Reversibility of Ischemic Findings on 3-T T_2^* -Weighted Imaging After Emergency Superficial Temporal Artery-Middle Cerebral Artery Anastomosis in Patients With Progressive Ischemic Stroke

—Two Case Reports—

Yoshiteru TADA, Masaaki UNO, Shunji MATSUBARA,
Atsuhiko SUZUE, Kenji SHIMADA, Naomi MORITA*,
Masafumi HARADA**, and Shinji NAGAHIRO

Departments of Neurosurgery, *Radiology, and **Radiologic Technology, School of Medicine,
Institute of Health Biosciences, The University of Tokushima Graduate School, Tokushima

Abstract

Vascular ischemic signs, i.e. multiple hypointense vessels in the ischemic territory, were identified by gradient echo-type 3-T T_2^* -weighted magnetic resonance (MR) imaging in 3 patients with acute ischemia due to major vessel occlusion. Emergency superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis was performed in 2 patients with progressive stroke caused by bleeding-type moyamoya disease or severe MCA stenosis. Both patients were initially treated conservatively, but their neurological signs deteriorated. 3-T T_2^* -weighted MR imaging detected funicular low signals in both patients indicating enhancement of cortical vessels or medullary veins. The area of the vascular ischemic signs was almost the same or smaller than the hypoperfusion area on perfusion-weighted MR imaging or single-photon emission computed tomography. Postoperatively, the vascular ischemic signs disappeared in both patients, suggesting a relationship with severe ischemia due to high-risk misery perfusion. Their postoperative course was uneventful, and MR imaging revealed no new cerebral ischemic lesions or cerebral hyperperfusion. The patient without surgery developed cerebral infarction in the area of the vascular ischemic signs. Vascular ischemic signs detected by 3-T T_2^* -weighted MR imaging may represent a new predictor of high-risk misery perfusion, and may disappear after STA-MCA anastomosis performed in the subacute stage.

Key words: emergency superficial temporal artery-middle cerebral artery anastomosis, progressing stroke, reversibility, 3-tesla T_2^* -weighted magnetic resonance imaging, vascular ischemic sign

Introduction

The Japanese EC-IC (extracranial-intracranial) Bypass Trial (JET) is a randomized, double-blind trial of 206 selected patients with severe hemispheric hemodynamic failure due to cerebral artery occlusive disease,⁵⁾ which showed that EC-IC bypass surgery reduced the incidence of major stroke or death in the 2 years after surgery (JET Study Group, personal communication). However, superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis for acute or subacute cerebral ischemia remains controversial. The most important factors for choosing urgent revascularization are progressive symptoms and the reversibility of ischemic tissue damage.

Gradient echo-type T_2^* -weighted magnetic resonance

(MR) imaging detects acute hemorrhage⁷⁾ and provides evidence of earlier microbleeds⁶⁾ in patients with cerebral ischemia. These images can also show intra-arterial clots as areas of hypointense signal intensity in an artery, known as the susceptibility vessel sign in acute ischemic stroke.^{1,10)} T_2^* -sensitive MR imaging can detect local hypointensity in the vascular territory of the occluded cerebral artery, which may result from increased deoxygenation of hemoglobin in blood, indicating misery perfusion.¹³⁾ Previously, we showed that 3-T T_2^* -weighted MR imaging showed vascular ischemic signs, i.e. hypointense cortical vessels or vessels in the deep white matter, in patients with acute ischemia due to major vessel occlusion.⁸⁾ However, the resolution of vascular ischemic signs after emergency STA-MCA anastomosis and the clinical importance have not been investigated.

Here we describe the reversibility of ischemic findings

on 3-T T_2^* -weighted MR imaging after emergency STA-MCA anastomosis in patients with progressive ischemic stroke.

Case Reports

Case 1: A 44-year-old woman with a history of hypertension experienced transient ischemic attacks of the right arm over a period of 6 months. She also complained of headache, nausea, and dysarthria. On admission to our hospital 3 days after the ictus, she was alert with dysarthria but no motor paresis. Routine laboratory tests including coagulation tests found no abnormalities. Computed tomography revealed intraventricular hemorrhage, predominantly in the left lateral and the third ventricle (Fig. 1A). Diffusion-weighted MR imaging showed no ischemic lesion (Fig. 1B). Cerebral angiography on the 2nd hospital day revealed moyamoya disease (right side, stage 2; left side, stage 3) (Fig. 1C, D).¹²⁾ Right carotid angiography demonstrated severe stenosis of the terminal portion of the internal carotid artery and moyamoya vessels at the base of the brain.

