Urgent Endarterectomy Using Pretreatment With Free Radical Scavenger, Edaravone, and Early Clamping of the Parent Arteries for Cervical Carotid Artery Stenosis With Crescendo Transient Ischemic Attacks Caused by Mobile Thrombus and Hemodynamic Cerebral Ischemia
—Case Report—

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Abstract

A 68-year-old man with left cervical internal carotid artery stenosis suffered crescendo transient ischemic attacks caused by mobile thrombus detected by carotid echography and secondary impairment of cerebral hemodynamic reserve demonstrated by positron emission tomography. Urgent carotid endarterectomy (CEA) was performed following pretreatment with edaravone and early clamping of the carotid arteries without intraluminal shunting. The postoperative course was uneventful, and postoperative magnetic resonance imaging and single-photon emission computed tomography revealed no new cerebral ischemic lesions and no findings of cerebral hyperperfusion, respectively. The risks associated with CEA are higher for patients with evolving stroke or crescendo transient ischemic attacks than that for patients with stable disease. This case demonstrates that urgent endarterectomy for cervical carotid artery stenosis with crescendo transient ischemic attacks caused by mobile thrombi and hemodynamic cerebral ischemia can be successfully performed following pretreatment with edaravone and early clamping of the carotid arteries.

Key words: carotid endarterectomy, mobile thrombus, hemodynamic cerebral ischemia, crescendo transient ischemic attacks

Introduction

Carotid endarterectomy (CEA) is an effective method for preventing stroke in appropriately selected patients. Most complications following CEA are ischemic in nature, and occur secondary to embolization or inadequate cerebral protection in patients with poor collateral supply. Mobile or floating thrombi are easily detected by routine carotid echography and are associated with increased risk of perioperative stroke in patients undergoing CEA. Postoperative neurological dysfunction may also be related to cerebral hyperperfusion, which is defined as a major increase in ipsilateral cerebral blood flow well above the metabolic demands of the brain tissue following correction of carotid artery stenosis. Further, preoperative impairment in cerebral hemodynamic reserve is a significant risk factor for the development of post-cea hyperperfusion.

We successfully treated a patient who underwent urgent CEA using pretreatment with free radical scavenger, edaravone, and early clamping of the parent arteries for cervical carotid artery stenosis after sudden onset of crescendo transient ischemic attacks (TIAs). Preoperative carotid echography and positron emission tomography confirmed mobile...
thrombus and impaired cerebral hemodynamic reserve, respectively.

Case Report

A 68-year-old man with a history of hypertension experienced two minor completed strokes causing right hemiparesis over a period of 6 months. Magnetic resonance (MR) imaging and cerebral angiography with arterial catheterization performed at a local hospital revealed multiple infarcts in the left cerebral hemisphere and 95% stenosis of the left cervical internal carotid artery (ICA) (Fig. 1). No collateral flow was evident via the anterior or posterior communicating arteries. The patient received anti-platelet agents and was admitted to our hospital for further evaluation and treatment 2 months after the last stroke.

On admission, neurological examination revealed mild right hemiparesis, and modified Rankin scale score of 2. Brain single-photon emission computed tomography (SPECT) study using $^{[123]}$I-N-isopropyl-p-iodoamphetamine$^{15}$ showed reduced cerebral blood flow in the left cerebral hemisphere (Fig. 2 left). Brain positron emission tomography study using $^{15}$O-labeled O$_2$ and CO inhalation and H$_2$O autoradiography$^{20}$ showed reduced cerebrovascular reactivity to acetazolamide (center), and increased oxygen extraction fraction (right) in the left cerebral hemisphere (Fig. 3). Carotid echography revealed ulcerated plaque with mobile thrombus in the left cervical ICA (Fig. 4). After completion of these examinations, the patient suffered sudden onset of recurrent TIAs. Diffusion-weighted MR imaging revealed acute
infarcts in the deep white matter and the cortex of the left cerebral hemisphere (Fig. 5 left column). Intravenous administration of argatroban was initiated, but the patient experienced greater frequency of TIAs as well as further evidence of new infarcts in the left cerebral hemisphere (Fig. 5 center column).

