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Cerebral ischemia: evaluation with contrast-enhanced MR imaging.

M R Crain, W T Yuh, G M Greene, D J Loes, T J Ryals, Y Sato and M N Hart

Cerebral Ischemia: Evaluation with Contrast-Enhanced MR Imaging

Martin R. Crain[1]
William T. C. Yuh[1]
George M. Greene[2]
Daniel J. Loes[1]
Tony J. Ryals[1]
Yutaka Sato[1]
Michael N. Hart[3]

Eighty patients with a total of 82 ischemic lesions were examined with contrast-enhanced MR imaging 1 hr to 1 month after onset of symptoms. The studies were reviewed retrospectively to determine the presence of arterial enhancement and the patterns of parenchymal enhancement. Arterial enhancement was often detected on the initial MR examination (45%), was frequently demonstrated in cortical infarction (86%), in some cases preceded the development of signal changes on T2-weighted images, and resolved by 11 days. The presence of arterial enhancement appeared to be a better indicator of clinical severity than was the presence of proximal vessel occlusion on MR or angiographic studies. Two patterns of parenchymal enhancement were seen: progressive enhancement and early and/or intense enhancement. In patients with the progressive pattern, parenchymal enhancement on postcontrast T1-weighted images was rarely seen before 7 days, while signal abnormalities on T2-weighted images were intense during the first few days. The early and/or intense enhancement pattern was usually present within the first 3 days, approximated or exceeded the area and intensity of signal changes on T2-weighted images, and was usually associated with minimal or reversible neurologic sequelae (except when located in or near a watershed zone), suggesting a lesser degree of ischemic insult than was associated with the progressive pattern. Three additional general relationships between MR findings were observed: (1) an inverse relationship between the extent of arterial enhancement and parenchymal enhancement in acute and subacute phases, (2) an inverse relationship between the area of postcontrast parenchymal enhancement and the area of signal change on T2-weighted images in the acute phase, and (3) a direct relationship between arterial enhancement and the degree of signal changes on T2-weighted images in the acute phase.

We conclude that patterns of enhancement appear to reflect the underlying pathophysiology in acute cerebral ischemia and may have prognostic significance. In contrast to results of previous reports, gadopentetate dimeglumine appears to be useful in the MR evaluation of early ischemia and its response to intervention.

[1] Department of Radiology, The University of Iowa College of Medicine, Iowa City, IA 52242. Address reprint requests to W. T. C. Yuh.

[2] Department of Surgery, Division of Neurosurgery, The University of Iowa College of Medicine, Iowa City, IA 52242.

[3] Department of Pathology, Division of Neuropathology, The University of Iowa College of Medicine, Iowa City, IA 52242.

The location and time course of enhancement with CT contrast agents in the evaluation of patients with cerebral infarction is well documented [1–4]. Although the use of gadopentetate dimeglumine–enhanced MR imaging has been reported in patients with cerebrovascular disease [5–9], the usefulness of MR contrast agents and the patterns of enhancement that occur, especially early in cerebral ischemia, are not well established. While some investigators have reported that gadopentetate dimeglumine does not improve the sensitivity of MR in acute cerebral ischemia [10], others have suggested that contrast material may be useful in the detection of this entity [8, 11]. Our purpose was to investigate the usefulness of contrast-enhanced MR imaging in the evaluation of acute cerebral ischemia. In particular, we wished to study the degree and pattern of enhancement with respect to location, duration, and temporal progression of ischemia and to relate the findings on enhanced MR images to underlying pathophysiology.

Materials and Methods

Eighty-two ischemic lesions in 80 patients were studied. All patients who presented between November 1988 and February 1990 with symptoms of acute cerebral ischemia (i.e., motor and sensory deficits, loss of consciousness, aphasia) and who also received IV administration of gadopentetate dimeglumine during their MR examination were reviewed retrospectively. Ages ranged from 18 to 89 years (mean, 55 years). There were 44 men and 36 women. The timing of the onset (either the acute onset of symptoms in a previously asymptomatic patient or the rapid progression of intermittent symptoms in a symptomatic patient) was determined from the best available clinical history. The MR time was defined as the interval between the onset of symptoms and the start of the initial MR examination (rounded off to the closest hour). Criteria for inclusion in the final study group included reliably defined onset of acute ischemic symptoms, IV administration of gadopentetate dimeglumine, and MR findings referable to the clinical distribution of ischemia. Patients with intraparenchymal hematoma by initial CT or MR, those without definable clinical symptoms corresponding to MR findings, and those without a reliably defined time of onset were excluded.

All examinations were performed on either a 0.5-T (Picker International, Highland Heights, OH) or a 1.5-T (General Electric, Milwaukee, WI) superconductive scanner. At least one T1-weighted, 350–750/20 (TR range/TE), and one T2-weighted (2000–2300/90–100) spin-echo pulse sequence were obtained with a 3–10-mm slice thickness. There was a 10–50% slice gap in the examinations performed at the higher field strength. At least two orthogonal planes were imaged. Postcontrast imaging was performed immediately after IV injection of 0.1 mmol/kg of gadopentetate dimeglumine (Magnevist, Berlex Laboratories, Inc., Wayne, NJ). Postcontrast pulse parameters and imaging planes were identical with those of the precontrast T1-weighted sequences.