Fig. 1 Case 1. A: Computed tomography (CT) scan on admission showing intraventricular hemorrhage. B: Diffusion-weighted magnetic resonance image on admission showing no ischemic lesions. C: Right carotid angiogram showing severe stenosis of the terminal portion of the internal carotid artery and moyamoya vessels at the base of the brain (anteroposterior view). D: Left carotid angiogram showing middle cerebral artery occlusion, severe A_1 stenosis, and moyamoya vessels at the base of the brain (anteroposterior view).

sels at the base of the brain. Left carotid angiography disclosed occlusion just distal to the MCA, severe stenosis of the A_1 , and moyamoya vessels at the base of the brain. The diagnosis was intraventricular hemorrhage caused by moyamoya disease. She was conservatively treated with intravenous administration of isotonic electrolyte solution (1500 ml/day). Her blood pressure was stable at 160–180

Fig. 2 Case 1. A: Diffusion-weighted magnetic resonance (MR) image showing a high-intensity area in the left frontal lobe 5 days after stroke onset (arrow). B: Perfusion-weighted MR image showing a large hypoperfusion area almost identical to the left middle cerebral artery distribution. C, D: T_2^* -weighted MR images showing vascular ischemic signs, hypointense cortical vessels (arrows) or vessels in the deep white matter (arrowheads), consistent with the hypoperfused area. E: Preoperative N-isopropyl-p-(iodine-123) iodoamphetamine single-photon emission computed tomography scan showing reduced cerebral blood flow in the left cerebral hemisphere. F: Diffusion-weighted MR image showing the area of infarction had increased 7 days after stroke onset (arrow).

(systolic)/80–100 (diastolic) mmHg.

She manifested minimal right hemiparesis on the 5th day after the ictus. Diffusion-weighted MR imaging showed a high-intensity area in the left frontal lobe (Fig. 2A). Perfusion-weighted MR imaging demonstrated evidence of a large area of hypoperfusion almost identical to the left MCA distribution (Fig. 2B). 3-T T_2^* -weighted MR imaging detected vascular ischemic signs at the site of this area of hypoperfusion (Fig. 2C, D). Single-photon emission computed tomography (SPECT) using *N*-isopropyl-*p*-(iodine-123) iodoamphetamine (^{123}I -IMP) obtained on the 5th day after the ictus revealed hypoperfusion in the left hemisphere (Fig. 2E). Intensive care, including hypervolemia and hemodilution, was continued, but her symptoms progressed. Diffusion-weighted MR imaging performed on the 7th post-onset day showed the area of infarction had increased (Fig. 2F).

Based on these results, we considered the left hemisphere to be in the state of misery perfusion and performed emergency left STA-MCA anastomosis on the same day. Her blood pressure was controlled to normoten-

sive after the operation. Her right hemiparesis and aphasia gradually improved. Postoperative MR angiography showed the STA-MCA bypass was patent, and diffusion-

Fig. 3 Case 1. A: Follow-up T_2^* -weighted magnetic resonance (MR) image obtained 10 days after the operation showing no vascular ischemic signs. B: Postoperative perfusion-weighted MR image obtained 10 days after the operation demonstrating reperfusion. C: Postoperative *N*-isopropyl-*p*-(iodine-123) iodoamphetamine single-photon emission computed tomography scan revealing cerebral blood flow increase.

Fig. 4 Case 2. A, B: Diffusion-weighted magnetic resonance (MR) images on admission showing infarction in the insular cortex. C: Preoperative carotid angiogram revealing severe stenosis (arrow) in the proximal segment of the left middle cerebral artery (MCA) (anteroposterior view). D: Perfusion-weighted MR image showing a large hypoperfusion area almost identical to the left fronto-temporo-parietal lobe. E, F: T_2^* -weighted MR images showing vascular ischemic signs, hypointensity of the cortical vessels (arrows) and the vessels in the deep white matter (arrowheads). The extent of the vascular ischemic signs was almost the same or smaller than the area of hypoperfusion. G: Preoperative *N*-isopropyl-*p*-(iodine-123) iodoamphetamine single-photon emission computed tomography scan indicating low perfusion in the territory of the left MCA. H, I: Serial diffusion-weighted MR images on the 8th day after onset showing progression of infarction in the corona radiata.

weighted MR imaging showed no further ischemic lesions. SPECT found no reduction in cerebral blood flow (CBF) in the right hemisphere, so we did not perform revascularization surgery on the right. Follow-up 3-T T_2^* -weighted MR imaging obtained on the 10th day after the operation showed the vascular ischemic signs had disappeared (Fig. 3A). Postoperative perfusion-weighted MR imaging and SPECT performed on the same day demonstrated CBF recovery (Fig. 3B, C). She was discharged 15 days after the operation without neurological deficits, and she experienced no neurological deterioration during the follow-up period of 14 months.

