

Vascular MR Contrast Enhancement in Cerebrovascular Disease

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PURPOSE: To determine the significance of vascular enhancement in stroke patients with and without permanent neurologic deficit. **METHODS:** We prospectively studied two groups of patients with spin-echo MR imaging before and after injection of gadopentetate dimeglumine. In the patients in group 1 (12 women, 22 men; age range, 32 to 76 years), who had permanent neurologic deficit caused by recent ischemic brain infarction, we obtained 3 to 13 serial MR images during follow-up examination. Group 2 consisted of 26 patients (14 women, 12 men; age range, 54 to 81 years) with transient neurologic deficit caused by angiographically proved high-grade stenosis or occlusion of the internal carotid artery. **RESULTS:** Vascular enhancement was present in 59% of patients in group 1 and in 65% of patients of group 2. In group 1, the frequency of vascular enhancement declined steadily over several weeks, but it was still present in single cases even after 3 months. Vascular enhancement correlated positively with the extent of brain infarction in group 1 and with the degree of carotid stenosis in group 2. **CONCLUSION:** Vascular enhancement as shown by MR imaging may herald ischemic brain infarction and could persist over several weeks in areas that show collateral flow after infarction has occurred.

Index terms: Brain, infarction; Brain, magnetic resonance; Magnetic resonance, contrast enhancement

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The high vulnerability of the brain makes early treatment of cerebral ischemia crucial. A prerequisite for early treatment is an immediate assessment of the pathogenesis of sudden focal neurologic deficit before brain infarction is complete. At present, computed tomography (CT) is generally the first diagnostic step in making this assessment because of its wide availability, its relative insensitivity to movement, and its ability to detect ischemic alterations of brain parenchyma within the first 6 hours after the onset of symptoms (1-3). Magnetic resonance (MR) imaging has certain advantages over CT: it provides better tissue contrast and detection of flow phenomena; there are no beam-hardening artifacts causing blurring of the basal brain structures; and it allows multiplanar imaging,

angiography, fast imaging with advanced gradient-echo techniques or echo-planar imaging, perfusion imaging, and probably direct detection of brain viability by means of diffusion-weighted sequences (4).

In a few studies, conventional spin-echo MR imaging and CT have been compared directly in terms of their usefulness in evaluating early hemispheric stroke (5-7). These authors found no clear superiority of one method over the other in detecting early signs of cerebral ischemia. Both CT and MR imaging have been shown to be sensitive in discerning ischemic alterations of brain parenchyma during the first hours after stroke (1-3, 5, 8). Compared with CT, MR imaging has an additional advantage of being able to depict the underlying vascular disease and can show dissection, intramural hematoma, or occlusion of cervical and intracranial arteries (9).

Intracranial vascular enhancement in association with cerebral ischemic infarction has been described as a sign of early infarction (10-13). We prospectively studied this sign in patients with cerebrovascular disease to find out whether it is in fact associated with early brain infarction

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or only with the derangement of cerebral arterial flow, in which case it would be a precursory and probably a warning sign of complete ischemia.

Subjects and Methods

We prospectively studied two groups of patients with cerebrovascular disease: Group 1 consisted of 52 consecutive patients with acute onset of permanent neurologic deficits. Selection criteria included the exclusion of hemorrhagic infarction by CT, the ability to perform the first MR examination within 48 hours of the onset of symptoms, the ability of the patients to give their informed consent for initial and follow-up MR imaging, their availability for and ability to tolerate repeated studies, and equipment availability. The time of onset of symptoms was determined from the best available clinical history. The study was designed to obtain subsequent MR images at the end of the first week, during the second, third, and fourth weeks, and 3 months after the stroke. Eighteen patients were excluded from the study because more than 2 follow-up studies could not be obtained. Thus, data were analyzed for 34 patients in this group (12 women, 22 men; 32 to 76 years old). Three to 13 MR images (average, 6) were obtained for each patient.