MR examinations were reviewed retrospectively by two radiologists without knowledge of the MR time. Special attention was given to the presence of arterial enhancement, pattern and degree of parenchymal enhancement, parenchymal signal abnormalities on unenhanced images, and vascular distribution of ischemic changes. Vascular distribution was defined as predominant involvement of the anterior cerebral artery (ACA) territory, middle cerebral artery (MCA) territory, or vertebrobasilar circulation. Note was made if abnormal parenchymal signal was located within or near a major watershed zone (watershed infarction). Parenchymal abnormalities were categorized according to location: cortical abnormalities involved predominantly cortical structures with or without involvement of deep structures, and noncortical ones were limited to noncortical structures and included those in the brainstem, subcortical gray matter (basal ganglia and thalamus), and deep white matter. We also categorized the duration of ischemic symptoms using 7 days as the cutoff point between the acute and subacute phases. This definition has been
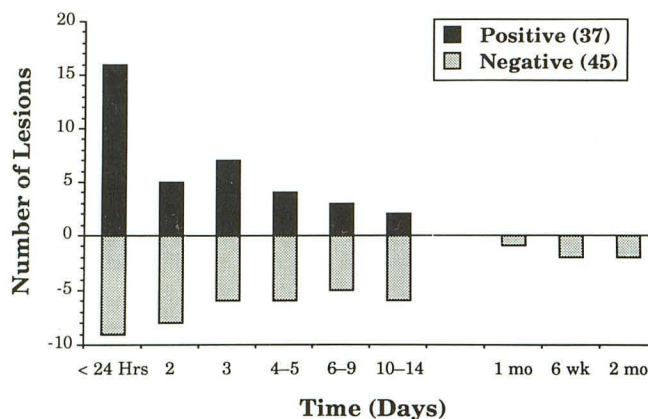

Fig. 1.—Graph depicting the number of lesions that demonstrated arterial enhancement at the time of initial MR examination. Arterial enhancement was frequently detected within the first 24 hr, rarely after 7 days, and not at all after 11 days, suggesting reestablishment of circulation or development of collateral circulation.
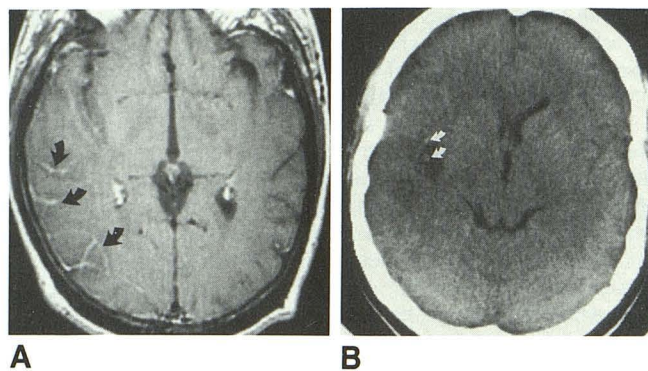

A   **B**

Fig. 2.—Comparison of vascular abnormalities depicted by contrast MR imaging and CT.

A, Postcontrast axial T1-weighted image (750/20/1) obtained 3 days after onset shows abnormal arterial enhancement in distribution of right middle cerebral artery (*arrows*). Specifically noted is obvious enhancement of distal peripheral small branches.

B, Axial unenhanced CT image at corresponding level of parietal lobes shows "dense artery sign" (*arrows*) in region of proximal middle cerebral artery. However, no vascular abnormality in distal arterial branches can be appreciated. The extent of the vascular abnormality is much more apparent on enhanced MR image.

used by other authors [5, 6]. Angiograms were reviewed if they were obtained within 24 hr of the MR examination.

Results

The distribution of the MR times is presented in Table 1. Eleven patients had more than one contrast-enhanced MR examination.

Arterial Enhancement

Arterial enhancement on the initial MR examination was detected in 37 (45%) of 82 ischemic lesions (Figs. 1–5). It was found in 30 (83%) of 36 cortical infarctions, five (16%) of 31 noncortical infarctions, and two (20%) of 10 watershed infarctions (Table 2). The five noncortical lesions with arterial

TABLE 1: MR Time (Time from Onset of Ischemic Symptoms to Initial MR Examination)

Time	No. of Lesions
<24 hours	25
2 days	13
3 days	13
4–5 days	10
6–9 days	8
10–14 days	8
≥1 month	5
Total	82[a]