Case 2: A 48-year-old man experienced numbness in his right arm. He was admitted to a local hospital and a diagnosis of small cerebral infarction in the left insular cortex was made (Fig. 4A, B). Cerebral angiography revealed severe stenosis of the M_1 portion of the left MCA (Fig. 4C). His symptoms gradually worsened despite anti-platelet therapy, so he was transferred to our hospital for further evaluation and treatment on the 4th day after onset. On admission, neurological examination revealed mild motor aphasia and perfusion-weighted MR imaging showed a large area of hypoperfusion almost identical to the left fronto-temporo-parietal lobe (Fig. 4D). 3-T T_2^* -weighted MR imaging detected vascular ischemic signs almost the

same or smaller than this area of hypoperfusion (Fig. 4E, F). ^{123}I -IMP SPECT indicated hypoperfusion in the territory of the left MCA (Fig. 4G). He received additional volume expansion therapy with free radical scavengers and anti-platelet therapy. However, his neurological signs deteriorated gradually and he developed complete right hemiparesis. Serial diffusion-weighted MR imaging on the

Fig. 5 Case 2. A: Follow-up T_2^* -weighted magnetic resonance (MR) image 9 days after the operation indicating disappearance of the vascular ischemic signs. B: Postoperative perfusion-weighted MR image showing increased perfusion. C: Postoperative N-isopropyl-p-(iodine-123) iodoamphetamine single-photon emission computed tomography scan showing cerebral blood flow similar to the flow on the contralateral side.

Fig. 6 Case 3. A: Diffusion-weighted magnetic resonance (MR) image on admission showing multiple hyperintense areas in the territory of the right middle cerebral artery (MCA). B: Perfusion-weighted MR image revealing hypoperfusion in the territory of the right MCA. C, D: T_2^* -weighted MR images showing the extent of vascular ischemic signs was almost the same or smaller than the area of hypoperfusion (arrows). E: N-isopropyl-p-(iodine-123) iodoamphetamine single-photon emission computed tomography scan revealing hypoperfusion in the territory of the right MCA. F: Right carotid angiogram revealing severe stenosis (arrow) in the distal segment of the right MCA (anteroposterior view). G: Follow-up diffusion-weighted MR image showing infarction at a site corresponding to the area of the vascular ischemic signs.

8th day after onset showed progression of infarction in the corona radiata (Fig. 4H, I). He underwent emergency left STA-MCA anastomosis on the 9th day after onset. Postoperatively, his right hemiparesis improved and he was able to resume his normal activities. Diffusion-weighted MR imaging showed no evidence of ischemic enlargement, and MR angiography demonstrated patency of the STA-MCA bypass. Follow-up 3-T T_2^* -weighted MR imaging obtained on the 9th day after the operation showed that the lesion had disappeared (Fig. 5A). Postoperative perfusion-weighted MR imaging and SPECT demonstrated reperfusion (Fig. 5B, C).

Case 3: A 74-year-old woman with a history of arterial hypertension, hyperlipidemia, and diabetes mellitus was admitted to our hospital with dysarthria and left minimal hemiparesis. Diffusion-weighted MR imaging showed multiple hyperintense lesions in the right MCA area (Fig. 6A). Perfusion-weighted imaging and ^{123}I -IMP SPECT revealed hypoperfusion in the territory of right MCA (Fig. 6B, E). 3-T T_2^* -weighted MR imaging detected vascular ischemic signs of almost the same or smaller extent than the area of hypoperfusion (Fig. 6C, D). Cerebral angiography revealed severe stenosis of the M_1 portion of the right MCA (Fig. 6F). Her neurological signs deteriorated despite conservative therapy using free radical scavengers and antiplatelet drugs, so we decided to administer anticoagulation therapy. However, she developed severe left hemiparesis on the 4th day after onset and follow-up diffusion-weighted MR imaging showed progression of infarction to almost the same area as the area of the vascular ischemic signs seen by the initial T_2^* -weighted MR imaging (Fig. 6G).