To evaluate the origin of the cerebral ischemia, we assessed the vascular status during the first week after onset of symptoms by extracranial and transcranial Doppler sonography of all brain-supplying arteries in each patient and by digital subtraction angiography (DSA) in 18 patients. Angiography was performed within 2 days of one of the MR examinations during the first week after the onset of symptoms. To evaluate the source of emboli, all patients were additionally examined by transthoracic sonography and by electrocardiography with a 24-hour Holter monitor. In a few cases, transesophageal cardiac sonography was done. The causative factors were determined retrospectively from radiologic and clinical findings. Causes of infarction were categorized as follows: an embolic infarction pattern on MR images and a potential embolic source for the ischemia placed the source in the *embolic* category. A hemodynamic pattern on MR images and no potential embolic source were categorized as *hemodynamic*. And a microangiopathic infarction pattern in conjunction with a history of hypertension or diabetes characterized the source as *microangiopathic*. To assess a standardized clinical follow-up examination, we scored all patients according to the Scandinavian Stroke Scale (SSS) (14) parallel to each MR examination.

Group 2 consisted of 26 consecutive patients (14 women, 12 men; 54 to 81 years old) referred to our institution because of high-grade stenosis or occlusion of at least 1 carotid artery. Selection criteria included evidence of stenosis of greater than 75% according to criteria established by the North American Symptomatic Carotid Endarterectomy Trial (15) or evidence of occlusion of the internal carotid artery on Doppler sonograms, absence of permanent neurologic deficits, and no clinical history of

reversible cerebral ischemia within 6 months preceding admission. Informed consent was obtained from all patients.

After Doppler sonographic evaluation of the cranial arteries, all patients were examined by MR imaging and DSA within 2 days of each other. In a subgroup of 12 patients we performed Doppler sonography to assess carbon dioxide reactivity of the middle cerebral artery using the technique described by Widder (16).

The MR protocol was standardized for both groups: MR imaging was performed at a field strength of 1 T using spin-echo sequences without flow compensation. Precontrast T1-weighted, proton density-weighted, and T2-weighted images were routinely obtained in axial planes with an 8-mm section thickness, a 24-cm field of view, a 256 × 256 matrix, and 1 or 2 excitations. In patients with infratentorial lesions, additional T1-weighted images were obtained in 3.5-mm-thick sagittal sections. After injection of 0.1 mmol/kg of gadopentate dimeglumine, we repeated the T1-weighted spin-echo sequences with the same parameters as mentioned above.

The images were evaluated by consensus of two experienced neuroradiologists using standardized evaluation forms. Neither reviewer was blinded to the medical history and clinical signs. Particular attention was directed to the pattern of cerebral infarction, parenchymal enhancement, and vascular enhancement.

Vascular enhancement was defined as tubular appearing enhancement of at least two vessels, which were hypointense relative to brain parenchyma on the precontrast T1-weighted image within or in the vicinity of ischemic lesions if present. Parenchymal abnormalities were categorized according to extent, location, and vascular distribution.

The association between clinical and neuroradiologic baseline characteristics and vascular enhancement was tested by Fisher's Exact Test and the unpaired *t*-test. A *P* value of less than .05 was accepted as significant.

Angiograms were evaluated for evidence and location of slow arterial blood flow. Because of the variability of filming rates, circulation times were not calculated. In agreement with the definitions described by Mueller et al (12), the angiographic criterion for slow flow was either delay in antegrade filling of distal vessels in the compartment of obstructed proximal vessels or retrograde filling of the distal compartment by collateral arteries with delayed wash-out of contrast agent as compared with similar-size arteries of the same area or the contralateral area.

Angiographic and MR findings were compared with respect to evidence and location of slow flow and vascular enhancement.

