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# MR Contrast Enhancement in Brainstem and Deep Cerebral Infarction

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**MR imaging with IV administration of gadopentetate dimeglumine was performed in 89 patients with 100 clinically and radiologically documented brainstem or deep cerebral (basal ganglia/internal capsule) infarctions to determine the patterns and time course of contrast enhancement. By location, there were 61 deep cerebral, eight midbrain, 23 pontine, and eight medullary infarctions. The age of the infarctions ranged from 1 day to 3½ years, with 22% of the patients scanned within 4 days and 43% scanned within 2 weeks of clinical ictus. Abnormalities on T2-weighted images were encountered in every case. Mass effect was seen in 10 infarctions, most commonly noted between days 2 and 6, but persisting to day 20 in a single case. Parenchymal contrast enhancement was seen in 43 cases, occurring predominately between days 2 and 80. By postinfarction day 3 only half the strokes enhanced, although all did after day 6. Intravascular enhancement within the vertebral or basilar arteries was noted in five cases; all were brainstem infarctions imaged during the first week following ictus. Meningeal enhancement adjacent to the infarction was not seen in any case.**

**Our results indicate that MR contrast enhancement of brainstem and deep cerebral infarctions typically occurs over a period from about 3 days to 3 months following ictus. Lack of both parenchymal and intravascular enhancement is thus to be expected for several days after a brainstem or deep cerebral infarction.**

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The value of MR imaging for the detection and characterization of cerebral infarction is now well established [1–7]. High-signal abnormalities on T2-weighted images are reliably seen within the first 24 hr of most cerebral infarctions [5], a time when CT may be normal or demonstrate only subtle changes [8]. MR has proved particularly valuable in brainstem and lacunar infarctions, where the detection rate of MR over CT appears to be even greater [9–11].

Contrast enhancement with gadopentetate dimeglumine has been shown to be a useful adjunct to routine MR imaging of stroke, especially in its ability to reveal altered hemodynamics associated with acute cortical infarction [12–16]. The time course for parenchymal enhancement in cortical infarctions appears to be similar on both iodine-enhanced CT and gadopentetate-enhanced MR [15]. However, Elster and Moody [16] have recently described two new types of enhancement seen on MR that precede the appearance of classic parenchymal enhancement. These two new types of enhancement were named the *intravascular enhancement sign* and *the meningeal enhancement sign*, and were identified in up to three fourths of patients scanned within the first few days following a cortical cerebral infarction.

The role of contrast enhancement with gadopentetate dimeglumine in the MR imaging of brainstem and deep lacunar infarctions remains largely uninvestigated [17]. We therefore set out to examine prospectively a group of patients with clinical and radiologic evidence of such infarctions by contrast-enhanced MR imaging. Our main goals were to establish standards for the expected time course of parenchymal enhancement in these types of infarctions and to determine whether intravas-

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cular or meningeal enhancement signs could be seen with strokes in these locations.

## Subjects and Methods

The study population initially comprised 123 patients referred for cranial MR imaging over a 2½ year period. Each patient enrolled into the study had been initially referred either for evaluation of a suspected new brainstem or deep cerebral infarction or for an unrelated reason but who, by history, had a clinically definite old infarction in one of these regions. By "deep cerebral infarction" we mean specifically infarctions of the basal ganglia, thalamus, cerebral peduncle, or internal capsule. Patients with cortical and subcortical white matter infarctions were specifically excluded from this study group and will form the subject of a separate report.

Before imaging, each patient was examined by a neurologist, who established the time of clinical ictus by means of medical history and the probable location of the infarction by means of physical examination. To minimize selection bias, each referred patient with a suspected cerebral infarction was prospectively enrolled to undergo MR imaging both with and without gadopentetate dimeglumine.

After imaging, neurologic histories and MR images were reviewed to select a cohort of patients with definite clinical and radiologic evidence of a deep cerebral or brainstem infarction. From the original 123 patients, six were eliminated because motion artifacts or other technical problems resulted in poor-quality MR images that were deemed uninterpretable. Twelve patients proved to have cortical rather than brainstem infarctions, as suspected clinically; these patients were also excluded from the analysis. Finally, in 16 patients the MR scans were normal or showed nonspecific changes of brainstem white matter disease leukoaraiosis. Since a precise focal lesion could not be identified to account for their symptoms, these patients were also excluded from the analysis.