[a] 80 patients.
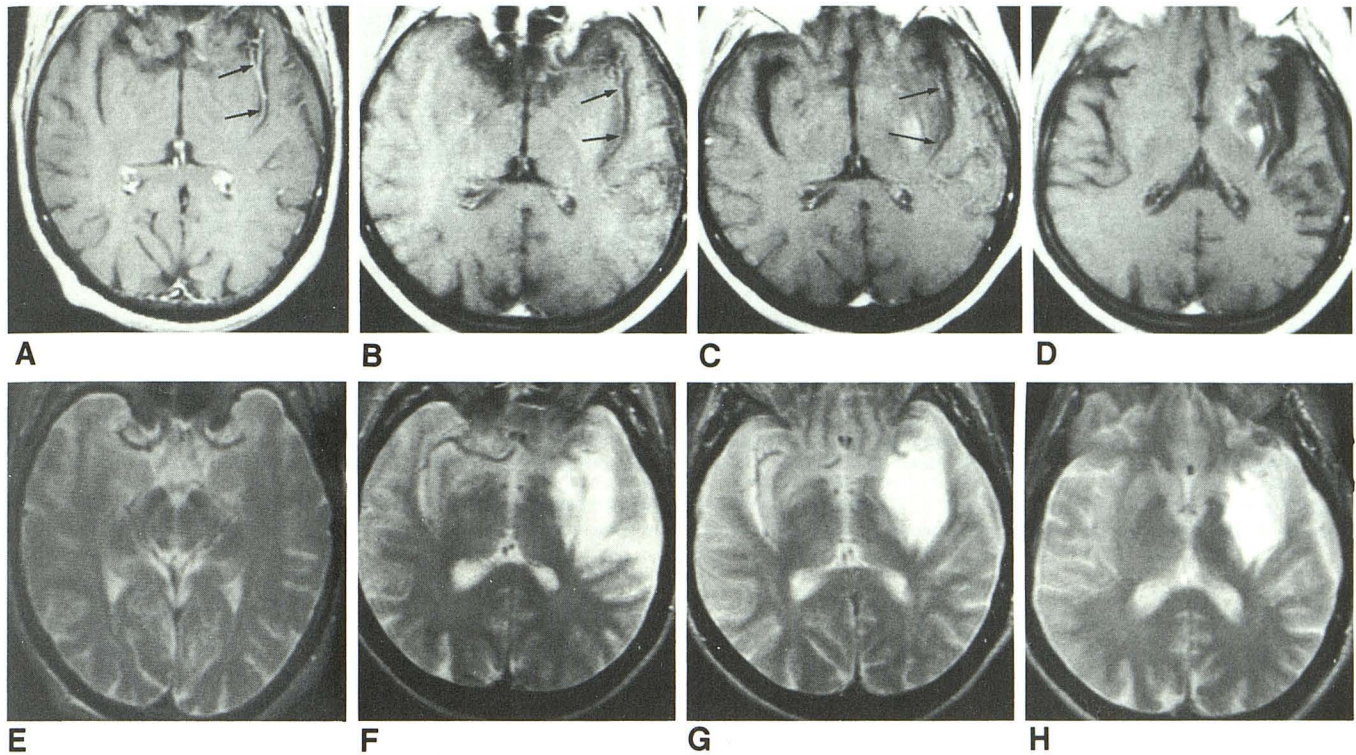
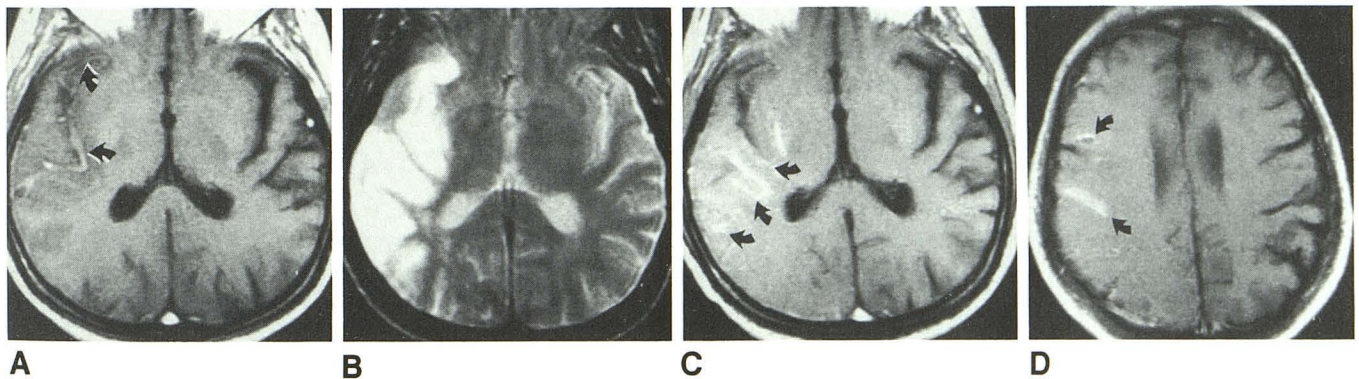Fig. 3.—Example of early arterial enhancement and progressive parenchymal enhancement in a cortical infarction.

A–H, Postcontrast axial T1-weighted images (750/20) obtained at 2 hr (A), 24 hr (B), 7 days (C), and 3 months (D), and the corresponding axial T2-weighted images (2000/100) obtained at the same time intervals (E–H) after the onset of acute ischemic symptoms. In typical complete ischemia, arterial enhancement (arrows) in distribution of left middle cerebral artery is most prominent at 2 hr (A) in the left sylvian fissure, is persistent at 24 hr (B), is only partially detected at 7 days (C), and is absent at 3 months (D). Parenchymal enhancement is absent at 2 hr (A) and 24 hr (B) and is only faintly seen in left basal ganglia but not in insular cortex at 7 days (C). At 3 months (D), enhancement is limited to margins of remaining viable tissue in left insular cortex and basal ganglia. Note the apparent inverse relationship between the degrees of arterial and parenchymal enhancement at all stages. The abnormality on T2-weighted images, undetected at 2 hr (E), was extensive at 24 hr (F) and progressively diminished from 7 days (G) to 3 months (H). The area of abnormality on T2-weighted images is much greater than that of parenchymal enhancement until the chronic stage.

Fig. 4.—Another example of cortical infarction with earlier resolution of arterial enhancement and development of parenchymal enhancement.

A and B, Postcontrast axial T1-weighted image (583/20) (A) and corresponding T2-weighted image (2000/100) (B) obtained within first 24 hr of ischemic symptoms. Arterial enhancement (arrows) is demonstrated in distribution of right middle cerebral artery (A). Intense signal on T2-weighted images without parenchymal enhancement is present at this time (A and B). These findings are typical of complete ischemia as seen in Fig. 3.

C and D, Follow-up postcontrast axial T1-weighted images (583/20) obtained 7 days after onset of acute ischemic symptoms when arterial enhancement has completely resolved and significant parenchymal gyriform enhancement has developed (arrows). The gyriform enhancement in this patient is more prominent than that seen at 7 days in the patient in Fig. 3. This is probably due to earlier reestablishment of circulation or development of collateral circulation.

enhancement were located in the posterior fossa and all were associated with basilar artery enhancement. There was no enhancement of terminal arterial branches in basal ganglia or deep white matter lesions.