Results

Vascular Enhancement in Patients with Cerebral Infarction (Group 1)

MR imaging revealed 52 ischemic lesions in the 34 patients of group 1. Twenty patients had

TABLE 1: Vascular enhancement and location, cause, and size of infarction among patients in group 1

Infarction Characteristics	No. of Patients	No. (%) of Patients with Vascular Enhancement	P Value
Supratentorial*	31	20 (65)	Not significant [†]
Infratentorial*	6	0	
Vascular Territory			
MCA [†]	23	16 (70)	
PCA [†]	7	4 (57)	
Watershed	1	0	
MCA/PCA [†]			
Location			Not significant [§]
Cortical [†]	16	11 (69)	
Subcortical [†]	14	9 (43)	
Cause			.036 [†]
Embolic [†]	14	12 (86)	
Hemodynamic [†]	7	2 (29)	
Microangiopathic [†]	5	2 (40)	
Unknown [†]	5	4 (80)	
Size			.009 [§]
Less than 5 cm [†]	17	8 (47)	
More than 5 cm [†]	14	12 (86)	

Note.—MCA indicates middle cerebral artery; PCA, posterior cerebral artery.

* Three patients had supratentorial and infratentorial lesions and were included in both groups.

[†] Evaluation was made on the basis of patients with supratentorial infarction (n = 31).

[‡] χ^2 test.

[§] Fisher's Exact Test.

1, 10 patients had 2, and 4 patients had 3 acute ischemic lesions. In 17 patients with a potential embolic source and an embolic infarction pattern, the cause of the infarction was categorized as embolic. The pattern of infarction indicated hemodynamic mechanism in 7 patients and disease of the small vessels in 5 patients. In the remaining 5 patients, the cause of infarction remained obscure.

Vascular enhancement was observed in 20 (59%) of the 34 patients. The association between extent, location, vascular territory, and cause of infarction in the patients of group 1 and the presence of vascular enhancement are summarized in Table 1. We did not observe vascular enhancement in association with infratentorial lesions in 6 patients. The frequency of vascular enhancement was significantly higher with embolic infarctions or with infarctions that were larger than 5 cm in diameter (Table 1).

Significant correlations between vascular enhancement and the site of infarction were not observed. The presence of vascular enhancement was independent of supratentorial vascular distribution or cortical versus subcortical location.

The time course of vascular enhancement among patients with acute infarction is shown in Figure 1. Vascular enhancement was most of-

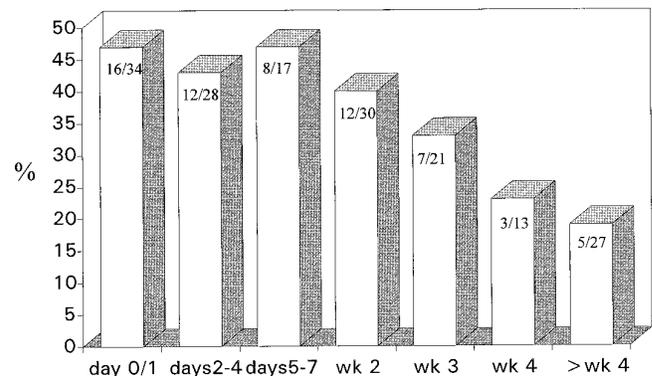


Fig 1. Time course of vascular enhancement in patients after cerebral infarction. Vascular enhancement occurred most often during the first week after symptom onset but persisted during the entire observation period in 19% of patients.

ten observed during the first week after stroke but in some cases it could be seen during the entire observation period (Fig 2). In four patients vascular enhancement was absent during the first 48 hours after stroke. In one of these patients, the appearance of vascular enhancement coincided with clinical deterioration during the third week. In another patient, vascular enhancement appeared together with a clinically asymptomatic occlusion of the middle cerebral artery trunk during follow-up; this was verified by angiography. In the remaining two

