

# **Endarterectomy for Mild Cervical Carotid Artery Stenosis in Patients With Ischemic Stroke Events Refractory to Medical Treatment**

## **—Two Case Reports—**

Masakazu KOBAYASHI, Kuniaki OGASAWARA, Takashi INOUE,  
Hideo SAITO, Yasunori SUGA, and Akira OGAWA

*Department of Neurosurgery, Iwate Medical University, Morioka, Iwate*

### **Abstract**

**A 62-year-old man and a 44-year-old man with unilateral cervical carotid artery stenosis (less than 50% with echolucent plaque and ulceration) suffered recurrent ischemic stroke events despite treatment with antiplatelet and anticoagulation drugs. Carotid endarterectomy (CEA) was performed under transcranial Doppler monitoring for the detection of micro-emboli using a microscope inserted through a skin incision to minimize pressure on the carotid arteries. The atheroma plaque included an ulcer with fresh thrombi in both patients. Both patients awoke from anesthesia without new neurological deficits, and no ischemic stroke events have recurred since CEA. Endarterectomy is an effective method for preventing stroke in patients with severe carotid stenosis (>70%), but the efficacy of this procedure for mild carotid stenosis (<50%) remains uncertain, regardless of carotid plaque characteristics. The present cases suggest that even mild stenosis of the cervical carotid artery may result in ischemic stroke events that are refractory to medical treatment if the stenosis is associated with echolucent plaque with ulceration. Endarterectomy is recommended to prevent further stroke in such patients.**

Key words: carotid artery stenosis, carotid endarterectomy, stroke recurrence

### **Introduction**

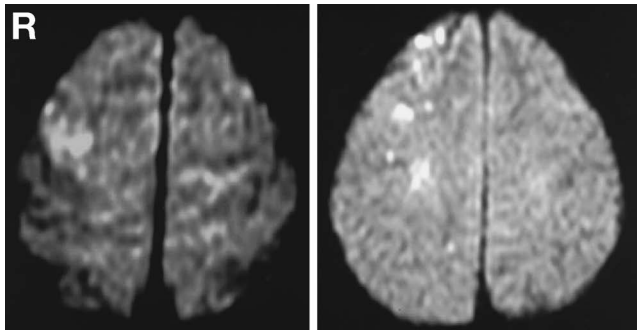
The severity of carotid artery stenosis is the factor most closely related to a high incidence of ischemic stroke events in patients with cervical carotid disease.<sup>5,10</sup> Certain carotid plaque characteristics, including the morphology and surface, are also associated with a high risk of stroke.<sup>1-4,6,7</sup> Endarterectomy is an effective method for preventing stroke in patients with severe carotid stenosis (>70%), but the efficacy of the procedure for mild carotid stenosis (<50%) remains uncertain, regardless of the carotid plaque characteristics.<sup>9</sup>

We treated two patients by carotid endarterectomy (CEA) for unilateral cervical carotid artery stenosis of less than 50% with plaque ulceration who suffered from recurrent ischemic stroke events despite treatment with antiplatelet and anticoagulation drugs.

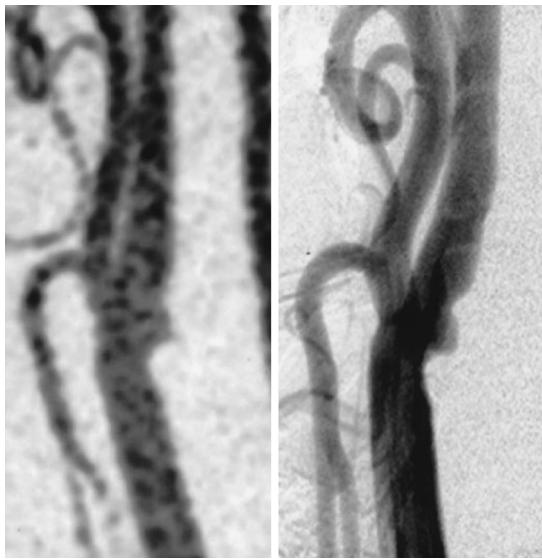
### **Case Reports**

**Case 1:** A 62-year-old man with a history of hypertension and hyperlipidemia experienced transient ischemic attack (TIA) manifesting as left hemiparesis and was treated with ticlopidine (200 mg/day). Five years later, the patient developed angina pectoris, and aspirin (100 mg/day) was added to the medication. Five months later, the patient experienced minor completed stroke manifesting as left hemiparesis, and the patient was hospitalized for further evaluation and treatment.

