Unilateral Leptomeningeal Enhancement After Carotid Stent Insertion Detected by Magnetic Resonance Imaging

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Background and Purpose—Percutaneous transluminal angioplasty combined with vascular stenting is currently being assessed in the treatment of patients with symptomatic, severe carotid stenosis. The immediate cerebral hemodynamic effects resulting from stenting are not fully understood. This article describes a novel finding: abnormal leptomeningeal enhancement after stenting shown by MRI.

Methods—Fourteen patients with symptomatic severe carotid bifurcation stenosis underwent MRI within 4 hours before and within 3 hours after attempted carotid stenting. Twelve patients were successfully stented. Part of the MR investigation consisted of the acquisition of T1-weighted images before and after administration of the contrast agent Gd-DTPA, both before and after the procedure.

Results—All 12 patients who underwent successful stenting did not have abnormal enhancement of the leptomeninges before stenting but developed unilateral enhancement following intervention but before the second injection of contrast agent. No contrast enhancement was detected in the 2 patients who had the angiographic procedure but were not stented.

Conclusions—These findings suggest that abnormal changes to the leptomeningeal vasculature occur during carotid stenting which are not associated with sudden development of neurological symptoms. The anatomic distribution of the enhancement suggests that it is a consequence of the sudden change in brain hemodynamics secondary to the improvement in carotid flow after stenting. (Stroke. 2000;31:848-851.)

Key Words: angioplasty ▪ blood-brain barrier ▪ carotid stenosis ▪ magnetic resonance imaging ▪ stenting

Atherosclerotic carotid stenosis is the leading cause of ischemic stroke in adults. The results of 2 large, multicenter studies have shown the relative advantages of medical and surgical treatment (carotid endarterectomy) in patients with severe, symptomatic carotid stenosis.1–3 Other interventional procedures aimed at improving blood flow to the brain such as percutaneous transluminal angioplasty4 and, more recently, the combination of balloon angioplasty and endovascular stent insertion,5 are also being used to reduce the risk of stroke. Stenting, like angioplasty, has the advantage of being less invasive than surgical intervention and may offer a low incidence of restenosis.6 The long-term effects of interventional procedures (≥2 years) have been reported in the case of endarterectomy, will presumably be shortly reported in the case of balloon angioplasty, and are yet to be assessed for stenting.

MR has become an invaluable tool for neurological research with use of structural imaging and “functional” techniques such as perfusion-weighted and diffusion-weighted imaging. The short-term cerebral effects of direct interventional treatments for carotid stenosis have not been extensively studied, although early reports show improvement of cerebral blood flow after endarterectomy.7 Chelates of gadolinium,8 a rare earth metal, are commonly used as an intravenous contrast agent in MRI. In neuroimaging they are used to depict breakdown of the blood-brain barrier or, with the advent of subsecond scanning times, as a tracer for investigating cerebral perfusion. The findings presented in this article are preliminary in that they are part of an ongoing study that includes an extensive MR protocol designed to study the immediate cerebral consequences of carotid stenting. As part of that protocol we monitored cerebral perfusion in patients who have undergone carotid stenting with dynamic first-pass gadolinium perfusion imaging. After perfusion imaging we routinely perform T1-weighted MRI, and it is in this context that the findings described in this article were made.

Subjects and Methods

Subjects
The study group consisted of 7 men and 7 women (mean age 68 ± 11 years) who had symptoms suggestive of cerebral or ocular ischemia: transient ischemic attacks (n = 4), amaurosis fugax (n = 3), minor stroke (n = 4), and major nondisabling stroke (n = 3). The patients were screened by Doppler ultrasound and received arch angiography if ultrasound showed a stenosis of >50%. Arch angiography was performed for 2 reasons: to confirm or refute the presence of severe...
carotid bifurcation stenosis and to look for significant atherosclerotic disease of the aortic arch and its branches (proximal disease). When a severe stenosis was confirmed (using the NASCET criteria\(^1\)) and there was no significant proximal disease, patients were randomized between endarterectomy and stenting, and those in the stenting group were recruited into this study. If there was significant proximal disease, the patients were offered endarterectomy only. One of the 14 patients had a previous carotid endarterectomy contralateral to stent insertion, and another had a previous carotid stent contralateral to the symptomatic side being treated during this study. The recruitment and protocol outlined below were approved by the local research ethics committee, and all subjects were provided informed, written consent before their participation in this study.

**Procedures**

**Percutaneous Transluminal Angioplasty/Stent Insertion**

A diagnostic angiographic catheter was placed in the common carotid artery from a standard right femoral artery approach, and a Compas wire (Mallinckrodt Medical Ltd) was inserted into the external carotid artery, followed by an Arrow Sheath (7F, 80- to 100-cm long) into the common carotid artery. Atropine (1.2 mg) was administered either via systemic intravenous injection (3 patients) or into the common carotid artery via the catheter (9 patients). A V18 (0.018\(^\circ\)) wire was fed through the stenosis into the internal carotid artery. Pre-stent dilation was achieved by a 3- or 4-mm diameter balloon inflated once, for approximately 15 seconds. An 8- or 9-mm-diameter Wallstent (Boston Scientific) was then inserted. Postdilation was achieved using a balloon 5 mm (or in 1 case 6 mm) in diameter inflated once for approximately 15 seconds.

