

Should We Treat a Patient's Symptoms or Angiography Image in TIA? Two Case Reports

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Objectives: Data on vascular status in the first hours after onset of transient ischemic attack (TIA) and its clinical significance are missing. Also, it is not known whether arterial occlusion, if present in TIA, should be the target for revascularization. We present 2 patients to demonstrate that TIA can be due to acute major intracranial arterial occlusion and to show how such arterial occlusion may affect the outcome.

Case reports: Two patients (54 and 63 years old) were diagnosed with TIA and at the same time had occlusion of the middle cerebral artery. No recanalization therapy was performed, as there was no or minimal neurological deficit. After several hours, the condition of both patients clinically deteriorated. One patient experienced spontaneous recanalization in the first 24 hours and clinical improvement over the subsequent days, resulting in complete resolution of the neurological deficit. The other patient did not recanalize and developed a significant brain infarction as well as hemorrhagic transformation requiring decompression surgery. Over the long term, the patient remained hemiplegic, unable to walk, and dependent on assistance for most activities of daily living.

Conclusions: The cases presented here raise important questions: (1) How frequently is arterial occlusion present in clinically asymptomatic patients? (2) If occlusion is present but not symptoms, is stroke a more correct diagnosis than TIA? and (3) What would be the benefit of recanalization therapy? Studies addressing these questions should be conducted.

Key Words: transient ischemic attack, middle cerebral artery occlusion, revascularization, outcome after transient ischemic attack

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OBJECTIVES

In recent years, the concept of transient ischemic attack (TIA) has changed as TIA is now seen as an emergent medical condition rather than a benign clinical syndrome. This changed concept is accompanied by the need for a new definition of TIA. The original definition was based solely on the presence of a neurological deficit lasting <24 hours. With the more

frequent use of new and advanced imaging techniques, especially magnetic resonance imaging (MRI), it was shown several years ago that many patients diagnosed with TIA based on clinical findings also had brain infarction revealed by imaging.^{1,2} A new tissue-based definition was proposed. This definition considers TIA to be a brief episode of neurological dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting <1 hour, and without evidence of acute infarction.³ However, before any infarction occurs, occlusion of a brain artery can be present and thus create potential target for recanalization treatment.

We present 2 patients with TIA and subsequent stroke who initially had a major intracranial arterial occlusion. Because the patients did not have clinical symptoms within the time window for recanalization therapy, the physician was confronted with a key question: Should the patient symptoms or an angiographic image be treated? The cases presented here also indicate that even a tissue-based definition of TIA cannot distinguish it from stroke because both patients had acute arterial occlusion that presented like TIA but eventually led to infarction. Finally, we can speculate that the mechanism of very early stroke occurrence after TIA may be in some cases due to acute arterial occlusion.

CASE REPORTS

Case Report #1

A 54-year-old woman with a history of paroxysmal atrial fibrillation, arterial hypertension, and hyperlipidemia was treated with aspirin, propafenone, losartan, and fenofibrate. The patient reported a brief episode of speech disorder 6 months previously (which, in retrospect, we consider to be due to expressive aphasia).

The patient visited the outpatient clinic at 6 PM for a sudden facial droop that occurred at 5 PM. At the onset of symptoms, the patient also reported “memory loss” lasting for 5 minutes. The results of a clinical examination were normal, and therefore the patient was diagnosed with TIA. An acute nonenhanced computed tomography (CT) was performed at 6:30 PM and was reported by the radiologist as normal (Fig. 1A). The patient was admitted for further examination and observation at a standard care unit. The long-term antiplatelet therapy (100 mg of aspirin daily for paroxysmal atrial fibrillation) was continued, but a switch to anticoagulation therapy was planned in the next 1 to 2 days. At 10 PM, a minor facial droop on the left side developed and the patient reported a slight weakness of the left arm. The patient was transferred to a stroke unit, where carotid and transcranial color-coded duplex ultrasound (TCCD) was performed. TCCD showed a missing signal on the color-coded imaging and systolic spikes on Doppler (transcranial in brain ischemia grade 1), corresponding with the diagnosis of occlusion of the right middle cerebral artery (MCA). The TCCD also showed a significant “flow diversion” to the anterior and posterior cerebral arteries on the side of occlusion, implying very good collateral flow.⁴ The diagnosis of MCA occlusion was immediately confirmed by CT-angiography (CT-AG) at 10:30 PM (Figs. 1C,