Discussion

The present cases illustrate two major findings. First, vascular ischemic signs on 3-T T_2^* -weighted MR imaging may represent a potential predictor for identifying imminent infarction and misery perfusion. Second, such vascular ischemic signs may be reversible by appropriate revascularization.

Misery perfusion is observed as increased brain oxygen extraction fraction (OEF) on positron emission tomography (PET) in brain regions with reduced CBF and relatively preserved oxygen metabolism. MR imaging is a potential alternative method for detecting misery perfusion. Increased OEF results in higher blood deoxyhemoglobin concentrations in the cerebral capillaries and veins. Deoxyhemoglobin is paramagnetic and oxyhemoglobin is diamagnetic, so changes in hemoglobin oxygenation levels affect MR signal intensities that depend on the blood oxygenation level. In our patients, the area of vascular ischemic signals was almost the same or smaller than the area of hypoperfusion identified by perfusion-weighted MR imaging or SPECT. These results indicate that hypoperfusion leads to a higher deoxyhemoglobin levels in vessels in the ischemic area, which results decreased signal intensity in these vessels on T_2^* -weighted MR imaging.

The physiological events were complex in our Case 1.

Ischemic complications secondary to bleeding-type moyamoya disease are rare.^{4,9,11} Dehydration,⁴ hypotension,⁴ increased intracranial pressure (ICP),⁴ coagulation anomalies,⁹ and vasospasm⁹ are all factors proposed to contribute to ischemic injury. Case 1 had a 6-month history of transient ischemic attacks, suggesting that the brain was hemodynamically compromised. We suggest that a rapid increase in ICP caused by the intraventricular hemorrhage was a major contributing factor in the occurrence of the ischemic complications. The increased ICP decreased cerebral perfusion, and CBF was diminished below the clinical baseline, probably in parallel with increased OEF. 3-T T_2^* -weighted MR imaging detected vascular ischemic signs at that time, which disappeared after revascularization. Improvement in these lesions may reflect normalization of the increased OEF by STA-MCA anastomosis.

1.5-T T_2^* -weighted MR imaging showed hypointense leptomeningeal vessels in patients with acute stroke, but only in 17 of 48 patients.³ In contrast, in our previous study, 3-T T_2^* -weighted MR imaging detected vascular ischemic signs in all 24 patients with major vessel occlusion, and the affected area contained not only cortical vessels but also medullary veins.⁸ The predictive value of the visualization of abnormal transcerebral veins on 1.5-T T_2^* -weighted MR imaging for further hemorrhagic transformation has also been found in acute stroke patients treated by intravenous thrombolysis.² However, neither of our patients with such vascular ischemic signs developed hemorrhagic transformation after emergency STA-MCA anastomosis. Postoperatively, their symptoms gradually improved, the vascular ischemic signs detected preoperatively disappeared, and did not progress to infarction. These findings suggest that the detectability of deoxyhemoglobin is different using 1.5-T and 3-T T_2^* -weighted MR imaging, and that the severity of CBF reduction and the increase in OEF are greater in hypointense areas on 1.5-T than 3-T T_2^* -weighted MR imaging. Therefore, detection of vascular ischemic signs by 1.5-T T_2^* -weighted MR imaging may be predictive of subsequent hemorrhagic events in patients scheduled for revascularization.

All hypointense areas detected by T_2^* -sensitive MR imaging obtained within 4 hours of symptom onset progressed to infarction.¹³ In our previous report,⁸ vascular ischemic signs seen on the initial 3-T T_2^* -weighted MR imaging decreased after recanalization by thrombolytic therapy in a patient with occlusion of a MCA branch. In our present Case 3, the area of vascular ischemic signs on the initial 3-T T_2^* -weighted MR imaging progressed to infarction. Our findings suggest that the vascular ischemic signs in the other 2 patients would not have disappeared spontaneously without surgery. However, we should be aware that some patients with vascular ischemic signs continue to be at high risk for complete infarction or hemorrhagic transformation after revascularization.

There are some limitations in our current study. Although we found that emergency bypass surgery produced improvement in the symptoms, we did not determine whether OEF was elevated in the area of vascular ischemic signs, or whether all areas of vascular ischemic

signs seen on 3-T T₂*-weighted MR imaging ultimately became infarction. As our study involved only 3 patients, larger patient populations are needed to address this issue.