**MRI**

MR examinations were performed on a 1.5-T system (Eclipse, Marconi Medical Systems). The full MR protocol consisted of a variety of sequences used to acquire data before and after stenting. For the purpose of this article, we will discuss only part of the MR imaging in detail. A fast fluid-attenuated inversion recovery (FLAIR) sequence (TE=95.9 ms; TR=6000 ms; inversion time=1800 ms; echo train length=8; acquisition matrix 192×256 over a 25-cm FOV; averages=1) was used to acquire 20 5-mm-thick contiguous axial images. These images were acquired before and after intravenous administration of 20 mL of the contrast agent Gd-DTPA (Magnevist, Schering AG). In 6 cases this was supplemented with standard spin-echo T1-weighted imaging (TE=16 ms; TR=501 ms; acquisition matrix 192×256 over a 25-cm FOV; averages=1). MRI was performed before and after the interventional procedure. Thus, 4 sets of MR images were acquired: preprocedure precontrast, preprocedure postcontrast, postprocedure precontrast, and postprocedure postcontrast.

The mean time between initial MR imaging and insertion of the stent was 137 minutes (range 43 to 235 minutes). The mean time between stent insertion and the poststenting MRI was 111 minutes (range 80 to 175 minutes).

Two patients did not undergo stent insertion, 1 due to the presence of tortuous vasculature and the other to occlusion of both internal carotid arteries. Both of these subjects were controlled as controls by having an initial MR examination, conventional arch angiography, and a second MR examination after the diagnostic angiogram.

**Results**

One patient had focal enhancement before stenting that was intraparenchymal, adjacent to an area of (presumably) recent infarction. No patient showed leptomeningeal enhancement after the introduction of Gd-DTPA before stenting.

All 12 patients who underwent stenting demonstrated areas of leptomeningeal enhancement on FLAIR imaging after stenting but before the administration of the second bolus of Gd-DTPA. In all cases the enhancement became more prominent after administration of the second bolus of contrast. In 11 of 12 patients, enhancement occurred only ipsilateral to the stented carotid artery; in 1 the enhancement was contralateral to the stent. In this case the opposite carotid artery was occluded. There were 2 distinct enhancement patterns: 6 of 12 cases demonstrated large areas of unilateral enhancement of the leptomeninges, primarily in the territory of the middle cerebral artery (Figure 1); the remaining 6 showed areas of focal enhancement (Figure 2), which tended to be adjacent to...
areas of old cortical ischemic damage. No patient showed leptomeningeal enhancement in the vascular territory of the anterior cerebral artery, and enhancement in the posterior cerebral artery territory was unusual and minimal.

Where T1-weighted spin-echo images were obtained (6 subjects), the same spatial distribution of enhancement was shown when compared with the FLAIR sequences. Contrast enhancement was more pronounced on images acquired with the FLAIR sequence than those acquired with the T1-weighted spin-echo sequence. The unilateral abnormal enhancement was present in cases in which the atropine was given peripherally as well as intra-arterially. None of the 12 patients had new neurological symptoms after the stenting, and all made uneventful recoveries.

No abnormal enhancement was seen in the 2 patients who had angiography and atropine but were not stented.

Discussion

Leptomeningeal enhancement refers to the abnormal accumulation of contrast media in the pia and/or arachnoid mater and is a comparatively unusual radiological finding. It can be seen in malignant infiltration of the meninges, meningeal infection, and Sturge-Weber syndrome (due to leptomeningeal angiomatosis). We believe that this is the first description of meningeal enhancement following carotid stenting.

Leptomeningeal enhancement can be seen on CT but MR is much more sensitive and specific. Standard T1-weighted spin-echo or fast spin-echo sequences with short repetition times are the most common method of depicting the presence of contrast agent and are used routinely in most centers. FLAIR is based on an inversion-recovery sequence that is heavily T1 weighted, as well as being T2 weighted. It has recently been reported that this sequence can be particularly useful for detecting superficial enhancement in areas such as the meninges, and this is confirmed by our early experience. When performed, enhancement seen on the T1-weighted spin-echo images spatially matched that seen with the FLAIR technique in our study. Thus, we believe that what we have observed is a shortening in the T1 of the leptomeninges caused by the dipole-dipole interactions of the paramagnetic gadolinium ion complex. Because the enhancement was seen after angioplasty/stenting but before the second injection of Gd-DTPA, the gadolinium complex must have originated from the pool of contrast injected before carotid intervention.

