculitis, mass lesion, aneurysm, or arteriovenous malformation which can, rarely, simulate migraine. Patients with any persistent unexplained neurological deficit, the very abrupt onset of severe headache, or associated seizures should also be investigated. Worsening headache pattern and strictly unilateral attacks occur in migraine and are less alarming than the complicated forms.

Abnormal CT Scans in Migraine
Abnormal CT brain scans have been reported with migraine. In these highly selected patients with severe and frequent migraine attacks, many with persistent neurological findings, the incidence of focal, infarct-like abnormalities has been higher than expected. However, areas of focal atrophy would be anticipated in patients with permanent deficits. The incidence of generalized cerebral atrophy in migraineurs was found to be less than in a general population. Unselected migraine subjects usually have normal CT scans.

Treatment
In addition to avoiding provocative factors, effective treatment for the migraine is available. The acute migraine attack can be aborted with prompt use of
erogotamine-containing medications and a variety of analgesics. Ergotamine should be avoided in patients with complicated migraine because of the possibility of aggravating the presumed vasospasm. Ergotamine can be used safely and is helpful in preventing or dampening the headaches of classic migraine. Inhalation of isoproterenol, a beta-adrenergic agonist, has been suggested as a treatment for the migraine aura.  

Antimigraine prophylaxis, termed interval therapy, is also effective for recurrent migraine headaches and their associated neurological symptoms. The frequency and severity of migraine attacks must be sufficient to warrant the regular use of these preventive type medications, which are beneficial in up to two-thirds of patients. The treatments include (1) beta-adrenergic blocking agents such as propranolol, (2) antiserotonergic medications such as methysergide and cyproheptadine, (3) antidepressants including amitriptyline and in resistant cases monoamine oxidase inhibitors, (4) biodegradation technique training, and possibly (5) antiplatelet aggregating agents such as the nonsteroidal antiinflammatory drugs. Finally, the calcium channel blockers may prove useful in the prevention of migraine or its complications.

Conclusion

Migraine is a very common disorder which usually follows a benign course despite the frequent occurrence of disturbing, transient neurological dysfunction. Rarely, persistent neurological impairment ensues which cannot be reliably avoided with interval therapy such as propranolol. Nevertheless, attempts at prophylactic therapy are warranted to prevent both migraine attacks and the exceptional permanent deficits, particularly in patients with frequent classic migraine or a past history of complicated migraine. In addition, while antiplatelet aggregating drugs such as aspirin are questionably effective in migraine prophylaxis, their use should be considered to prevent arterial occlusions with platelet aggregates, thought to account for the persistent neurological damage.

Acknowledgment

The author wishes to thank Dr. J. K. Campbell for reviewing the manuscript.

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Stroke. 1984;15:383-386
doi: 10.1161/01.STR.15.2.383

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/15/2/383.citation

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