Arterial enhancement was most likely to be found if the MR examination was obtained within a few days of the onset of symptoms; it was seen in only two of 15 lesions when the MR examination was obtained after 7 days and was not
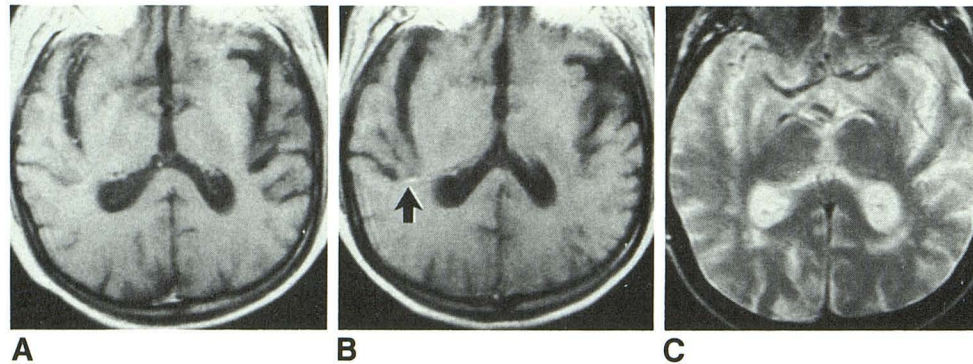
A   **B**   **C**

Fig. 5.—Example of rapid resolution of arterial enhancement in a patient with transient neurologic symptoms.
A and *B*, Postcontrast T1-weighted images (583/20) obtained 4 hr (*A*) and 24 hr (*B*) after onset of hemispheric ischemic symptoms. Arterial enhancement in distribution of right middle cerebral artery within the sylvian fissure is seen at 4 hr (*A*) but has resolved completely by 24 hr (*B*). Faint parenchymal enhancement near posterior watershed area (*arrow*) can be seen as early as 24 hr, probably due to the early reestablished blood flow to the ischemic region (*B*).
C, Axial T2-weighted image (2000/100) obtained 1 week after onset of symptoms shows minimal signal abnormality, suggesting less severe ischemic tissue insult. The rapid resolution of arterial enhancement paralleled the rapid and complete neurologic recovery of this patient within hours of admission.

detected after 11 days. In no instance did arterial enhancement occur on a follow-up examination if the initial MR failed to demonstrate this finding.

In patients with arterial enhancement who had multiple MR examinations, the enhancement usually persisted for 7 days, although prompt resolution occurred in two patients (Fig. 5). In both patients, arterial enhancement was present in the first 24 hr but resolved by the second day. Resolution of arterial enhancement paralleled rapid neurologic recovery (within 24–48 hr) in both patients. One developed modest signal abnormality on T2-weighted images that appeared on the second examination at 24 hr and nearly resolved by 1 week (Fig. 5). The other showed no signal change on T2-weighted images on either the initial or follow-up MR examinations up to 3 months after onset.

Eleven patients had angiography within 24 hr of the initial MR examination. Of the six patients who had arterial enhancement, only two had complete proximal occlusion on angiography. All six showed slow antegrade or retrograde flow on the angiogram. One patient with complete angiographic occlusion proximally showed no arterial enhancement on enhanced MR. Complete angiographic proximal vessel occlusion did not relate well to the presence of distal arterial enhancement on MR.

Parenchymal Enhancement

Contrast enhancement of ischemic brain parenchyma followed either of two patterns (Table 2): slowly progressive enhancement (Figs. 3, 4, 6) and early and/or intense enhancement (Figs. 7–9).

Progressive enhancement. Thirty-six cortical lesions (Figs. 2–4) and 31 noncortical lesions (Fig. 6) showed minimal or no parenchymal enhancement on initial MR (Table 2). The areas that did enhance were usually much smaller than the areas

TABLE 2: Summary of Typical Patterns of Enhancement

MR Findings and Outcome	Complete Ischemia (Progressive Enhancement)		Incomplete Ischemia (Early/Intense Enhancement)
	Cortical (*n* = 36)	Noncortical (*n* = 31)	Both (*n* = 15)[a]
Parenchymal enhancement			
Pattern			
Acute (≤7 days)	Usually absent[b] (1/27)[c]	Infrequent[d] (9/30)	Early (10/10)
Subacute (>7 days)	Progressive gyriform	Peripheral→central	Intense (5/5)
Extent (area involved)	Contrast material < T2 signal	Contrast material < T2 signal	Contrast material ≥ T2 signal (13/
Acute	(34/36)	(26/31)	15)
Arterial enhancement			
Acute	Frequent (30/36)	Infrequent[e] (5/31)	Infrequent (2/15)
Clinical outcome	Infarction	Infarction	Reversible/minimal neurologic dysfunction vs irreversible/infarction[f]

[a] Five cases of transient ischemia, 10 cases limited to a watershed zone.
[b] Single case with faint enhancement at 6 days.
[c] Number of positive cases/number of cases imaged.
[d] All enhancing lesions were small and had faint peripheral enhancement.
[e] When positive, usually involved basilar artery.
[f] Infarction in many cases of watershed zone ischemia.
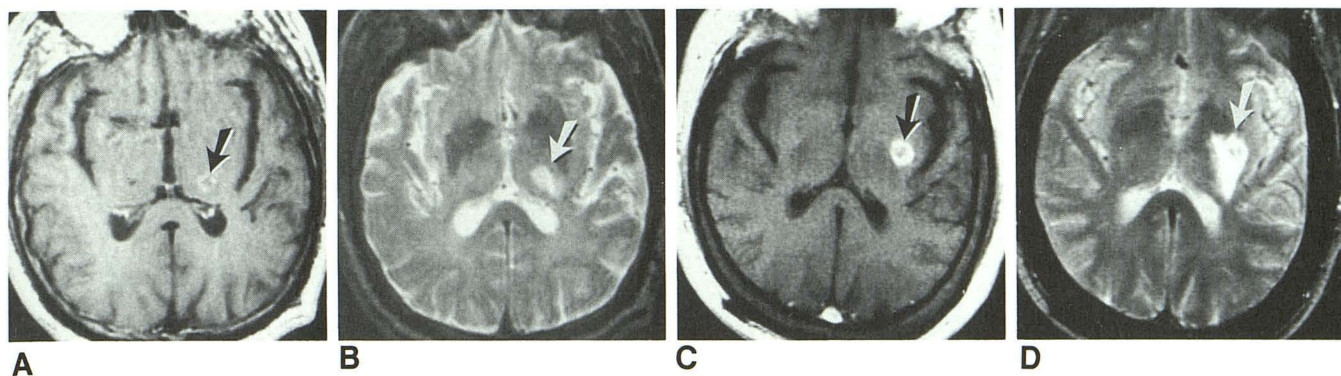
A   B   C   D

Fig. 6.—Examples of progressive parenchymal enhancement in noncortical infarctions.