Diffusion-weighted magnetic resonance (MR) imaging revealed cortical infarcts in the right frontal lobe (Fig. 1 *left*). MR angiography showed stenosis of less than 50% with plaque ulceration at the right common carotid artery (CCA) bifurcation (Fig. 2 *left*). Warfarin was added to the antiplatelet agents to maintain the prothrombin international normalized ratio (PT-INR) at 2.0 to 2.5. However, 3 months later, the patient experienced recurrent minor completed stroke manifesting as left hemiparesis, and the patient was re-hospitalized. The PT-INR obtained 6

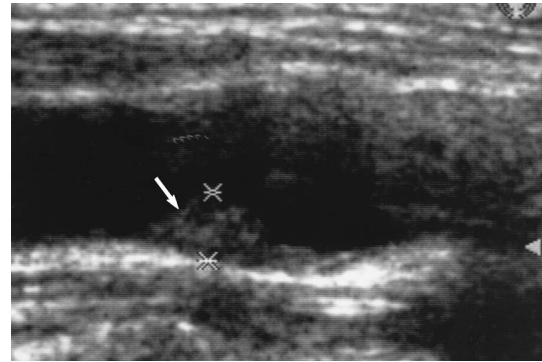


**Fig. 1 Case 1.** Diffusion-weighted magnetic resonance images showing fresh infarcts in the cerebral cortex of the right frontal lobe 5 hours after a second ischemic event manifesting as left hemiparesis (*left*), and fresh multiple infarcts in the right cerebral hemisphere at 7 hours after a third ischemic event manifesting as left hemiparesis (*right*).



**Fig. 2 Case 1.** Magnetic resonance angiogram after the second ischemic event (*left*), and carotid angiogram with arterial catheterization after the third ischemic event (*right*) showing 35% stenosis with ulceration at the right common carotid artery bifurcation.

hours after stroke recurrence was 2.08. Diffusion-weighted MR imaging revealed multiple infarcts in the right cerebral hemisphere (Fig. 1 *right*). Cerebral angiography with arterial catheterization showed 35% stenosis with plaque ulceration at the right CCA bifurcation (Fig. 2 *right*). No steno-occlusive lesions were observed in the intracranial arteries. Carotid



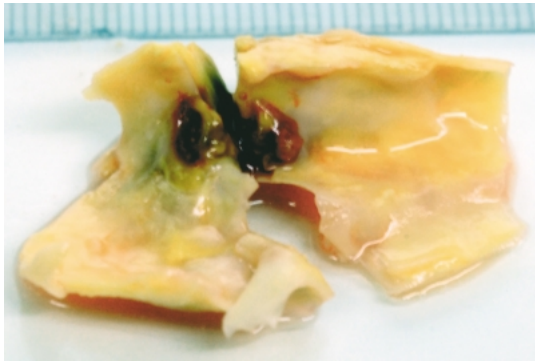
**Fig. 3 Case 1.** B-mode ultrasonogram of the right cervical carotid artery showing echolucent plaque (*arrow*).

echography revealed echolucent plaque in the right CCA (Fig. 3). Transesophageal echocardiography and Holter electrocardiography showed no abnormal findings.

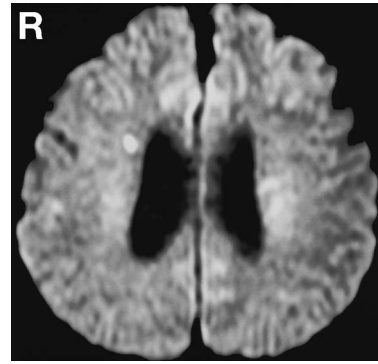
The patient underwent right CEA under general anesthesia. Transcranial Doppler monitoring for detection of micro-emboli was initiated after induction of anesthesia, and the procedure was performed under the operating microscope inserted through a skin incision to minimize the pressure on the carotid arteries during dissection. Dissection of the carotid arteries from the surrounding tissues was accomplished without the development of micro-emboli, and endarterectomy was performed successfully. Macroscopic examination of the atheroma plaque revealed an ulcer with fresh thrombi (Fig. 4), which corresponded to the ulceration on preoperative angiography and echolucent plaque on preoperative carotid echography.