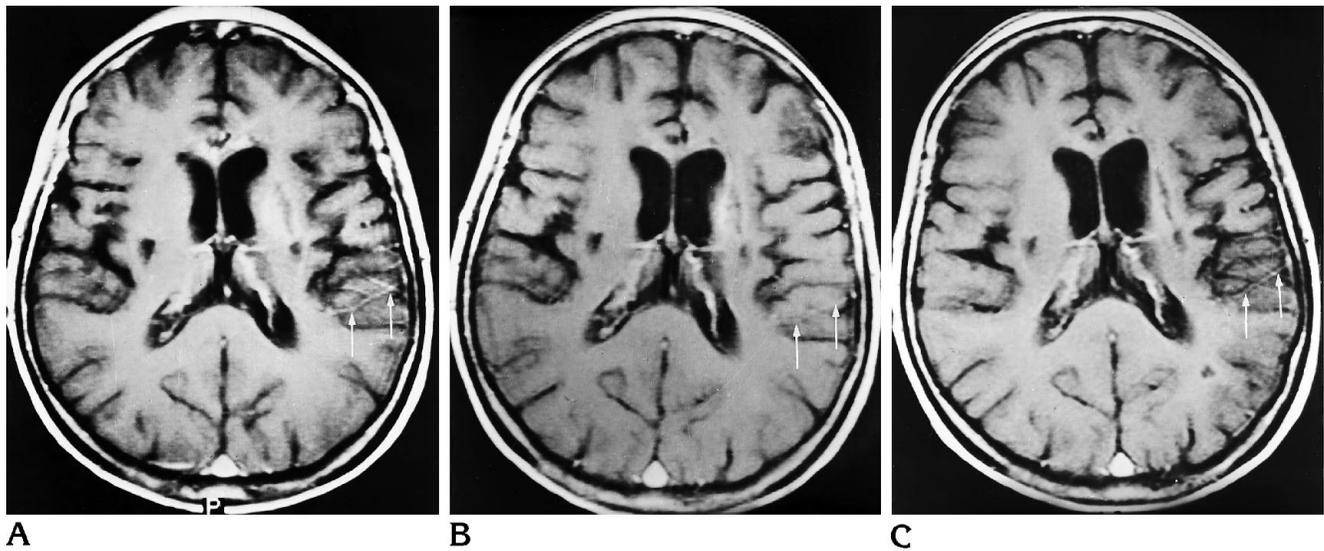


Fig 2. Serial T1-weighted MR images 1 day (A), 4 days (B), and 104 days (C) after stroke. Note persisting vascular enhancement at the left planum temporale (arrows).

TABLE 2: Vascular enhancement and angiographic findings among patients in group 1

	No. of Patients with Slow Flow	
	Delay in Antegrade Filling	Retrograde Collateral Filling
Patients with vascular enhancement (n = 11)	1	8*
Patients without vascular enhancement (n = 7)	0	1

Note.—Only patients who had angiography are included (n = 18).
* $P < .05$, Fisher's Exact Test.

patients vascular enhancement appeared at the second MR examination on day 4 and at the third examination on day 13, respectively; there were no changes in the clinical or vascular status.

The correlation of angiographic findings with MR evidence of vascular enhancement after cerebral infarction is summarized in Table 2. Angiography showed delayed wash-out in retrogradely filled leptomeningeal collateral arteries as the most important pathophysiological correlate in these patients (Fig 3). In two patients with vascular enhancement, slow flow could not be identified. Both patients had a hemodynamic infarction pattern and angiographically high-grade stenosis of the internal carotid artery. Retrograde collateral filling of a few vessels without MR evidence of vascular enhancement was

seen in one patient with a small embolic infarction.

We did not find an association between vascular enhancement and clinical signs and symptoms. At the initial MR examination on day 0 or 1 after stroke, the SSS score was 40 ± 14 in patients with vascular enhancement and 45 ± 10 in patients without vascular enhancement ($P > .22$, unpaired t test). Four weeks later, the SSS score was 55 ± 3 and 54 ± 8 , respectively ($P > .80$, unpaired t test).

Vascular Enhancement in Patients without Cerebral Infarction (Group 2)

Seventeen (65%) of 26 patients with high-grade stenosis or occlusion of one or both internal carotid arteries had vascular enhancement. Table 3 presents the angiographic findings in patients of group 2. Vascular enhancement was located in the insular region and was associated with slow flow in collateral arteries in all patients (Fig 4). The degree of carotid occlusion and the frequency of vascular enhancement correlated positively ($P = .002$, Fisher's Exact Test). Slow flow could not be documented angiographically in only two patients with MR evidence of vascular enhancement.

