

Transtentorial Herniation After Unilateral Infarction of the Anterior Cerebral Artery

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Background—Fatal cerebral herniation is a common complication of large (“malignant”) middle cerebral artery infarcts but has not been reported in unilateral anterior cerebral artery (ACA) infarction.

Case Description—We report a 47-year-old woman who developed an acute left hemiparesis during an attack of migraine. Cranial CT (CCT) was normal but demonstrated narrow external cerebrospinal fluid compartments. Transcranial Doppler sonography was compatible with occlusion of the right ACA. Systemic thrombolytic therapy with tissue plasminogen activator was initiated 105 minutes after symptom onset. Follow-up CCT 24 hours after treatment revealed subtotal ACA infarction with hemorrhagic conversion. Two days later, the patient suddenly deteriorated with clinical signs of cerebral herniation, as confirmed by CCT. An extended right hemispherectomy was immediately performed. Within 6 months, the patient regained her ability to walk but remained moderately disabled.

Conclusions—This is the first reported case of unilateral ACA infarct leading to almost fatal cerebral herniation. Narrow external cerebrospinal fluid compartments in combination with early reperfusion, hemorrhagic transformation, and additional dysfunction of the blood-brain barrier promoted by tissue plasminogen activator and migraine may have contributed to this unusual course. (*Stroke*. 2001;32:649-651.)

Key Words: brain edema ■ migraine ■ stroke, ischemic ■ thrombolysis

Cerebral herniation is a common and often fatal complication of large (malignant) middle cerebral artery infarcts.¹ Infarction involving the much smaller territory of the anterior cerebral artery (ACA) is usually not expected to cause life-threatening cerebral herniation. We report a case of unilateral ACA infarction in which a combination of potentially edema-promoting factors led to marked mass effect requiring surgical intervention.

Case History

A 47-year-old woman suddenly collapsed while she had a typical attack of migraine. She had a 29-year history of migraine without aura, a positive family history of migraine, but no other cardiovascular risk factors besides 20 pack-years of cigarette smoking. She did not take any medication except paracetamol and aspirin for migraine attacks, but none was taken on the day of the event. She did not use oral contraceptives. On admission, she complained of a right-sided pulsating headache of moderate intensity, accompanied by photophobia. She was drowsy and had a left leg plegia, a mild paresis of the left arm, left-sided hemihypesthesia, and anosognosia. Cranial CT 55 minutes after symptom onset was normal; however, the external cerebrospinal fluid (CSF) compartments appeared to be narrow (Figure 1). On transcranial Doppler sonography, the right ACA was not detectable, whereas normal flow signals were seen in the remaining

major intracranial arteries. Intravenous thrombolytic therapy was initiated with recombinant tissue plasminogen activator (Alteplase) according to the National Institute of Neurological Disorders and Stroke Study protocol² 105 minutes after symptom onset. On transcranial Doppler sonography, a normal flow signal was detected in the right ACA 12 hours after thrombolysis. Routine follow-up cranial CT after 24 hours revealed subtotal right ACA infarction with hemorrhagic conversion and a mild midline shift. Twelve-lead ECG, Holter monitoring, transesophageal echocardiography, and laboratory tests were normal. The patient's condition remained stable during the next 48 hours, and her mean arterial blood pressure was between 90 to 100 mm Hg. Migrainous symptoms subsided completely within 1 day. Forty-eight hours after the ictus, the patient became drowsy. Within 15 minutes, she was deeply comatose and had a dilated and fixed right pupil. Immediate administration of mannitol led to normalization of the right pupil within 10 minutes, but the patient remained unconscious. Cranial CT demonstrated increased infarct edema, complete obstruction of the external CSF spaces, and marked horizontal as well as axial herniation (Figure 2). The patient immediately underwent right hemispherectomy. No further lesions in other arterial territories of the brain were detected by MRI and diffusion-weighted imaging a few days after surgery. MR angiography and venography showed no abnormalities of the major cerebral

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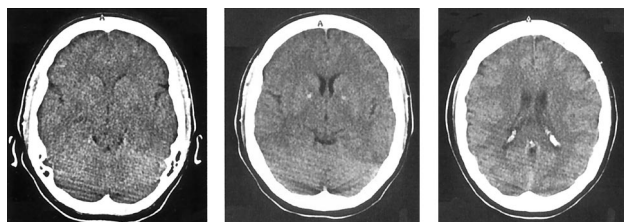


Figure 1. CT 55 minutes after symptom onset without early signs of cerebral infarction. Note narrow external CSF spaces.

arteries and veins. After surgery, the patient had a mild left facial paresis and a severe left hemiparesis equally affecting her arm and leg. During the next 6 months, she partially recovered, regaining her ability to walk and carry out most of the activities of daily living, but she remained moderately disabled (modified Rankin scale 3).

