Migraine With Vasospasm and Delayed Intracerebral Hemorrhage

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Three women with well-documented migraine associated with intracerebral hemorrhage are described. In each case, migraine headaches began during adulthood. Unusually severe and protracted headache heralded the onset of fixed neurological deficits associated with lobar intracerebral hemorrhage. Striking carotid artery tenderness was characteristic. Except for a history of migraine, no cause for intracerebral hemorrhage could be established. In each case arteriography showed extensive spasm of the appropriate extracranial or intracranial artery. Surgical pathology following evacuation of two hematomas demonstrated signs of vessel wall necrosis associated with subacute inflammatory changes. Vasospasm associated with severe migraine attacks may result in ischemia of intracranial vessel walls, leading to necrosis and subsequent vessel rupture when perfusion pressure is restored.

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Charcot, in 1881, suggested that any of the transient neural dysfunctions of migraine could become permanent.1 Since then, migraine has been associated with residual neurological deficits in a large number of cases, and the concept of complicated migraine has become widely accepted.2-4 Retinal, cortical, and brain-stem lesions have each been described. In the majority, neurological dysfunction is attributed to ischemic stroke, presumably secondary to vascular spasm. Intracerebral hemorrhage in migrainous patients has only rarely been reported,1 and has sometimes been associated with preexisting arteriovenous malformations.13 This article describes a group of patients, all of whom are female, affected with migraine who presented with lobar intracerebral hemorrhage either during or immediately following typical migraine attacks. All patients were investigated in detail; no evidence of underlying vascular malformation or tumor was discovered. Radiologic studies suggested that early and severe vasospasm of either the intracranial or extracranial vessels was important in the development of hemorrhage.

REPORT OF CASES

Case 1.—A 61-year-old woman had a 4-year history of migraine headaches preceded by an aura of left-sided paresthesias. She presented to the emergency department complaining of severe bitemporal headache, similar to previous attacks. A neurological consultant found the patient to be normotensive, and the examination results to be entirely normal. A lumbar puncture was performed and the results revealed normal cerebrospinal fluid. She was discharged on analgesics and propranolol.

Two days later she returned complaining of severe headache, and, on this occasion, had a mild left hemiparesis with a left Babinski’s sign. Blood pressure was again normal. Computed tomographic scans of the brain, with and without contrast infusion, were normal (Fig 1, left), and she was discharged on prednisone therapy in an effort to abort a severe migraine attack.

Twenty-four hours later her headache worsened. The following morning she was difficult to arouse, and was again brought to the emergency department. She was hypertensive, bradycardic, and stuporous, but, after stimulation, was able to follow simple commands. She had a dense left hemiplegia associated with a left-sided homonymous hemianopia and right gaze preference. Brain computed tomographic scanning demonstrated a right frontoparietal intracerebral hemorrhage (Fig 1, center). A carotid arteriogram showed narrowing of the M1 segment of the right middle cerebral artery (Fig 1, right). There was mass effect related to the hematoma, but no evidence of arteriovenous malformation, aneurysm, or tumor. A right frontoparietal craniotomy was performed with evacuation of the hematoma. Pathologic examination of the surgical material showed areas of cerebral necrosis surrounding partially necrotic ruptured small arteries without evidence of vascular malformation, tumor, or amyloid angiopathy. She made a slow recovery and was discharged with a persistent neurological deficit.

Case 2.—A 45-year-old woman suffered from common migraine headaches associated with photophobia and nausea for several years. She took no medications and used no illicit drugs. One day prior to admission she had an attack similar to her usual headaches, but somewhat more severe. Twenty-four hours later, she suddenly developed a left hemiparesis, associated with left hemihypesthesia. On admission, her blood pressure and heart rate were normal. She was alert and cooperative. There was striking tenderness over the right carotid artery, but the pulse was normal and there were no bruits. She had a dense left hemiplegia.

Brain computed tomographic scanning showed a homogeneous, well-defined, round hyperdensity in the right frontoparietal region consistent with an intracerebral hematoma (Fig 2, left). A right-sided internal carotid arteriogram demonstrated an avascular mass in the right frontal lobe. There was headlike narrowing of the extracranial

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that a weakness, tenderness and headache, with nausea and photophobia, which was similar to her usual attacks, but increased progressively over several days. She was treated with analgesics that provided partial relief. Four days later, after-continued headache, she noted left face and arm weakness and numbness, and came to the emergency department. Blood pressure and heart rate were normal. Carotid pulses were full, but there was tenderness over the right carotid artery. She had right-gaze preference associated with a left hemiparesis involving the face and arm more than the leg and a left Babinski’s sign. Computed tomographic scan showed a right-sided frontoparietal hematoma (Fig 4, left). A selective digital right-sided carotid arteriogram demonstrated severe narrowing of the extracranial portion of the internal carotid artery (Fig 4, center). There was no evidence of arteriovenous malformation. Over the next 24 hours, severe right-sided headache persisted and was associated with tenderness over the scalp on the right side. She was discharged with residual left-sided weakness, and continued to make a slow recovery. Three months later she underwent a repeated right-sided carotid arteriogram that showed resolution of the narrowing that had been present on the first study (Fig 4, right).

COMMENT

These patients all manifested a relatively stereotyped pattern of headache associated with intracerebral hemorrhage (Table). Two had common migraine and one suffered from classic migraine. Suddenly, following typical attacks, each suffered major lobar intracerebral bleeding.