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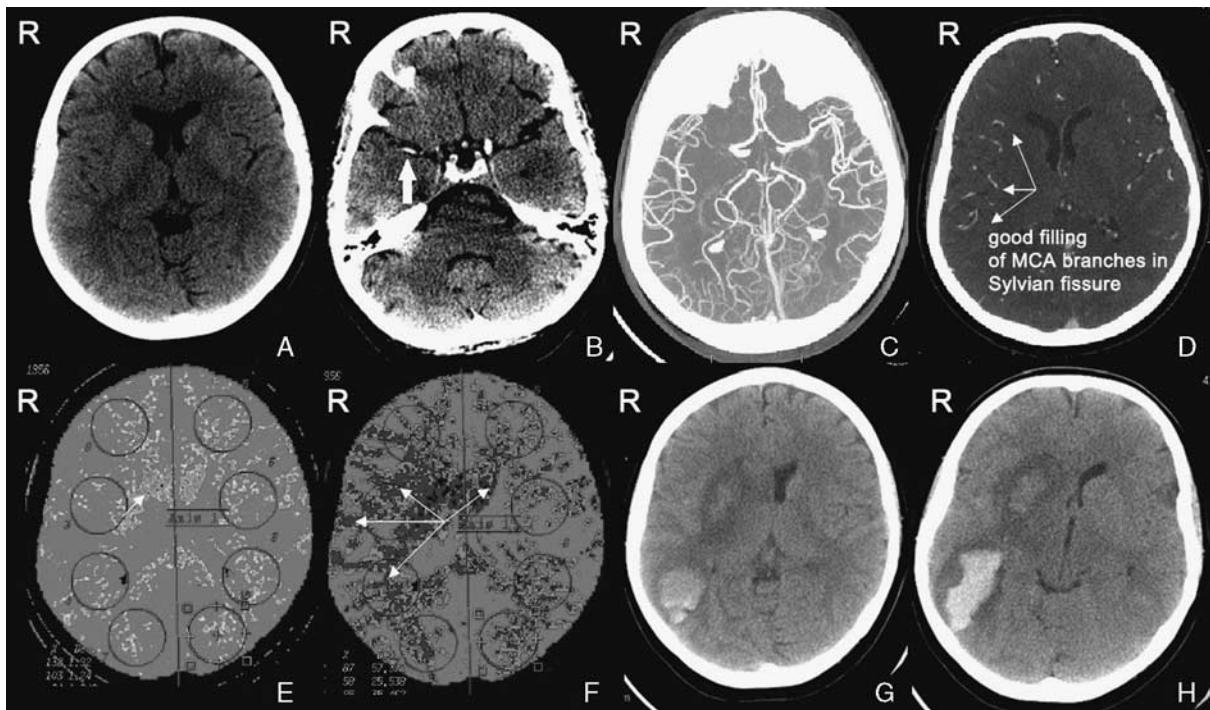


FIGURE 1. A and B, Unenhanced CT outpatient examination (1.5 h after symptom onset): originally read as normal finding, but later reread because the dense arterial sign of the right MCA was noticed (arrow). C, CT-angiography 5.5 hours after symptom onset demonstrates occlusion of the right MCA. D, CT-angiography 5.5 hours after symptom onset: good collateral flow (arrows). E, CBV 18 hours after symptom onset: localization of the infarction (arrow). F, CBF 18 hours after symptom onset: penumbra and benign oligemia surrounding the infarct core (arrows). G, Unenhanced CT 38 hours after symptom onset: hemorrhagic transformation of ischemia in the right temporal and occipital lobe. H, Unenhanced CT on the fourth day after symptom onset: edema of the right hemisphere due to ischemia and hemorrhagic transformation. CBF indicates cerebral blood flow; CBV, cerebral blood volume; CT, computed tomography; MCA, middle cerebral artery.

D). After the CT-AG was available, we retrospectively identified the dense arterial sign of the right MCA on the very first CT scan (Fig. 1B), indicating that MCA occlusion had been present during the outpatient examination.

At that point, 5.5 hours after symptom onset, the benefit of recanalization therapy with tissue plasminogen activator or mechanical thrombectomy was weighted against the risk. Because of minimal neurological deficit and potential risks such as intracranial bleeding due to thrombolysis or interventional procedure, no such therapy was performed.