Our study was terminated when technically satisfactory MR images were obtained in 100 radiologically definite brainstem and deep cerebral infarctions where the clinical age was certain. Five patients were examined on two occasions. Six patients had infarctions in more than one region (medulla, pons, midbrain, basal ganglia). Overall, therefore, the 100 infarctions studied came from a population of 89 patients, 40 men and 49 women, ranging in age from 32 to 93 years (median, 63 years).

MR imaging was performed exclusively at high field strength (1.5 T). Precontrast T1-weighted, T2-weighted, and spin-density images were obtained routinely with the use of spin-echo protocols. Precontrast T1-weighted images in axial and sagittal planes were obtained with the following parameters: 600/20/2 (TR/TE/excitations); section thickness, 5 mm; intersection gap, 1.5 mm; field of view, 24 cm; matrix, 256 × 256. Spin-density and T2-weighted images were also obtained before the administration of contrast material and with the use of a double-echo variable bandwidth protocol: 2500/20,80/1; matrix, 192 × 256; and other parameters similar to those of the T1-weighted images. Gradient moment nulling was used to minimize flow-related artifacts on the 80 TE sequence only. No flow compensation gradients were used on the T1-weighted sequences, which might confound interpretation of an intravascular enhancement sign.

After precontrast images were obtained, gadopentetate dimeglumine (Magnevist, Berlex Imaging, Cedar Knolls, NJ) was administered to each patient by IV infusion at a dose of 0.1 mmol/kg. Multiplanar (axial and coronal; sagittal, as needed) postcontrast T1-weighted images with the same parameters as listed above were obtained within 15 min after infusion. The images were reviewed by an experienced neuroradiolgist who, at the time of the readings, was unaware of the precise clinical age of the infarction. This reader recorded his observations concerning general features of the infarction seen on the precontrast portion of the study (such as signal abnormality, mass effect, location, vascular territory, and evidence of hemorrhage). Next, the reader recorded his observations concerning the contrast-enhanced portion of the examination. Particular attention was directed to the timing and pattern of the appearance of contrast material within vessels, within the adjacent meninges, and within brain parenchyma. Because it is well recognized that some cerebral vessels and portions of the dura mater may show mild enhancement normally, only asymmetric enhancement of these structures seen on two adjacent sections was scored as abnormal. The patient's contralateral (normal) side thus served as an internal control against which to judge abnormalities of contrast enhancement at the site of the infarction.

## Results

Abnormalities on T2-weighted images were encountered in each patient. By location, the number of infarctions analyzed were deep cerebrum (61), midbrain (eight), pons (23), and medulla (eight). There were no statistically significant trends or biases in the distribution of patients with strokes in each location by sex, patient age, or age of the infarction.

The age of the infarctions ranged from acute (4 hr) to remote (2½ years). Because many patients were referred for symptoms of relatively recent onset, a majority (63/100) of the infarctions studied were less than 3 months old. Overall, 22 infarctions were considered to be acute (studied within 4 days of clinical ictus). An additional 11 patients were scanned between days 4 and 7, while 10 more patients were examined during the second week after infarction.

Mass effect was appreciated in one medullary, four pontine, and five deep cerebral infarctions. It was not seen in any of the midbrain strokes analyzed. Mass effect was only noted with larger infarctions (not lacunae), such as in the pontine lesion of Figure 1. Mass effect occurred predominately between days 2 and 6, with the maximum time of visualization at day 2. One large pontine infarction showed slight residual mass effect at day 10, while one large basal ganglia infarction still showed moderate mass effect on the lateral ventricle at day 20.

Parenchymal contrast enhancement was noted in 48 cases, occurring predominately between days 2 and 80 (Fig. 2). The time course for the appearance of contrast enhancement is presented in Table 1. Note that for the two infarctions studied within 24 hr, neither showed contrast enhancement; by the second day only three of nine cases were enhancing. It was not until day 4 that the majority of brainstem and deep cerebral infarctions were enhancing. By the end of the first week, however, all infarctions demonstrated enhancement.

Meningeal enhancement associated with the infarctions was not observed in any case. Intravascular enhancement of the vertebral or basilar arteries was seen in only five cases, all were moderately sized brainstem infarctions imaged during the first week (Figs. 3 and 4). In one additional case where complete thrombosis of a vertebral artery was present, high signal was noted within the artery before and after contrast enhancement. It was not possible to ascertain by visual inspection whether this presumed intravascular thrombus also enhanced.