A relationship between preexisting migraine and intracerebral hemorrhage in each of these patients can only be inferred. Intracerebral hemorrhage is most commonly associated with hypertension, aneurysmal bleeding, rupture of macroscopic or cryptic vascular malformations, tumor necrosis, primary vasculopathy, or, in populations at risk, amphetamine or cocaine abuse. None of these conditions was demonstrated by either the clinical, arteriographic, or pathologic studies.

The finding of tenderness over the appropriate carotid artery was strik-
ing in two of the patients, and suggested that carotid vessel pathologic findings were important in the development of intracerebral hemorrhage. Carotidynia has been associated with carotid artery dissection, carotid artery occlusion, carotid artery aneurysm, giant cell arteritis, and migraine.10,11 None of our patients had a vessel biopsy performed to rule out giant cell arteritis, but normal sedimentation rates argued against this diagnosis. There was no evidence of occlusion or aneurysm in any of these cases. Spontaneous carotid artery dissection, a diagnosis that might be suggested by the arteriographic findings in case 3, remains a possibility in that case, but has typically been associated with ischemic stroke.12

Brain computed tomographic scanning was highly suggestive of spontaneous hemorrhage in two patients, and in one case (case 2) suggested the possibility of underlying tumor. The images were not consistent with the diagnosis of hemorrhagic infarction in that the hematomata were dense, well circumscribed, and did not show the patchy hyperdensity usually associated with that condition. In one case (case 1), a computed tomographic scan, performed 2 days before the hemorrhage occurred, was entirely normal. There was no evidence of ischemia or of vascular malformation.

All patients underwent arteriographic studies of appropriate vessels. In each case there was evidence of significant spasm of a major vessel supplying the area in which hemorrhage occurred. In the two patients with carotidynia, spasm was apparent in the extracranial portion of the internal carotid artery. In those patients the possibility of catheter-induced spasm seemed unlikely in view of both its persistence on repeated injections and the existence of carotidynia prior to the arteriogram. In the third patient, spasm was seen in the proximal segment of the middle cerebral artery.

Subarachnoid hemorrhage, cerebral trauma, central nervous system infection, drug abuse, toxemia, fibromuscular dysplasia, carotid artery dissection, and cerebral vasculitis have all been associated with the radiographic appearance of spasm of the cerebral arteries. In the present cases, only the latter three possibilities could be reasonably entertained.

One patient (case 3) in whom the diagnoses of fibromuscular dysplasia or carotid artery dissection were considered underwent follow-up study 3 months after intracerebral hemorrhage. At that time, spasm had completely resolved, and the vascular appearance was normal. Follow-up angiographic studies in fibromuscular dysplasia have demonstrated either stable or progressive pathologic findings, but resolution of that process has not been described.13-17 Carotid artery narrowing due to dissection may dis-

Fig 3.—Case 2. Brain specimen from area adjacent to intracerebral hemorrhage showing subacute inflammatory infiltrate. Arrows point to macrophages. Note perivascular lymphocytic infiltration (hematoxylin-eosin, X115).

Fig 4.—Case 3. Left, Brain computed tomographic scan without contrast showing right-sided frontoparietal intracerebral hemorrhage. Center, Digital angiogram showing extensive narrowing of extracranial portion of right internal carotid artery. Right, Right common carotid arteriogram 3 months later, showing resolution of spasm.
appear over time, thus the diagnosis remains possible in the present case, although spontaneous hemorrhage resulting from dissection, as opposed to hemorrhagic infarction, has not previously been reported (to our knowledge).\textsuperscript{12}

None of these patients had clinical or serologic evidence of systemic vasculitis. Recently, several reports have described a condition known as acute benign cerebral vasculitis characterized by the occurrence of transient focal neurological deficits, often associated with severe headache and mild abnormalities of the cerebrospinal fluid.\textsuperscript{12,13} Angiography in those patients disclosed narrowing of multiple intracranial and extracranial cerebral arteries, which largely improved when repeated examinations were done weeks or months later. Serdaru et al\textsuperscript{12} have described a patient in whom a biopsy of the narrowing portion of a temporal artery, as documented by angiography, was performed. Based on the absence of inflammation, those authors suggested that "benign cerebral vasculitis" may represent a vasospastic phenomenon related to an underlying migrainous diathesis. Two such patients presented with intracerebral hemorrhage. While not described in detail in their article,\textsuperscript{14} those patients resemble ours in their outline, and it is likely that the condition we have described represents one extreme of the spectrum of "benign" cerebral vasospasm.

A migrainous cause for the arteriographically demonstrated spasm of vessels, either extracranial or intracranial, in each of the patients can only be suspected because of the similarity of each patient's prodromal symptoms to those associated with her typical attacks. It is possible that intracerebral hemorrhage was the result of temporary ischemia of vessel walls followed by sudden reperfusion with subsequent rupture of ischemic vessels. An analogous process, as recently suggested by Caplan,\textsuperscript{15} may explain intracerebral hemorrhage associated with toxemia,\textsuperscript{24} and has been suggested to explain intracerebral hemorrhage associated with sympathomimetic drug abuse,\textsuperscript{25} trigeminal nerve stimulation with resultant abrupt hypertension,\textsuperscript{26} cold exposure,\textsuperscript{27} and carotid endarterectomy with subsequent reperfusion.\textsuperscript{21}

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