Carbon dioxide reactivity of the middle cerebral artery was $6.5\% \pm 4.0$ in patients with vascular enhancement (n = 7) and $10.7\% \pm 4.3$ in patients without vascular enhancement (n = 5) ($P = .053$, unpaired t test).

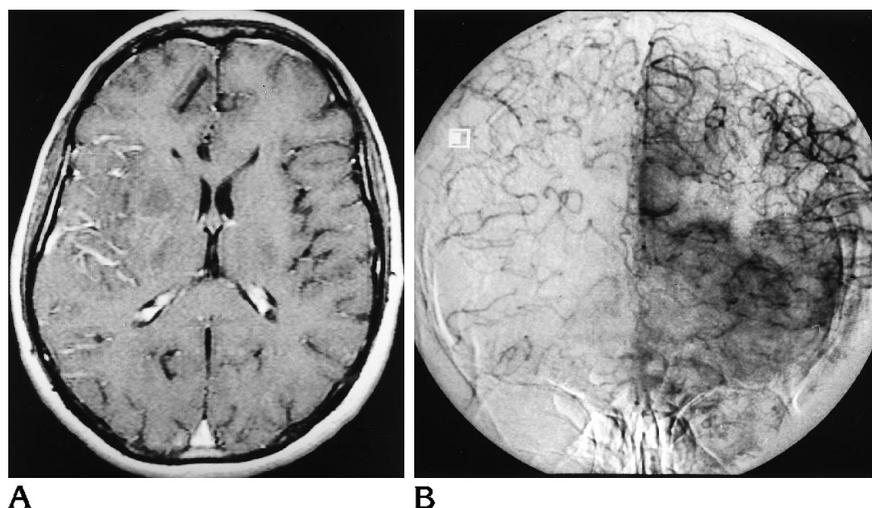


Fig 3. Contrast-enhanced MR images and angiograms in a 35-year-old man after embolic occlusion of the right middle cerebral artery.

A, Contrast-enhanced T1-weighted MR image obtained on third day after symptom onset shows vascular enhancement of the insular and parietal cortex near and within an area of hypointense parenchyma.

B, Angiogram obtained on second day after symptom onset shows slow flow in leptomeningeal collaterals between right anterior and middle cerebral arteries after injection of contrast material in the left internal carotid artery.

TABLE 3: Vascular enhancement and angiographic findings among patients in group 2

	Degree of Carotid Stenosis \pm SD	No. of Patients with Slow Flow	
		Delay in Antegrade Filling	Retrograde Collateral Filling
Patients with vascular enhancement (n = 17)	93 \pm 8.0*	0	15
Patients without vascular enhancement (n = 9)	80 \pm 12.2*	0	0

* $P = .002$, Fisher's Exact Test.

Presence of acute ischemic lesions as determined by clinical or radiologic criteria was not observed in patients of group 2. MR imaging showed old ischemic lesions in eight patients with a history of reversible cerebral ischemia. Five of these patients had MR evidence of vascular enhancement.

Discussion

After cerebral ischemia, MR imaging may show two types of contrast enhancement: parenchymal and vascular (11). As is known from CT studies (17), parenchymal contrast enhancement represents extravasation of contrast material caused by a major breakdown of the blood-brain barrier and is not usually seen until 6 days after the ischemic event (18, 19). Vascular enhancement in the acute stage of cerebral infarction has been described as an early sign of infarction, and it is most often detected within the first 24 hours and not later than 11 days after the event (10–13). According to these authors, vascular enhancement is defined as contrast enhancement of arteries in or near ischemic lesions; it was detected in nearly half

the examined ischemic lesions in those studies. Vascular enhancement was most likely to be found in cortical lesions and was rarely detected in deep white matter and noncortical gray matter lesions (11). Crain et al (10) also described vascular enhancement of the vertebral and basilar arteries in association with lesions of the brain stem.