A–D, MR images of noncortical infarctions obtained 7 days after onset of symptoms in one patient (A and B) and 2 weeks after onset of symptoms in another patient (C and D). Postcontrast axial T1-weighted images (750/20) (A and C) show that parenchymal enhancement of noncortical infarctions (*arrow*) is faint at the periphery in the early stage (A) and later progresses toward the center and becomes more dense (C). As in the case of complete cortical ischemia, the areas of signal change (*arrow*) seen on axial T2-weighted images (2000/100) (B and D) exceed the areas of enhancement in complete noncortical ischemia.
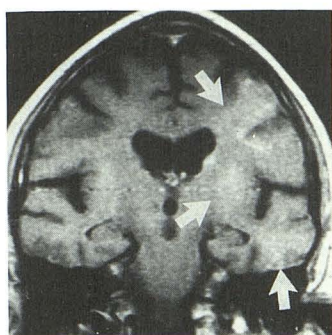

Fig. 7.—Example of early parenchymal enhancement in a patient with transient neurologic symptoms. This patient developed transient left hemispheric symptoms after 2 min of test balloon occlusion of left internal carotid artery.

A, Postcontrast coronal T1-weighted image (583/20) obtained at 2 hr shows diffuse parenchymal enhancement (*arrows*) in distribution of left middle cerebral artery without arterial enhancement. Also noted is enhancement of caudate nucleus.

B, Axial T2-weighted images (2000/100) show no apparent signal change at this time.

C, Postcontrast axial T1-weighted images (583/20) at 24 hr show no evidence of parenchymal or arterial enhancement. No signal abnormality in left middle cerebral artery distribution was present on T2-weighted images at 24 hr (*not shown*). The resolution of parenchymal enhancement by 24 hr parallels the rapid neurologic improvement in this patient. This case demonstrates the inverse relationship between parenchymal enhancement and arterial enhancement, as well as between the areas of parenchymal enhancement and T2 signal abnormality.

A
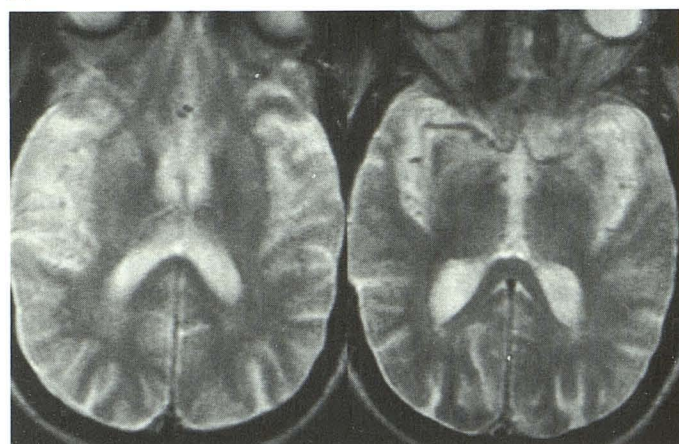
B   C

of abnormal signal on T2-weighted images. These patients tended to have more severe clinical outcomes than did those with early and/or intense enhancement.

Typical completed cortical infarctions did not develop parenchymal enhancement for about 1 week (Figs. 3 and 4), and signal abnormalities on T2-weighted images predominated in the first weeks. Twenty-six (96%) of 27 cortical lesions showed no parenchymal enhancement when the initial

MR examination was obtained within 1 week (Table 2). The only lesion with enhancement before 1 week was seen in a 62-year-old man with minimal gyriform enhancement of an occipital infarction 6 days after the onset of visual symptoms.

After 1 week, thin, faint enhancement of the cortex usually began near the pial surface or margins of the ischemic zone and progressed to thicker, denser gyriform enhancement in the subacute phase (Fig. 4). Not until the subacute to chronic

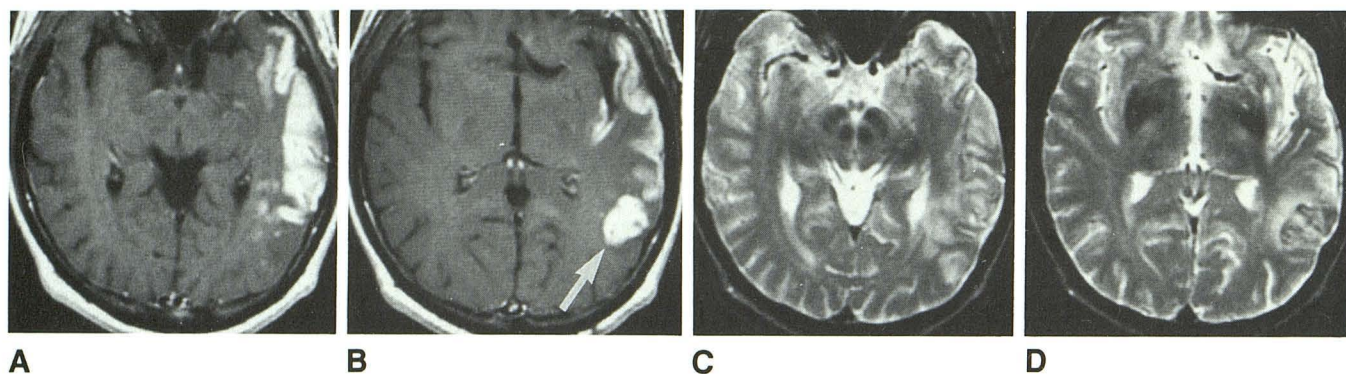**A**   **B**   **C**   **D**

Fig. 8.—Example of early, intense parenchymal enhancement in a patient with reversible ischemic neurologic deficit. MR examination performed 10 days after transient ischemic episode with right-sided weakness and aphasia that resolved almost completely in 2 hr.

A and *B*, Postcontrast axial T1-weighted images (700/20) show diffuse, intense cortical enhancement in distribution of left middle cerebral artery without evidence of arterial enhancement.