The next morning, the patient awoke with severe hemiparesis on the left side. At 11 AM—that is, 18 hours after onset—the CT-AG showed persistent MCA occlusion, unenhanced CT showed ischemia, and CT perfusion showed perfusion (cerebral blood flow/cerebral blood volume) mismatch indicating persisting penumbra surrounding the infarct core (Figs. 1E, F). Again, recanalization with mechanical thrombectomy was considered but was not performed because of the significant delay from symptom onset and the brain infarction on unenhanced CT. Antiplatelet therapy with aspirin was continued, and low-molecular-weight heparin (LMWH) was started as a prophylaxis of deep vein thrombosis.

On the third day after admission, the patient became disoriented and had nausea, vomiting, hyposaturation, and tachypnea. Unenhanced CT (38 h after onset) showed hemorrhagic transformation of ischemia in the right temporal and occipital lobe, edema of the right hemisphere, compression of the right lateral ventricle, and dislocation of midbrain structures (Fig. 1G). The neurosurgeon did not indicate decompression surgery. LMWH was discontinued because of hemorrhage.

On the next day (fourth day), the patient became somnolent. Follow-up CT revealed progression of the edema of the right hemisphere (Fig. 1H). The decompression surgery was now performed. After the surgery, the patient regained consciousness and underwent extensive rehabilitation for several weeks due to hemiplegia, inability to walk, and dependence on assistance [Modified Rankin Scale (MRS)

score 4]. Months later, the patient was able to walk with assistance and had mRS 3.

Case Report #2

A 63-year-old overweight female patient with a history of paroxysmal atrial fibrillation, arterial hypertension, and hypothyroidism was treated with aspirin, propafenone, sotalol, and levothyroxine.

The patient experienced a sudden hemiparesis on the left side that occurred at 10:30 AM and lasted for 5 minutes. At 11:45 AM, she visited the outpatient clinic. The results of a clinical examination were normal; however, acute nonenhanced CT (performed 1.5 h after symptom onset) showed a dense right MCA sign, implying arterial occlusion (Fig. 2A). The patient refused hospitalization, although she was informed of potential risks.

Four hours after symptom onset, severe hemiparesis reoccurred on the left side. The patient returned to the hospital and was immediately admitted to a stroke unit. Neurological examination demonstrated dysarthria and hemiplegia on the left side [National Institute of Health Stroke Scale (NIHSS) 10].

CT-AG was performed at 3:45 PM (5.25 h after symptom onset) and demonstrated occlusion of the M1 segment of the right MCA (Fig. 2B) and hypodensity in the temporal lobe. Because ischemic changes in the territory of the right MCA were already present, neither thrombolysis nor mechanical recanalization was indicated. Medication with aspirin was continued and a prophylactic dose of LMWH was administered (to prevent deep vein thrombosis).

A mild improvement in neurological deficit (NIHSS 8) was observed at 7 PM (8.5 h after symptom onset). The next day, CT-AG (26.5 h after symptom onset) showed complete recanalization of the right MCA (Fig. 1C).

The third day after symptom onset, the patient had only a mild facial droop on the left side (NIHSS 1). The seventh day, only a small ischemia of the capsula externa area on the right side was apparent on

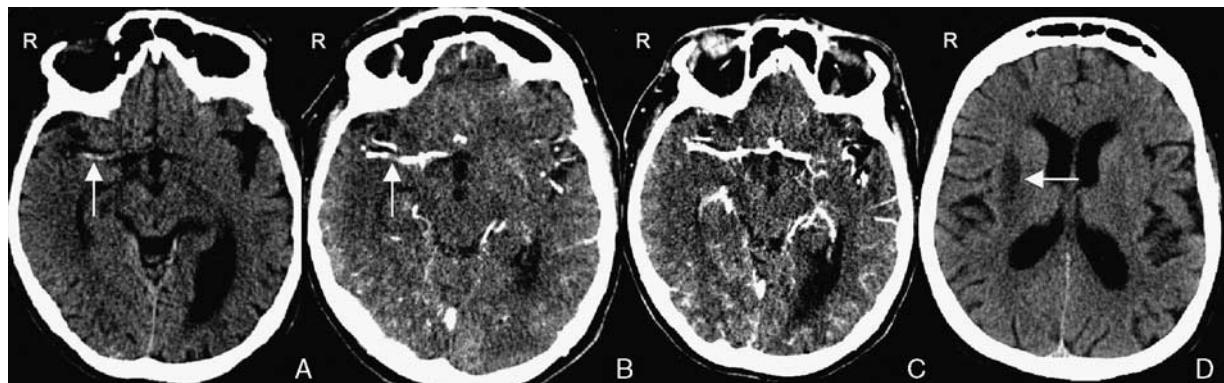


FIGURE 2. A, Unenhanced CT outpatient examination (1.5 h after symptom onset): dense right MCA sign (arrow). B, CT-angiography 5.25 hours after symptom onset: occlusion of the M1 segment of the right MCA (arrow). The distal part of the MCA is filled with leptomeningeal collaterals. C, CT-angiography on the second day after symptom onset: complete recanalization of the right MCA. D, Unenhanced CT on the seventh day after symptom onset: small ischemia of the capsula externa area on the right side (arrow). CT indicates computed tomography; MCA, middle cerebral artery.