Our angiographic observations support the findings of others (12, 13) that slow flow is the pathophysiological correlate of vascular enhancement after cerebral infarction. When flow is slow, as in cortical veins and dural sinuses, enhancement of blood could be observed routinely owing to the loss of flow voids, resulting in a symmetric picture of tubular structures in both hemispheres (20). We observed that slow flow in leptomeningeal collateral arteries is the most important reason for the focal vascular enhancement sign (Fig 3). Retrograde collateral circulation via leptomeningeal anastomoses from adjacent vascular territories offers a potential source of blood supply in distal vessels that are obstructed and develops rapidly after cerebral ischemia (21, 22). In our study only one patient without vascular enhancement had an-

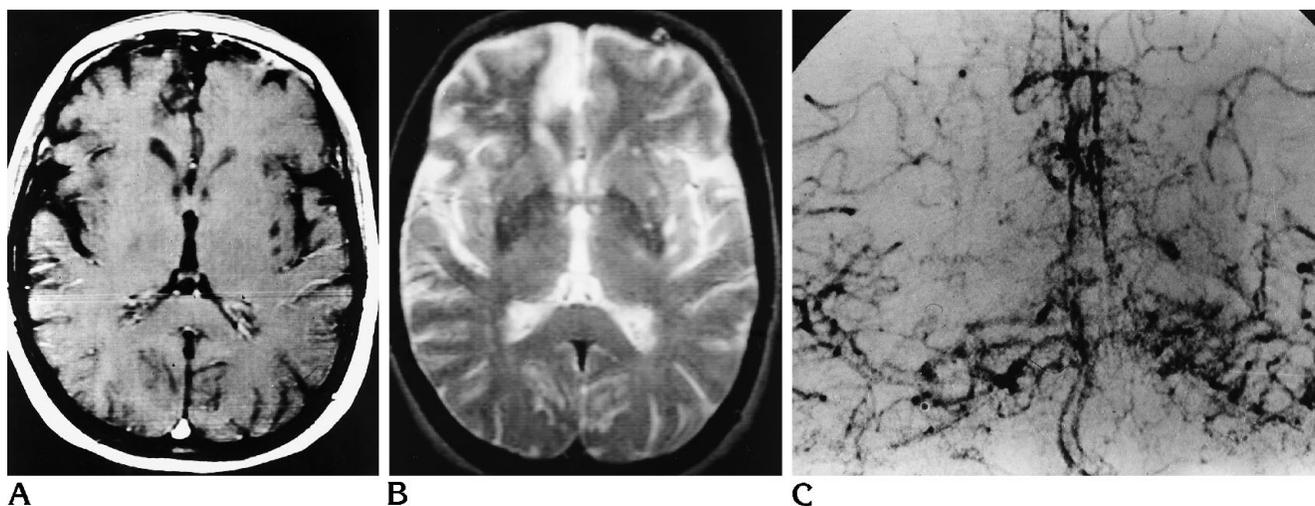


Fig 4. Contrast-enhanced MR images and angiograms in a patient with occlusions of both internal carotid arteries but with no permanent neurologic deficit.

A, Contrast-enhanced T1-weighted MR image shows vascular enhancement of the insular and temporal cortex bilaterally. Additionally, an old infarction in the distribution of the right anterior cerebral artery can be seen.

B, T2-weighted MR image shows an old infarction in the distribution of the anterior cerebral artery, which occurred 12 months previously.

C, Angiogram with contrast injection of the left vertebral artery, obtained within 1 day of MR study, shows collateral flow via both posterior communicating arteries into anterior circulation and slow flow in the major branches of both middle cerebral arteries.

giographic evidence of slow flow and only two patients with vascular enhancement had evidence of slow flow. The reason for this could be the timing of MR imaging and DSA within 2 days of each other. It could be that a change in the hemodynamic status of these patient had occurred between the MR imaging and DSA studies.