Three days after the onset of crescendo TIAs, absence of development of hemorrhagic transformation was confirmed on computed tomography scans and the patient underwent urgent left CEA under general anesthesia. To prevent the development of artery-to-artery embolism, the operation was performed under the operating microscope through a skin incision and stress to the carotid arteries was minimized. The carotid sheath was opened, and the ICA was identified just behind the external carotid artery, so an intraluminal shunt could not be employed without manipulation of the carotid arteries. Therefore, drip infusion of edaravone (60 mg) and single bolus of heparin (5000 units) were administered, and the common and external carotid arteries were clamped without intraluminal shunting. The carotid arteries including the ICA were dissected, and endarterectomy was performed. The atheroma plaque included an ulcer and thrombi. The carotid clamping time was 57 minutes. Intraoperative transcranial regional cerebral oxygen saturation monitoring using near-infrared spectroscopy (TOS 96; Tostec, Tokyo) with the sensors bilaterally and symmetrically placed over the forehead revealed decreased left regional cerebral oxygen saturation immediately after the carotid clamping (Fig. 6). Subsequently, regional cerebral oxygen saturation recovered gradually. Intraoperative electroencephalography monitoring revealed no abnormal changes during the carotid clamping.

The patient did not experience new neurological deficits upon recovery from anesthesia. Brain SPECT performed immediately after surgery showed improvement of cerebral blood flow and no findings of cerebral hyperperfusion in the left cerebral hemisphere (Fig. 2 right). Diffusion-weighted MR imaging performed on the 1st postoperative day showed no new ischemic lesions (Fig. 5 right column). The patient’s postoperative course was uneventful.

**Discussion**

CEA can be performed safely within 2 weeks of non-disabling ischemic stroke and the benefit from CEA declines rapidly with increasing delay. Urgent CEA in the acute stage may also be beneficial for patients with evolving stroke or crescendo TIAs if they did not suffer major disturbances of consciousness and hemorrhagic transformation. However, the surgical risks associated with urgent CEA in such patients is several times greater than that in patients with stable disease. The present patient suffered crescendo TIAs caused by mobile thrombus...
and hemodynamic cerebral ischemia despite medical treatment and did not exhibit major disturbances of consciousness and hemorrhagic transformation, so urgent CEA was indicated in the acute stage.

The present patient had several surgical risk factors. Preoperative carotid echography revealed mobile thrombus in the affected carotid artery. The presence of mobile thrombus can result in artery-to-artery embolism caused by manipulation of the carotid arteries during CEA. Therefore, the common and external carotid arteries were clamped before manipulation of the carotid arteries, resulting in reversal of blood flow in the ipsilateral ICA and prevention of artery-to-artery embolism. However, early clamping of the carotid arteries resulted in a longer duration of cerebral ischemia, and transcranial cerebral oxygen saturation measurements indicated consequent severe global ischemia in the affected cerebral hemisphere, although intraoperative electroencephalography monitoring revealed no abnormal changes. The ICA was located just behind the external carotid artery in the operative field, so an intraluminal shunt could not be employed without manipulation of the carotid arteries. Therefore, a free radical scavenger, edaravone, was administered for neuroprotection in anticipation of the prolonged duration and increased severity of cerebral ischemia. Edaravone improves outcomes in patients with acute stroke and exerts a neuroprotective effect if administered before ischemic insults in animal models.

Further, pretreatment with edaravone can prevent the development of cognitive impairment caused by cerebral ischemia during carotid clamping in patients undergoing CEA.

This patient also had reduced cerebrovascular reactivity to acetazolamide and elevated oxygen extraction fraction in the affected hemisphere. Impairment of cerebral hemodynamic reserve is a significant predictor of post-CEA hyperperfusion. The development of cerebral hyperperfusion after CEA is also associated with cerebral ischemia during carotid clamping, and patients with reduced preoperative cerebrovascular reactivity and significant cerebral ischemia during carotid clamping always develop post-CEA hyperperfusion. However, pretreatment with edaravone can prevent the occurrence of cerebral hyperperfusion after CEA. Therefore, the administration of edaravone may have prevented the development of post-CEA hyperperfusion in the present patient, despite the preoperative impairment of cerebral hemodynamic reserve and significant cerebral ischemia during carotid clamping.

In conclusion, urgent endarterectomy for cervical carotid artery stenosis with crescendo TIAs caused by mobile thrombi and hemodynamic cerebral ischemia can be successfully performed following pretreatment with edaravone and early clamping of the carotid arteries.

References

Urgent CEA


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