The patient did not experience any new neurological deficits on recovery from anesthesia. Diffusion-weighted MR imaging performed on the 1st postoperative day showed no new ischemic lesions. Ischemic stroke events have not recurred with administration of aspirin (100 mg/day) for 3 years after the surgery.

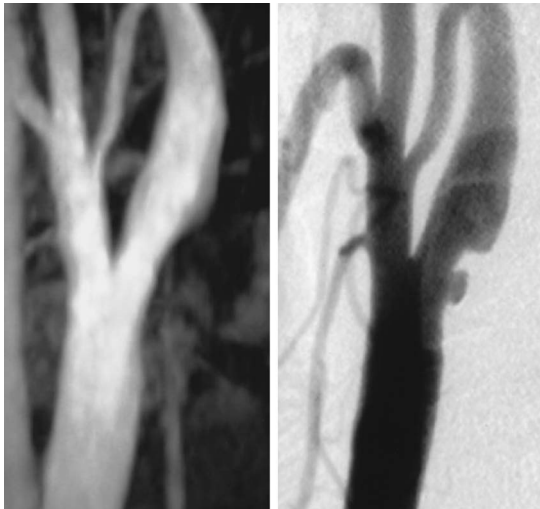
**Case 2:** A 44-year-old man with a history of diabetes mellitus suffered acute myocardial infarction and underwent percutaneous transluminal coronary angioplasty. He was treated with aspirin (100 mg/day) and ticlopidine (200 mg/day). Three years later, the patient presented with right amaurosis fugax. MR angiography showed stenosis of less than 50% at the right CCA bifurcation (Fig. 5 *left*). Oral warfarin was initiated to maintain the PT-INR at 2.0 to 2.5. However, 3 months later, the patient experienced two episodes of TIA manifesting as left hemiparesis, and was hospitalized for further evaluation and



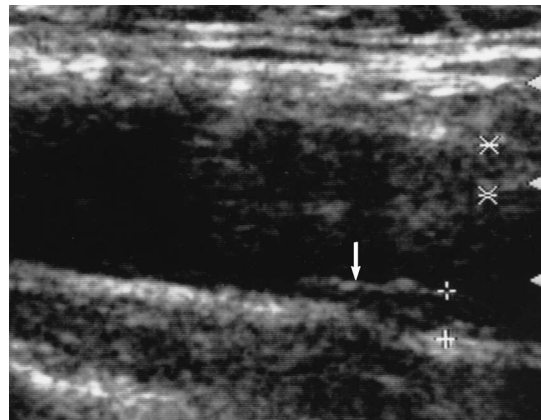
**Fig. 4** Case 1. Photograph of the surgical specimen showing atheroma plaque including an ulcer with fresh thrombi.



**Fig. 6** Case 2. Diffusion-weighted magnetic resonance image showing a fresh infarct in the white matter of the right cerebral hemisphere at 8 hours after the last ischemic event.



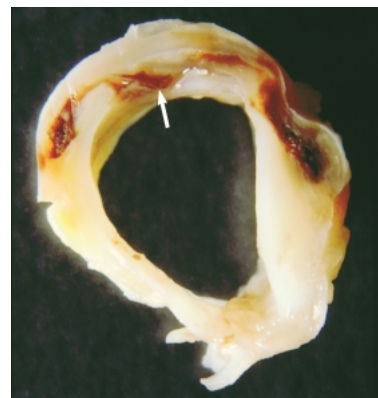
**Fig. 5** Case 2. Magnetic resonance angiogram after the first ischemic event (left), and carotid angiogram with arterial catheterization after the second ischemic event (right) showing 40% stenosis at the right common carotid artery bifurcation and ulceration in the lesion.