C and *D*, Corresponding axial T2-weighted images (2000/100) show a much less extensive area of signal abnormality. The enhancement appears more intense near the watershed zone (*B, arrow*), which may reflect greater availability of contrast material in this region. This case again shows that parenchymal enhancement is inversely related to the appearance of arterial enhancement and signal abnormality on T2-weighted images.

phases were reached did the area of enhancing parenchyma approximate that of the signal change on T2-weighted images, and the enhancement remained moderate in intensity (Fig. 3). Enhancement eventually disappeared in the chronic phase.

Most (21 of 30) noncortical lesions evaluated within 1 week of onset showed no parenchymal enhancement (Fig. 6) (Table 2). In nine lesions enhancement appeared before 1 week and was faint and peripheral. Four of the nine patients had posterior fossa infarctions ranging in age from 1 to 6 days, and three of these presented with intermittent ischemic symptoms preceding the onset of the infarction. The other five had thalamic or basal ganglia infarctions of 48 hr to 7 days duration.

After 1 week, faint peripheral enhancement of noncortical infarctions became dense and thick, similar to the progression seen in cortical lesions (Fig. 6). Later, progression to uniform enhancement of the lesion was seen. As in cortical infarctions, parenchymal enhancement in typical noncortical infarctions usually lagged behind signal abnormality on T2-weighted images in both intensity and area of involvement. However, these lesions were usually much smaller than cortical ischemic lesions.

Early and/or intense enhancement. Fifteen lesions demonstrated a pattern of early and/or intense enhancement; 10 were imaged on MR within the first week of onset (Figs. 7–9) (Table 2). Enhancement was usually noted within the first 2–3 days, and its area equaled or exceeded the area of abnormality on T2-weighted images in most lesions (87%). Only 13% of lesions with this pattern were associated with arterial enhancement (Fig. 9C) (Table 2).

Two distinct groups of patients had lesions with early and/or intense enhancement. One group had minimal symptoms or reversible neurologic deficits (Figs. 7 and 8), and the other group tended to have persistent neurologic deficits (i.e., infarctions) (Fig. 9). In the former group, one patient had onset of hemispheric ischemic symptoms after 2 min of balloon test occlusion of the internal carotid artery (ICA) preoperatively,

which almost completely resolved within 2 hr (Fig. 7). Diffuse parenchymal enhancement was seen without signal changes on T2-weighted images at 2 hr and had resolved later. Abnormal signal on T2-weighted images was not demonstrated on the 24-hr, 48-hr, or 7-day follow-up examinations. Another patient with reversible symptoms was an 18-year-old man who collapsed and had right hemiparesis that improved over the first 24–48 hr. An enhanced MR examination at 3 days showed early, intense gyriform enhancement in the left MCA distribution without arterial enhancement, similar to the patient shown in Figure 8. An angiogram obtained at 3 days showed no evidence of vessel occlusion. In a third patient, occlusion of the ICA resulted in acute blindness but no ipsilateral hemispheric clinical symptoms. MR obtained 18 hr after onset of symptoms showed an occluded proximal left ICA without ipsilateral hemispheric abnormality. However, early anterior watershed enhancement was seen in the contralateral (right) hemisphere. A fourth patient had a reversible ischemic neurologic deficit that resolved by 48 hr. Early homogeneous enhancement of the thalamus was demonstrated on MR at 4 days. A fifth patient had had percutaneous balloon occlusion of the ICA for treatment of an aneurysm. The patient developed no neurologic symptoms. An MR obtained 2 hr after the procedure showed faint enhancement without signal change on T2-weighted images in the posterior watershed zone.

The second group with early and/or intense enhancement tended to have more persistent and severe neurologic sequelae than the first, and lesions in these patients were limited to or adjacent to watershed regions (watershed infarctions) (Fig. 9). Five of these patients had MR within 1 week of onset of ischemic symptoms. The area of enhancement equaled or exceeded the size of the area of signal change on T2-weighted images as was seen in transient ischemic lesions, but more intense signal abnormalities were usually present. Five other patients had initial MR examinations between 7 and 14 days after onset of symptoms and also showed an area of intense enhancement equaling or exceeding the area
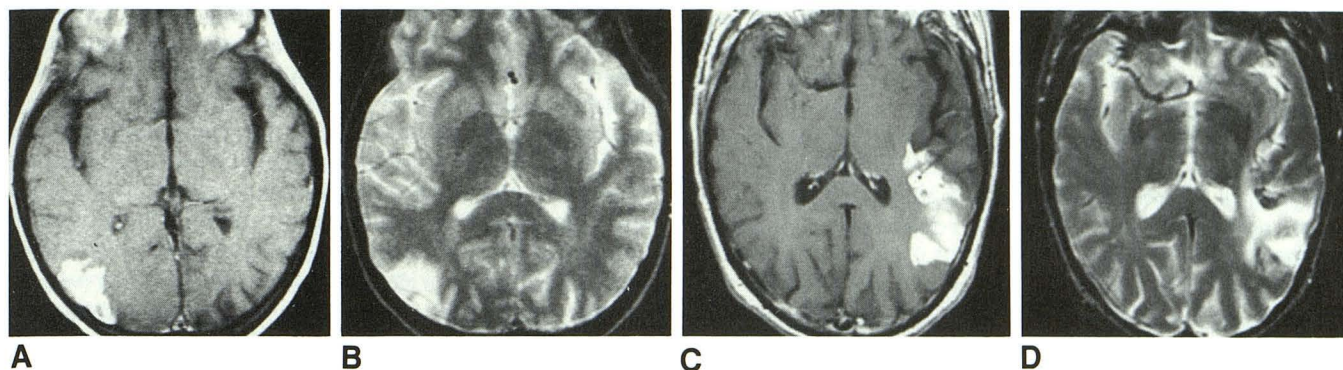
A   **B**   **C**   **D**

Fig. 9.—Examples of early, intense parenchymal enhancement in region of watershed zones in patients with severe neurologic sequelae. MR examination performed 14 days after gradual onset of symptoms in a patient with hypercoagulable state and angiographic evidence of thrombus in petrous portion of right internal carotid artery.