CT (Fig. 1D). The patient was discharged from hospital with normal neurological findings and no significant disability (NIHSS 0, mRS 0). A long-term anticoagulant treatment was started.

CONCLUSIONS

The cases presented here demonstrate that even patients who meet the definition of TIA (normal neurological examination and no sign of infarction on CT scan after a brief attack of neurological deficit) can have major arterial occlusion. Such occlusion, if not recanalized, can result in clinical deterioration and progression into extensive infarction and permanent neurological disability.

These cases raise the important question of whether patients with arterial occlusion can be diagnosed as TIA. This is because ischemia can develop due to occlusion, even when the patient does not have a neurological deficit and there is no infarction shown on the CT scan. The most likely explanation of why occlusion remains clinically silent for a certain amount of time is a good collateral flow that can temporarily compensate for the diminished flow behind the occlusion. Well-developed collateral flow was observed in the first case on TCCD and CT-AG (Fig. 1G). Therefore, recanalization of such an occlusion would be a therapeutic measure (as in patients with stroke) rather than a preventive measure (as it would be if a patient had TIA). There is currently no good terminology for a situation in which arterial occlusion is present but is not yet causing symptoms. A disadvantage in stroke patients, as compared with patients with coronary ischemia, is that there is no “troponin for stroke” that could detect clinically not-yet-manifested ischemia with sufficient sensitivity to differentiate TIA from stroke.

Several studies have demonstrated the efficacy and safety of endovascular treatment in patients with acute ischemic stroke caused by an occluded intracranial artery.⁵⁻⁹ Hypothetically, recanalization of intracranial occlusions in patients diagnosed with TIA may in a similar way improve outcome through the prevention of either stroke progression or stroke recurrence. Whether the benefit of acute treatment outweighs the possible complications in patients with TIA is, however, not known. The actual guidelines from the American Heart Association and American Stroke Association refer to the insufficiency of data on the benefit of endovascular treatment in patients with NIHSS <6.¹⁰ In the first case, we considered

recanalization therapy for the first time 5.5 hours after symptom onset. Although there was no ischemia on the CT scan (ASPECT score 10) and treatment was thus possible, the patient had a mild neurological deficit (NIHSS 1). If we had decided the opposite and endovascular treatment had been performed but resulted, for example, in intracerebral hemorrhage, aggressive treatment would have been considered unnecessary given the minimal neurological deficit at the time of our decision. In the second case, such a therapy was not considered at the time of patient examination after TIA because of absence of neurological deficit. Later, 5.25 hours after symptom onset, the presence of ischemia on the CT scan contraindicated recanalization therapy despite the severity of neurological deficit (NIHSS 10).

Several classification scores have been developed for predicting stroke risk after TIA: age, blood pressure, clinical features of TIA, duration of TIA (ABCD)² score, ABCD³-I score, and ABCD² score + MRI. However, none of these scores is applicable to our patients, because the ABCD² score does not consider the vascular status,¹¹ ABCD³-I score considers the status of extracranial (carotid stenosis $\geq 50\%$) but not intracranial arteries,¹² and ABCD² score + MRI is based on MR-angiography that was performed too late (24 h) for any recanalization therapy.¹³

The mechanism by which occlusion causes subsequent impairment of functional outcome needs to be better understood. The first step toward this understanding could be to use vascular imaging for all TIA patients to improve knowledge of the connection between acute vascular status and outcome. It may be that vascular occlusion is a target for acute revascularization, further underscoring the concept of TIA as an emergency medical condition. It is possible that we need to treat “vessels” rather than “symptoms,” because patients may not have symptoms but may experience ischemia, which can be temporarily clinically silent, opening the window for acute intervention. The provocative question is whether arterial occlusion means that the patient is having a stroke rather than TIA. If this is the case, the next step would be to consider the information on vascular status (obtained within the time window for intervention) in the definition of vascular diseases such as TIA or stroke.

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