A number of explanations for the leptomeningeal enhancement exist, including a reaction to the iodinated contrast media used for angiography, a reaction to the atropine used during the stenting procedure, or a result of the carotid intervention itself. The provisional nature and small numbers of this study do not allow firm conclusions; however, a number of indicators are apparent.

It would seem unlikely that iodinated angiography contrast media (in this case Optiray, Mallinckrodt Medical Ltd) was the cause. Because MRI is not usually performed immediately after an angiogram, there is no “human” literature for reference, although animal models have been studied. However, the 2 patients in our study who had arch carotid angiography and no stenting did not show leptomeningeal enhancement. More control data would be needed to further limit the possibility that x-ray contrast media is the causative agent that leads to the observed enhancement.

Similarly, it seems unlikely that atropine is the cause of the enhancement. It was routine to administer the atropine via the catheter in the carotid artery under treatment. In the latter part of this study, 3 patients had intravenous atropine and also showed only unilateral enhancement.

An alternative explanation could be that the abnormal enhancement occurred as a result of diffuse cerebral microembolism. Cerebral microembolism is well described in the literature pertaining to Doppler ultrasound. None of the

Figure 2. Sample images showing leptomeningeal enhancement localized around the medial and posterior orbital gyrus of the right frontal lobe, ipsilateral to the stented artery. (a) FLAIR precontrast, prestenting; (b) FLAIR postcontrast, prestenting (no enhancement); (c) conventional angiogram of the carotid bifurcation, prestenting; (d) conventional angiogram of the carotid bifurcation, poststenting; (e) FLAIR before second contrast bolus, poststenting (focal enhancement from the prestenting contrast bolus [arrow]); and (f) FLAIR after second contrast bolus, poststenting, showing stronger enhancement (arrow).
patients in this study had any clinical evidence of embolic stroke after intervention. Also, the enhancement could not be a marker for subacute stroke since it was observed within 3 hours of the interventional procedure. It is also unlikely to represent areas of acute infarction because the anatomic location suggests leptomeninges rather than cortical gray matter, and areas of acute infarction do not enhance after the administration of MR contrast. However, the hypothesis could be tested further with diffusion-weighted imaging, a marker for acute ischemic change.

The most likely cause appears to be directly related to the arterial inflow allowed by the stenting. The lack of any leptomeningeal enhancement before the procedure confirms the integrity of the blood-brain barrier prior to stenting. Gadolinium is excreted promptly from the body (half life of approximately 90 minutes) but some of the original bolus would be present during the stenting procedure. It should be noted that delayed MR imaging after Gadolinium does not produce leptomeningeal enhancement itself.

The physiological mechanisms that cause the observed enhancement are not obvious. However, the lack of enhancement seen in territory supplied by the anterior cerebral artery suggests that the phenomenon is hemodynamic in nature, because this area may be supplied from the contralateral supply via the anterior cerebral communicating artery. In all but 1 case the enhancement was ipsilateral to the treated stenosis, which suggests that changes in blood-brain barrier integrity occur in areas that are under low arterial pressure and have low flow rates as a result of carotid stenosis. This is likely to produce dilatation of the leptomeningeal collateral vessels, which may also explain the contralateral enhancement in the patient with contralateral carotid occlusion, where the circulation and meninges within that hemisphere may be most susceptible to sudden hemodynamic changes bought about by revascularization.

If leptomeningeal arterial vasodilation has occurred, intervention in severely occluded carotid vessel disease would probably produce hyperemia, characterized by a sudden increase in blood flow with loss of compensatory autoregulation. If leptomeningeal "leakiness" might lead to leptomeningeal enhancement. It is expected that this would be transient, but the exact time course cannot be defined by the data presented here. In a recent study, patients were monitored by MRI 1 to 2 days after endarterectomy, and enhancement was not seen at that time. In the present study, no symptoms were reported after the procedure, and thus this proposed enhancement mechanism needs to be distinguished from the hyperperfusion syndrome. Hyperperfusion syndrome is a known clinical complication of carotid endarterectomy that generally manifests itself 5 to 8 days after surgery. In a large study (1145 endarterectomies), the incidence of hyperperfusion syndrome was found to be approximately 2%. Fits, focal signs or headaches, and intracerebral hemorrhage or cerebral edema may be present. Pathological findings in a single case of intracerebral hemorrhage demonstrated hypercellularity with proliferation of endothelial cells and smooth muscle in the penetrating arteries of the affected hemisphere. The authors hypothesized that hyperperfusion can lead to an increased susceptibility to injury of the microcirculation in the hemisphere supplied by the stenosed artery. The formation of ipsilateral cerebral edema has previously been reported as a manifestation of the hyperperfusion syndrome, although edema was detected only in the deep white matter and by CT. Contrast-enhanced MRI may be a suitable technique to study the apparently complex relationship between the degree of arterial stenosis and blood flow/pressure reduction or to assess when blood pressure manipulators are indicated after carotid intervention.

A further understanding of this observed enhancement may help elucidate the hemodynamic physiological response to intervention in atherosclerotic carotid disease.

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