The present cases suggest that vascular ischemic signs detected on 3-T T₂*-weighted MR imaging disappeared after emergency bypass surgery, indicating that such areas are potentially viable brain tissue at high risk for infarction in patients with progressive stroke. Our preliminary data describe a relative and not yet quantifiable index of oxygen extraction, and the relevance must be ascertained by PET studies.

References

- 1) Flacke S, Urbach H, Keller E, Traber F, Hartmann A, Textor J, Gieseke J, Block W, Folkers PJ, Schild HH: Middle cerebral artery (MCA) susceptibility sign at susceptibility-based perfusion MR imaging: Clinical importance and comparison with hyperdense MCA sign at CT. *Radiology* 215: 476–482, 2000
- 2) Hermier M, Nighoghossian N, Derex L, Adeleine P, Wiart M, Berthezene Y, Cotton F, Pialat JB, Dardel P, Honnorat J, Trouillas P, Froment JC: Hypointense transcerebral veins at T2*-weighted MRI: A marker of hemorrhagic transformation risk in patients treated with intravenous tissue plasminogen activator. *J Cereb Blood Flow Metab* 23: 1362–1370, 2003
- 3) Hermier M, Nighoghossian N, Derex L, Wiart M, Nemoz C, Berthezene Y, Froment JC: Hypointense leptomeningeal vessels at T2*-weighted MRI in acute ischemic stroke. *Neurology* 65: 652–653, 2005
- 4) Iwama T, Kotani Y, Yamakawa H, Nagata I, Hashimoto N, Sakai N: Cerebral ischemic complications following intracranial bleeding in patients with moyamoya disease—three case reports. *Neurol Med Chir (Tokyo)* 41: 450–453, 2001
- 5) JET Study Group: [Japanese EC-IC Trial (JET Study): Study design and interim analysis]. *Surgery for Cerebral Stroke* 30: 97–100, 2002 (Japanese)
- 6) Kidwell CS, Saver JL, Villablanca JP, Duckwiler G, Fredieu A, Gough K, Leary MC, Starkman S, Gobin YP, Jahan R, Vespa P, Liebeskind DS, Alger JR, Vinuela F: Magnetic resonance imaging detection of microbleeds before thrombolysis: An emerging application. *Stroke* 33: 95–98, 2002
- 7) Lin DD, Filippi CG, Steever AB, Zimmerman RD: Detection of intracranial hemorrhage: Comparison between gradient-echo images and b(0) images obtained from diffusion-weighted echo-planar sequences. *AJNR Am J Neuroradiol* 22: 1275–1281, 2001
- 8) Morita N, Harada M, Uno M, Matsubara S, Matsuda T, Nagahiro S, Nishitani H: Ischemic findings of T2*-weighted 3-Tesla MRI in acute stroke patients. *Cerebrovasc Dis* 26: 367–375, 2008
- 9) Nakai Y, Hyodo A, Yanaka K, Nose T: Fatal cerebral infarction after intraventricular hemorrhage in a pregnant patient with moyamoya disease. *J Clin Neurosci* 9: 456–458, 2002
- 10) Schellinger PD, Chalea JA, Kang DW, Latour LL, Warach S: Diagnostic and prognostic value of early MR imaging vessel sign in hyperacute stroke patients imaged <3 hours and treated with recombinant tissue plasminogen activator. *AJNR Am J Neuroradiol* 26: 618–624, 2005
- 11) Su IC, Yang CC, Wang WH, Lee JE, Tu YK, Wang KC: Acute cerebral ischemia following intraventricular hemorrhage in moyamoya disease: Early perfusion computed tomography findings. *J Neurosurg* 109: 1049–1051, 2008
- 12) Suzuki J, Takaku A: Cerebrovascular “moyamoya” disease. Disease showing abnormal net-like vessels in base of brain. *Arch Neurol* 20: 288–299, 1969
- 13) Tamura H, Hatazawa J, Toyoshima H, Shimosegawa E, Okudera T: Detection of deoxygenation-related signal change in acute ischemic stroke patients by T2*-weighted magnetic resonance imaging. *Stroke* 33: 967–971, 2002

Address reprint requests to: Yoshiteru Tada, M.D., Department of Neurosurgery, Institute of Health Biosciences, The University of Tokushima Graduate School, 3-18-15 Kuramoto-cho, Tokushima, Tokushima 770-8503, Japan.
e-mail: yoshiteru.tada@hotmail.co.jp