A and B, Postcontrast axial T1-weighted image (516/20) (*A*) shows early and intense parenchymal enhancement in right posterior watershed zone without arterial enhancement. The area of enhancement approximates the area of signal abnormality shown on the axial T2-weighted image (2000/100) (*B*).

C and D, Postcontrast axial T1-weighted image (750/20) (*C*) of another patient 10 days after onset of acute aphasia with dense residual symptoms shows intense enhancement near watershed zone. Area of enhancement exceeds the extent of signal change on corresponding axial T2-weighted image (2300/90) (*D*). The small area of low signal intensity in posterior aspect of left temporal lobe corresponded to a focus of high signal intensity on precontrast T1-weighted images (not shown) and most likely represents petechial hemorrhage. Arterial enhancement of distal middle cerebral artery branches can also be seen (*C*).

of the signal abnormality on T2-weighted images. The signal intensity on T2-weighted images in these watershed infarctions related directly to the severity of clinical symptoms.

Discussion

MR has been proved more sensitive than CT in the detection of brain ischemia in its early and chronic stages [11–15]. This has been attributed to the high sensitivity of T2-weighted sequences. However, in our previous study [11], signal changes on T2-weighted images were not usually detected until approximately 8 hr after the onset of symptoms. Brain swelling detected on unenhanced T1-weighted images and the presence of abnormalities in large vessels frequently preceded the development of signal changes on T2-weighted images, improving the sensitivity of unenhanced MR in the detection of early cerebral ischemia.

Previous reports [10] have suggested that gadopentetate dimeglumine does not contribute significantly to the early detection of ischemic stroke. In the present series, findings of arterial and parenchymal enhancement suggest a potential use for contrast material in the detection and evaluation of cerebral ischemia.

Arterial Enhancement

Absence of flow void in major intracranial vessels has been shown to be an indicator of early cerebral ischemia [11, 16]. However, detection of diminished or absent flow in smaller arterial vessels (such as cortical branches of the MCA) may not be appreciated on unenhanced MR images. Recent reports have described a vascular abnormality demonstrated by CT (dense artery sign) [17–19], but this finding may not be as conspicuous as on contrast-enhanced MR images (Fig. 2).

Enhancement of arteries was detected in nearly half the ischemic lesions studied, usually in cortical lesions. Larger arterial size and low signal from surrounding CSF may be the reasons for more frequent detection of arterial enhancement in cortical than in noncortical lesions. Arterial enhancement was rarely detected in isolated noncortical ischemia of the deep white matter or the noncortical gray matter, probably because of the involvement of smaller terminal arterial branches that are not easily detected by either enhanced or unenhanced MR. Therefore, the only noncortical lesions with arterial enhancement were vertebrobasilar circulation lesions with involvement of the large vertebral and basilar arteries.

Theoretically, arterial enhancement should be detectable immediately after the onset of flow alteration, as this is a phenomenon of altered flow kinetics. The earliest arterial enhancement detected in this series was 2 hr after the onset of symptoms (the earliest that we were able to obtain a contrast study). Arterial enhancement may precede the development of parenchymal signal change on T2-weighted images (Fig. 3), suggesting that the addition of gadopentetate dimeglumine may further improve the sensitivity of MR in the detection of certain cases of acute cerebral ischemia in the first few hours after onset [11].

The mechanism of arterial enhancement in cerebral ischemia is unknown. Arterial structures usually lack intraluminal signal owing to rapid and/or turbulent flow, causing the so-called flow-void phenomenon. Slow flow in venous channels may be manifested on contrast-enhanced MR images by an increase of intravascular signal. Arterial enhancement in this series could be seen both in complete proximal occlusion with retrograde collateral flow and in incomplete occlusion with slow antegrade flow on the angiographic examination. Conversely, when rapid flow was maintained distal to an occlusion (either by collateral flow or by a limited "partial" occlusion), arterial enhancement was not demonstrated. Therefore, slow

flow appears to be the primary mechanism for arterial enhancement. Elster and Moody [20] have also recently speculated that sluggish arterial flow near an infarction is responsible for arterial enhancement. Although thrombi within the proximal ICA or basilar artery may enhance with the addition of contrast agent, this is not likely to account for enhancement of the distal vascular tree. Thrombi in our series were seen most frequently as isointense lesions on immediate postcontrast images.

Arterial enhancement was most often detected within the first 24 hr and was not seen after 11 days in this series (Fig. 1). The disappearance of arterial enhancement coincided with the appearance of significant parenchymal enhancement (Figs. 3 and 4). This may be due to the proliferation of collateral vessels [5, 21] or the recanalization of thrombosed vessels in the subacute phase, either mechanism resulting in the reestablishment of fast and/or turbulent flow in distal arterial vessels. It appears that the rate of development of collateral flow affects the time at which arterial enhancement dissipates and parenchymal enhancement develops. An extreme example of this relationship is seen in patients with "incomplete ischemia" (Fig. 7) in whom intense parenchymal enhancement occurs early and arterial enhancement does not develop because of the early reestablishment of flow. The fact that arterial enhancement in completed infarctions dissipates by 7 to 11 days also coincides with the well-documented onset of "luxury perfusion" on contrast-enhanced CT scans at approximately 1 week.

The presence of arterial enhancement appears to be a better indicator of clinical severity than is the presence of proximal vessel occlusion. There were asymptomatic patients in this series with complete proximal large-vessel occlusions who had no arterial enhancement on initial MR studies. These patients had excellent collateral flow on angiographic studies. We also saw two patients with arterial enhancement initially who showed dramatic clinical improvement and rapid resolution of the arterial enhancement (Fig. 5). A potential application of this relationship is in noninvasive monitoring of the response to treatment aimed at reestablishing flow, such as thrombolysis.