**Fig. 7** Case 2. B-mode ultrasonogram of the right cervical carotid artery showing echolucent plaque (arrow).

treatment. PT-INR obtained 3 hours after the stroke recurrence was 2.15.

Diffusion-weighted MR imaging revealed an infarct in the white matter of the right cerebral hemisphere (Fig. 6). Cerebral angiography with arterial catheterization showed 40% stenosis with plaque ulceration at the right CCA bifurcation (Fig. 5 right). No steno-occlusive lesions were observed in the intracranial arteries. Carotid echography revealed echolucent plaque in the right CCA (Fig. 7). Transesophageal echocardiography and Holter electrocardiography showed no abnormal findings.



**Fig. 8** Case 2. Photograph of the surgical specimen showing atheroma plaque including an ulcer with thrombi (arrow).

The patient underwent right CEA using the same procedure as described in Case 1. Dissection of the carotid arteries from the surrounding tissues was accomplished without development of micro-emboli, and endarterectomy was performed successfully. Macroscopic examination of the atheroma plaque revealed an ulcer with thrombi (Fig. 8), which corresponded with the ulceration on preoperative angiography and echolucent plaque on preoperative carotid echography.

The patient did not experience new neurological deficits on recovery from anesthesia. Diffusion-weighted MR imaging performed on the 1st postoperative day showed no new ischemic lesions. Ischemic stroke events have not recurred with administration of aspirin (100 mg/day) for 2 years after surgery.

## Discussion

In the present cases, preoperative MR imaging, cerebral angiography, transesophageal echocardiography, and Holter electrocardiography suggested that the ischemic stroke events resulted from artery-to-artery embolism associated with cervical carotid stenosis. Subsequently, ischemic stroke events recurred despite treatment with antiplatelet and anticoagulation drugs. Therefore, endarterectomy was selected despite the cervical carotid artery stenosis of less than 50%. Outcomes were good, and ischemic stroke events have not recurred following CEA.

In addition to the severity of stenosis, certain plaque characteristics, such as surface and morphology, are determinants of the risk of ischemic stroke events.<sup>1-4,6,7</sup> For example, plaque ulceration with symptomatic high-grade stenosis is associated with a several-fold increased risk of stroke.<sup>4</sup> Although plaque ulceration is usually detected in large high-grade carotid lesions, ulcers are sometimes found in early carotid atheroma (7% of low-grade stenosis).<sup>7</sup> The severity of carotid stenosis and stroke, and plaque ulceration and stroke are related.<sup>7</sup> The stroke event rate was higher in patients with low-grade stenosis and ulcer (9%) than in those without ulcer (2%), although there was no statistical significant difference between the two groups due to the relatively small number of patients studied.<sup>7</sup>

Plaque morphology is another factor associated with increased risk of stroke.<sup>1,2,6</sup> For example, echolucent plaque is significantly more common in symptomatic patients than in asymptomatic patients.<sup>6</sup> Other studies have also suggested an association between echolucent plaque and the subsequent development of neurologic symptoms.<sup>1,2</sup> In the present patients, preoperative cerebral angiography

and carotid echography revealed ulceration and echolucent plaque in the affected carotid artery, which was confirmed by postoperative macroscopic examination findings of ulcerated plaque with thrombi. The thrombi may have caused recurrent artery-to-artery embolism, resulting in medically-refractory ischemic stroke events in the context of mild carotid stenosis.

Our two patients underwent MR angiography but not carotid echography when first hospitalized at our institution for evaluation of their ischemic events. Even if carotid stenosis detected on MR angiography is mild, subsequent carotid echography should be performed to evaluate the plaque morphology. Inflammation is well known to be associated with plaque destabilization and eventually plaque rupture.<sup>8</sup> In fact, patients with elevated levels of high-sensitivity C-reactive protein exhibit increased risk for adverse cardiovascular outcome attributable to clinical adverse events associated with progressive atherosclerotic disease.<sup>11</sup> Therefore, a patient with ischemic events due to mild carotid stenosis, and exhibiting high levels of inflammatory biomarkers such as high-sensitivity C-reactive protein in addition to ulcerated and echolucent plaque, should undergo CEA before development of further ischemic events.