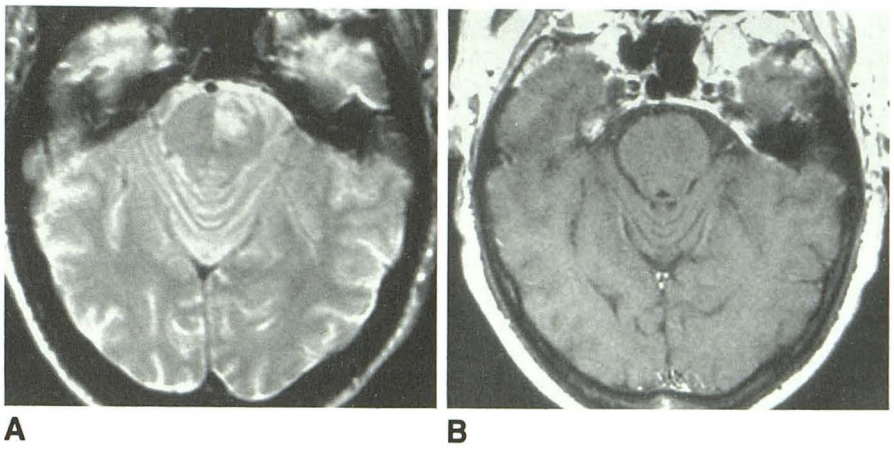



**Fig. 1.—Pontine infarction in a 70-year-old man with a 2-day history of right-sided weakness.**

***A*, T2-weighted image (2500/80) shows high signal on left side of upper pons with sharp medial border.**

***B*, Postcontrast T1-weighted image (600/20) shows swelling and subtle low signal in left pons, but no evidence of contrast enhancement.**

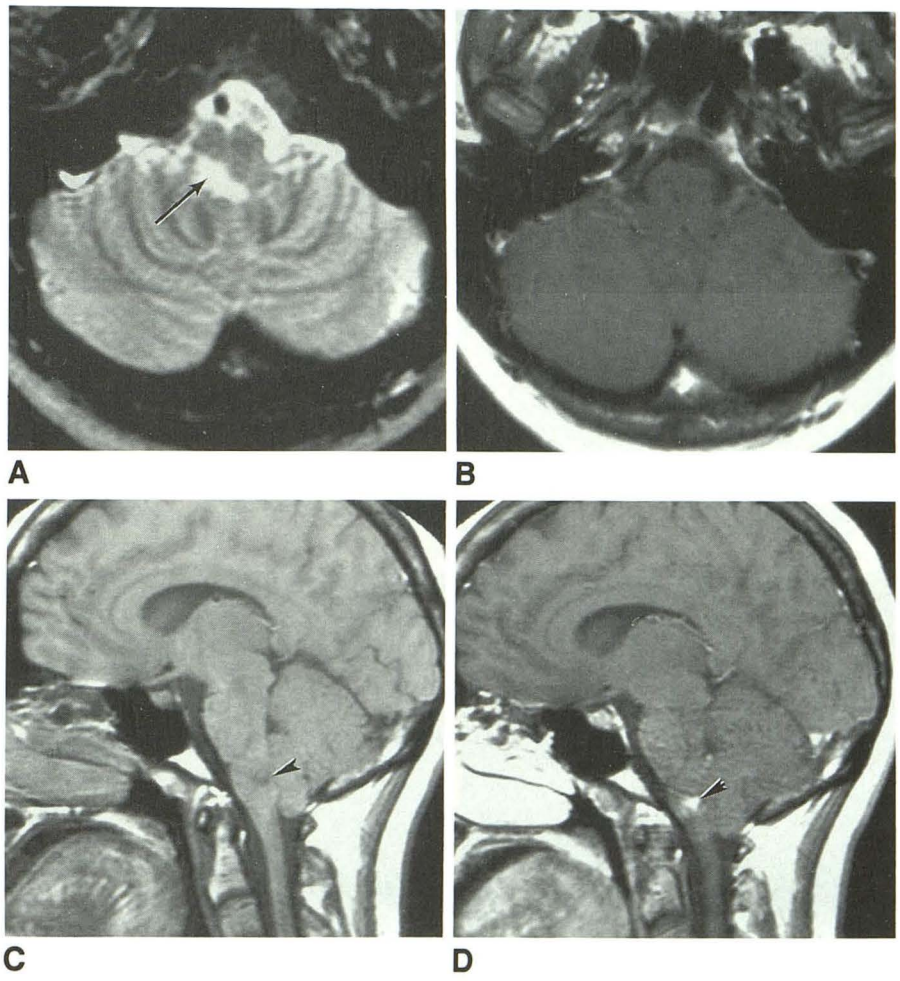



**Fig. 2.—32-year-old woman with angiographically proved spontaneous right vertebral artery dissection and Wallenberg syndrome.**