Parenchymal Enhancement

Patterns. Previous studies of enhanced MR in ischemic stroke have shown that parenchymal enhancement is not usually seen before 6 days [5, 7], is predominant in the subacute phase (7–30 days), slowly fades in the chronic phase (>30 days) [5, 7], and may persist for 6–8 weeks [22]. Although our data are in agreement with these findings, we have seen two distinct patterns of parenchymal enhancement after the administration of contrast material. In addition to the typical pattern of progressive parenchymal enhancement described previously, we also saw a pattern of early and/or intense parenchymal enhancement (Table 2).

The two patterns appear to reflect pathophysiologic processes similar to those described by Virapongse et al. [5] in a hypothetical model. They divided tissue perfusion during an acute ischemic insult into two categories: complete ischemia

(no perfusion) and incomplete ischemia (some perfusion) (Table 2). In their model of complete ischemia, diminished or absent perfusion would result in absence of early parenchymal enhancement owing to a significant interruption of contrast delivery to the ischemic tissue [5]. In our series, cases of complete ischemia tended to show no early parenchymal enhancement while signal abnormalities on T2-weighted images were more intense (Figs. 3, 4, 6). In the model of incomplete ischemia, they predicted that early enhancement may occur because a significant amount of contrast material continues to reach the ischemic tissue. We can substantiate this hypothesis with cases of incomplete ischemia that were characterized by early parenchymal enhancement with limited signal change on T2-weighted images (Figs. 7 and 8).

Three relationships that are compatible with this model of ischemia may be concluded from our observations. As mentioned in the discussion of arterial enhancement, there appeared to be an inverse relationship between arterial enhancement and parenchymal enhancement, with arterial enhancement present in the acute phase of ischemia only when perfusion was absent (complete ischemia). Arterial enhancement dissipated and parenchymal enhancement developed in the subacute phase as collateral flow was established. In the acute phase, the area of parenchymal enhancement also appeared inversely related to the area of signal abnormality on T2-weighted images. Parenchymal enhancement tended to be absent where the area and intensity of signal abnormality on T2-weighted images were greatest, both indicating a severe ischemic insult. A direct relationship between the degree of signal abnormality on T2-weighted images and the presence of arterial enhancement was also apparent in the acute phase of ischemia, with arterial enhancement again only found when the alteration of perfusion was severe (complete ischemia).

Mechanisms. Theoretically, the enhancement of ischemic brain parenchyma by gadopentetate dimeglumine depends on the availability of the contrast agent to the ischemic zone. Two basic sequential steps determine this availability: the adequate vascular delivery of contrast material and abnormal local tissue accumulation of the contrast agent [5, 10, 23].

Parenchymal enhancement can occur only when the delivery of contrast material is intact. In the setting of complete proximal vascular occlusion without preexisting collateral flow (complete ischemia), no early parenchymal enhancement occurs (Figs. 2–4). In incomplete ischemia with early parenchymal enhancement, delivery of contrast material during the acute stage may be maintained with partial vessel occlusion or may be promptly restored after interruption of flow in transient vessel occlusion (Figs. 7–9). In our series, lesions with early enhancement tended to have a better prognosis than did those with complete ischemia, reflecting the intact delivery of gadopentetate dimeglumine in lesser vascular insults. Signal changes on T2-weighted images were also less extensive in the incomplete ischemia cases, again consistent with lesser ischemic insults.

We agree with other authors [5, 7, 9] that progression of parenchymal enhancement in the subacute stages of complete ischemia is due to establishment of collateral blood flow. Delivery of contrast agent may thus resume with the disap-

pearance of arterial enhancement and the development of parenchymal enhancement. The collateral circulation may consist of previously existing vascular channels or proliferation of neovasculature at the border of viable tissue (marginal proliferation) and from the subarachnoid space (transmedullary proliferation). This is supported by the observation that development of gyriform enhancement tends to progress from the outer (pial) surface into the deeper structures and from thinner to thicker areas of involvement. Similarly, enhancement tends to progress from peripheral to central portions of noncortical lesions.

In this and other series [5, 22], enhancement of noncortical infarctions appears to develop earlier (4–7 days) than in cortical infarctions (>7 days). This is probably due to the fact that the blood supply to deep brain structures may have dual sources of supply (between ACA and MCA or between two vertebral arteries) and that there is more viable tissue surrounding these smaller lesions with less distance that the contrast material must penetrate.

Ischemia (Figs. 7 and 8) and infarction (Fig. 9) in or near watershed zones between major arterial distributions often resulted in the early, intense pattern of parenchymal enhancement. We postulate that infarction near these zones represents an equivalent of the incomplete ischemia model with regard to the delivery of contrast material but not the severity of ischemia. Delivery of contrast agent may be maintained by the dual nature of the blood supply from adjacent vascular territories. Therefore, although early and/or intense enhancement of watershed lesions may occur, the underlying insult often results in infarction, and the enhancement pattern is less likely to be predictive of clinical severity and/or reversibility.

After successful delivery of gadopentetate dimeglumine to a zone of ischemia, a subsequent mechanism for greater concentration of contrast material in the ischemic tissue than in normal tissue must be present for the lesion to be depicted by MR imaging. Although enhancement is most likely the result of an immature blood-brain barrier caused by neovascularity in the subacute phase of complete ischemia [5], the mechanism of early parenchymal enhancement is unknown. Breakdown of the blood-brain barrier due to irreversible damage to the vascular endothelium usually does not occur until approximately 6 hr after the insult [24–26], but we have seen cases with abnormal parenchymal enhancement as early as 2 hr (Fig. 7). Either local hyperemia (with blood pooling) caused by dysautoregulation [5] or extravasation of contrast material as a result of endothelial ischemia without frank breakdown of the blood-brain barrier [27, 28] may be postulated as responsible for an increased accumulation of contrast material. In either case, the total amount accumulated will ultimately depend on the overall rate of delivery of contrast agent by the vasculature.

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