To our knowledge, the time course of vascular enhancement after cerebral ischemia has not been studied so far. Furthermore, it is unclear whether vascular enhancement is associated with completed brain infarction or hypoperfusion of brain parenchyma, which may herald infarction.

Vascular Enhancement in Patients with Acute Cerebral Ischemia

After cerebral ischemia, we observed vascular enhancement as a common sign in large, embolic infarctions. There was better contrast between enhanced vessels and a large area of ischemic tissue with low signal on T1-weighted sequences and more collateral vessels were involved in large lesions. Development of collaterals may be delayed in embolic infarction, whereas collateral circulation is well developed in hemodynamic infarction (23). In newly

opened or in reopened collateral vessels, flow may be slower than in preexistent collateral vessels, and therefore vascular enhancement may be more common in embolic infarction. On the other hand, most of the hemodynamic infarctions in our study were small and located in the deep white matter with few collateral arteries involved and poor contrast between the enhanced vessels and the signal loss of infarcted tissue on T1-weighted MR images.

Vascular enhancement was highly (72%) associated with cortical lesions but appeared also in lesions of the subcortical gray or white matter. In such lesions the enhanced vessels were located at the adjacent brain surface. Angiographic studies in patients with subcortical lesions showed slow flow in leptomeningeal collateral arteries that ran from the surface to the infarcted regions. Like other authors (10), we believe that larger arterial size and low signal from surrounding cerebrospinal fluid may be the reason for the higher frequency of vascular enhancement in cortical as compared with subcortical lesions. We did not observe a significant association between vascular enhancement and the affected vascular territories or between vascular enhancement and infratentorial infarction.

Although other studies (10, 12) suggest that patients with vascular enhancement tend to

have more severe clinical symptoms, vascular enhancement was not associated with a poor clinical status in our patients. This observation suggests that cortical vascular enhancement indicates a sufficient collateral circulation via leptomeningeal arteries.

Figure 2 shows that vascular enhancement is present not only in the acute stage of brain infarction. Like other authors (10–13), we observed vascular enhancement most often during the first 2 weeks after the onset of symptoms. In contrast to these reports, however, vascular enhancement in our study did not disappear with the development of pathologic parenchymal enhancement. Vascular enhancement could be observed in all stages of ischemia and in combination with parenchymal enhancement. In single cases, vascular enhancement appeared on follow-up examinations parallel to changes in cerebral hemodynamics.

Vascular Enhancement in Patients with Stenosis or Occlusion of the Internal Carotid Artery

Our observations in patients with complete brain infarction suggest that vascular enhancement is related to impaired cerebral hemodynamics. We therefore also studied patients who did not have complete infarction but who did have a history of reversible ischemia and angiographically proved high-grade stenosis or obstruction of brain-supplying arteries. In these patients, cerebral hemodynamics depend on collaterals and their effectiveness. We found that slow retrograde flow in leptomeningeal collateral arteries is the most important pathophysiological correlate in these patients. None of our patients without vascular enhancement had angiographic evidence of slow flow, and all but two with MR evidence of vascular enhancement had criteria for slow flow. A reason for the lack of slow flow in patients with vascular enhancement could be a change in the hemodynamic situation that occurred between the MR imaging and DSA studies.

We observed a positive correlation between the presence of vascular enhancement and the grade of ipsilateral stenosis. In these patients, carbon dioxide stimulation revealed low vascular reactivity, indicating reduced perfusion reserve and probably hemodynamic decompensation (24, 25). In patients without complete

infarction we therefore interpret vascular enhancement as an indicator for hypoperfusion of dilated leptomeningeal collaterals. The risk of complete infarction in these patients may be high and should be determined by a prospective study.

In summary, our observations confirm that slow flow in leptomeningeal collaterals is the most important pathophysiological correlate of vascular enhancement. Vascular enhancement does not necessarily indicate a state of hemodynamic decompensation and infarction, but it may indicate a state of impaired cerebral hemodynamics. The assessment of vascular enhancement, therefore, may be of importance for patient treatment.

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