***A*, T2-weighted image (2500/80) obtained on day 2 shows high signal in right medulla (*arrow*).**

***B*, Contrast-enhanced T1-weighted image (600/20) shows no enhancement.**

***C*, Precontrast T1-weighted image (600/20) obtained on day 5 shows definite low signal and mild mass effect (*arrowhead*).**

***D*, Postcontrast T1-weighted image (600/20) shows strong enhancement of the infarction (*arrowhead*).**

Deep cerebral and basal ganglia infarctions demonstrated a similar time course for contrast enhancement. A typical example is presented in Figure 5.

## Discussion

MR imaging is now an established technique of proved benefit for the early diagnosis and characterization of cerebral infarction [1–17]. Positive MR findings may be present within a few hours of clinical ictus, a time when CT is traditionally negative or indeterminate [5]. The use of diffusion-sensitive MR sequences and paramagnetic contrast agents may potentially reveal physiologic information concerning the hemodynamics and full extent of brain injury unobtainable by other imaging methods [16, 18, 19].

Despite an extensive literature on the MR imaging of cortical

infarction, relatively few papers have appeared concerning the MR appearance of brainstem or lacunar infarction [9–11, 17]. This is in contrast to the relatively high clinical occurrence of lacunar strokes, which comprise up to 19% of all cerebrovascular pathologies [20]. Until the present era, CT has been the diagnostic method of choice for such lesions. Positive results obtained by this method have ranged from 30% to 69%, depending on the series chosen [21]. The high number of false-negative studies by CT relates both to the naturally small size of such infarctions as well as to the presence of bone artifacts that prevent proper viewing of the brainstem.

Little published literature is available concerning the expected time course of enhancement of brainstem or deep cerebral infarctions on contrast-enhanced MR. Virapongse et al. [13] first illustrated the utility of contrast enhancement in three patients with lacunar infarctions, while Miyashita et al. [17] recently presented another nine cases. Imakita et al. [15] studied the time course of gadopentetate enhancement in 35 patients with cerebral infarction. However, as judged by their illustrations, their series was overwhelmingly composed of supratentorial cortical infarctions, not brainstem strokes. Furthermore, only five patients were imaged during the first 4 days following ictus and only six had infarctions older than 28 days.

**TABLE 1: Time Course for Contrast Enhancement in Brainstem and Deep Cerebral Infarction**

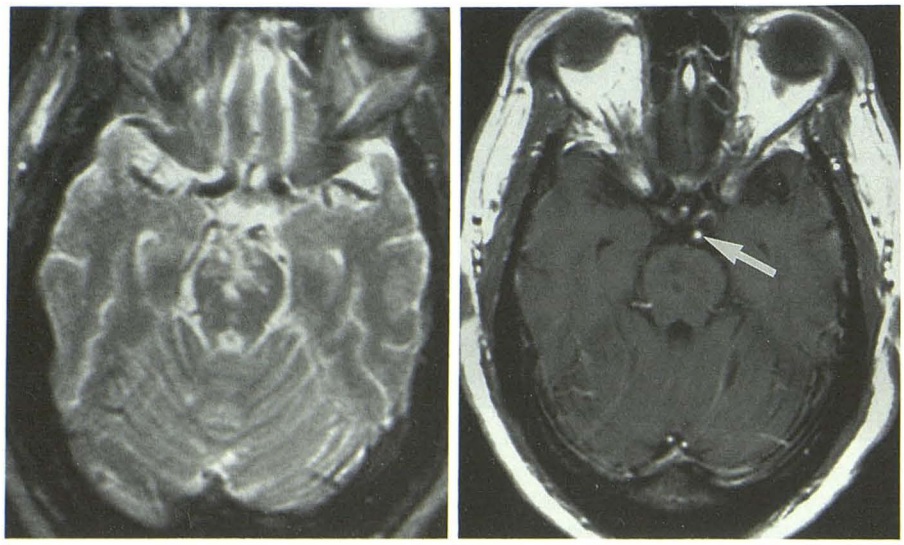
| Time After Infarction | Total No. of Infarctions | No. with Enhancement (%) |
|---|---|---|
| 0–1 days | 2 | 0 (0) |
| 1–2 days | 9 | 3 (33) |
| 2–3 days | 4 | 2 (50) |
| 3–4 days | 7 | 6 (86) |
| 4–7 days | 11 | 10 (91) |
| 7–14 days | 10 | 10 (100) |
| 14–28 days | 8 | 7 (88) |
| 1–3 mo | 12 | 10 (83) |
| >3 mo | 37 | 0 (0) |