Discussion

To the best of our knowledge, this is the first reported case of life-threatening herniation due to an acute unilateral ACA infarct. The combination of several factors may have contributed to this unusual course.

Younger age is known to predispose to fatal herniation in middle cerebral artery infarction, probably because of the lack of “protective” brain volume loss that is found in older subjects.³ Thus, our patient’s narrow external CSF compartments diminished the capacity to compensate for an intracranial space-occupying lesion. In addition, brain swelling beyond the ACA territory cannot be ruled out on the CT scan, demonstrating axial herniation (Figure 2). However, MRI, diffusion-weighted imaging, and MR venography performed only a few days after surgery gave no evidence of additional ischemic lesions in the middle cerebral artery territory, edema due to compressive brain trauma, or a coincidental sinus thrombosis.

Early reperfusion after spontaneous or fibrinolytic recanalization has to be considered as another potential contributor to edema increase after cerebral infarction. Follow-up transcranial Doppler sonography demonstrated early recanalization of the initially occluded ACA in our patient. In animal models, early reperfusion leads to damage of the blood-brain barrier with increased edema formation.⁴ Whether this assumption holds true in human ischemic stroke requires further investigation in a larger series. In a recent report, however, the incidence of malignant infarct edema was higher in ischemic stroke patients treated with tissue plasminogen activator compared with conventional therapy.⁵



Fig 2. Follow-up CT a few minutes after acute clinical deterioration (coma) demonstrating horizontal and axial herniation.

Hemorrhagic transformation of cerebral infarction is a common phenomenon, especially after thrombolytic therapy. However, a retrospective analysis of the first European Collaborative Acute Stroke Study data revealed that clinical worsening in patients with hemorrhagic conversion after thrombolysis is associated only with the most severe form of transformation (ie, parenchymal hemorrhage).⁶ Nevertheless, hemorrhagic conversion in our patient may have played a role, probably because of the coincidence of other potential factors increasing edema. Direct effects of blood products are known to alter the permeability of the blood-brain barrier, thereby triggering edema formation and possible clinical worsening.^{7,8} This assumption is confirmed by the CT-morphological course in our case, demonstrating an obvious increase of infarct edema coincidentally with signs of hemorrhagic transformation (Figures 1 and 2).

Direct and indirect effects of the thrombolytic agent itself may further have promoted local brain swelling. Tissue plasminogen activator specifically converts the thrombin-bound proenzyme plasminogen to the active enzyme plasmin.⁹ In vitro, plasmin causes an increase of permeability in human vein endothelial cells, directly damages cell membranes, and finally may lead to lysis of endothelial cells.¹⁰ Similar effects have been demonstrated in human arterial endothelium.¹¹ These findings suggest that activation of plasminogen, as in thrombolytic therapy for ischemic stroke, might damage the integrity of the blood-brain barrier in addition to the endothelial effects due to ischemia.⁷

Finally, the coincidence of a typical migrainous attack with the onset of ischemic symptoms gives rise to further considerations. The stroke in our patient did not fulfill the criteria of a migraine-induced cerebral infarct according to the International Headache Society but has to be considered as migraine-associated.^{12,13} Migraine is known to activate peripheral trigeminal fibers with consecutive neurogenic inflammation of the meninges, possibly leading to vasodilation and increased permeability of the blood-brain barrier.^{14–16} Clinical cases like the one reported by Meaney et al,¹⁷ who detected a reversible unilateral cerebral edema by MRI during an attack of hemiplegic migraine, give further evidence for this assumption.

In conclusion, only the coincidence of several factors that potentially intensify postischemic brain swelling, in combination with the patient’s limited capacity to compensate for an intracranial mass lesion, facilitated the atypical and unique course of unilateral ACA infarction leading to cerebral herniation and almost fatal outcome. However, the significance of each factor remains speculative and debatable. Whether special caution may be warranted in younger patients with migraine-associated cerebral infarction suitable for thrombolytic therapy requires further observations of similar cases.

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