Both our patients had similar surgical risk factors. Preoperative carotid echography revealed echolucent plaque, suggesting soft plaque, in the affected carotid artery. Such soft plaque is associated with a higher risk of artery-to-artery embolism during manipulation of the carotid arteries during CEA. Therefore, transcranial Doppler monitoring was employed intraoperatively for detection of micro-emboli, and pressure on the carotid arteries during dissection was minimized by using a microscope inserted through a skin incision. If transcranial Doppler monitoring detects micro-embolic signals before exposing the surgical fields for placing an intraluminal shunt, the CCA and external carotid artery should be clamped early to promote reversal of blood flow in the ipsilateral internal carotid artery and prevent artery-to-artery embolism.

The present cases show that patients with mild stenosis of the cervical carotid artery may develop medically-refractory ischemic stroke events in the presence of echolucent plaque with ulceration. Endarterectomy is recommended to prevent further stroke in such patients.

## References

- 1) Belcaro G, Laurora G, Cesarone MR, De Sanctis MT, Incandela L, Fascetti E, Geroulakos G, Ramaswami

- G, Pierangeli A, Nicolaides AN: Ultrasonic classification of carotid plaques causing less than 60% stenosis according to ultrasound morphology and events. *J Cardiovasc Surg (Torino)* 34: 287-294, 1993
- 2) Bock RW, Gray-Weale AC, Mock PA, App Stats M, Robinson DA, Irwig L, Lusby RJ: The natural history of asymptomatic carotid artery disease. *J Vasc Surg* 17: 160-171, 1993
  - 3) Egado JA: Benefits of modifying the predictive factors of stroke recurrence. *Cerebrovasc Dis* 20 Suppl 2: 84-90, 2005
  - 4) Eliasziw M, Streifler JY, Fox AJ, Hachinski VC, Ferguson GG, Barnett HJ: Significance of plaque ulceration in symptomatic patients with high-grade carotid stenosis. *Stroke* 25: 304-308, 1994
  - 5) European Carotid Surgery Trialists' Collaborative Group: MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70-99%) or mild (0-29%) carotid stenosis. *Lancet* 337: 1235-1243, 1991
  - 6) Golledge J, Cuming R, Ellis M, Davies AH, Greenhalgh RM: Carotid plaque characteristics and presenting symptom. *Br J Surg* 84: 1697-1701, 1997
  - 7) Handa N, Matsumoto M, Maeda H, Hougaku H, Kamada T: Ischemic stroke events and carotid atherosclerosis: results of the Osaka Follow-up Study for Ultrasonographic Assessment of Carotid Atherosclerosis (the OSACA Study). *Stroke* 26: 1781-1786, 1995
  - 8) Koenig W, Khuseyinova N: Biomarkers of atherosclerotic plaque instability and rupture. *Arterioscler Thromb Vasc Biol* 27: 15-26, 2007
  - 9) Moore WS, Barnett HJ, Beebe HG, Bernstein EF, Brener BJ, Brott T, Caplan LR, Day A, Goldstone J, Hobson RW 2nd, Kempeziński RF, Matchar DB, Mayberg MR, Nicolaides AN, Norris JW, Ricotta JJ, Robertson JT, Rutherford RB, Thomas D, Toole JF, Trout HH 3rd, Wiebers DO: Guidelines for carotid endarterectomy: a multidisciplinary consensus statement from the ad hoc Committee, American Heart Association. *Stroke* 26: 188-201, 1995
  - 10) North American Symptomatic Carotid Endarterectomy Trial Collaborators: Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 325: 445-453, 1991
  - 11) Schlager O, Exner M, Mlekusch W, Sabeti S, Amighi J, Dick P, Wagner O, Koppensteiner R, Minar E, Schillinger M: C-reactive protein predicts future cardiovascular events in patients with carotid stenosis. *Stroke* 38: 1263-1268, 2007
- 
- Address reprint requests to: Kuniaki Ogasawara, M.D., Department of Neurosurgery, Iwate Medical University, 19-1 Uchimaru, Morioka 020-8505, Japan.  
e-mail: kuogasa@iwate-med.ac.jp