In 1990, Elster and Moody [16] described what may be the two earliest signs of acute cortical cerebral infarction on contrast-enhanced MR: the *intravascular enhancement sign* and the *meningeal enhancement sign.* The intravascular enhancement sign was seen in about three quarters of their patients during the first 3 days, presumably representing sluggish flow within vessels supplying the infarction. The meningeal enhancement sign was seen commonly but somewhat less frequently than the intravascular sign, and only in association with larger infarctions.

In our present series of 100 brainstem and deep cerebral infarctions, an intravascular enhancement sign was encountered in only five patients. These cases were all larger brainstem infarctions such as that shown in Figure 4, and the intravascular enhancement appeared in the adjacent or more proximal vertebral and basilar arteries. In no case was a meningeal enhancement sign encountered.

The intravascular enhancement sign is thus quite uncommon in brainstem and deep cerebral infarctions, while it is extremely common in cortical infarctions. An additional confounding factor is that one may occasionally see this sign in the vertebrobasilar system in the absence of a stroke. In our experience this sign may incidentally be encountered in patents whose basilar arteries are ectatic and diseased by atherosclerosis, and in some patients with small, nondominant vertebral arteries. We believe, therefore, that the intravascular enhancement sign is an unreliable ancillary sign for brainstem and deep cerebral infarctions.

Consideration of relevant vascular anatomy may explain this discrepancy in the visualization rates of intravascular and meningeal enhancement signs when comparing cortical and brainstem infarctions. Cortical infarctions are frequently large, and may result from occlusion of either an entire carotid system or of a major cerebral artery. Conversely, a majority of brainstem and deep lacunar infarctions result from occlusion of small, penetrating branches of the vertebrobasilar system. It may be that if more critically ill patients with extensive vertebrobasilar thrombosis had been included in

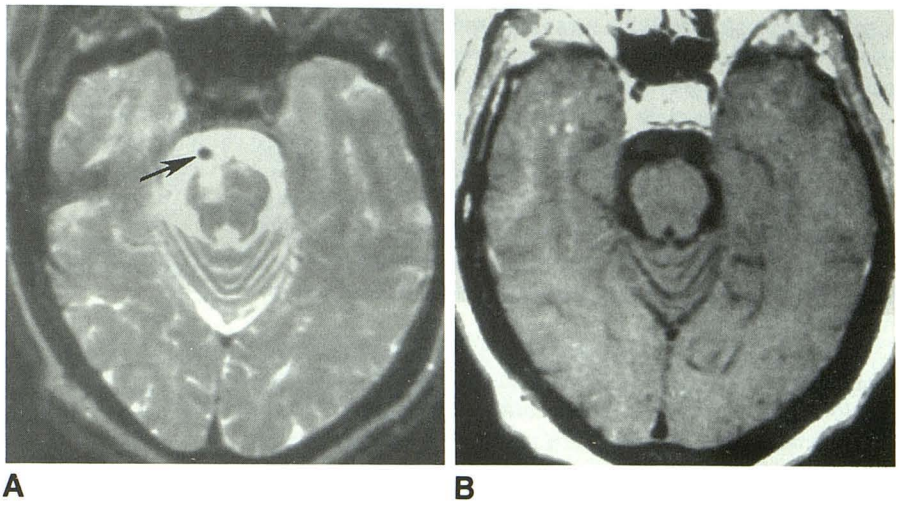


A B

**Fig. 3.—Intravascular enhancement sign in a patient with 3-day-old pontine stroke. The patient is a 55-year-old man with lower extremity weakness and abducens nerve palsy.**

***A*, T2-weighted image (2500/80) shows patchy high signal in upper pons.**

***B*, Postcontrast T1-weighted image (600/20) shows equivocal parenchymal enhancement, but definite enhancement within adjacent basilar artery (*arrow*).**



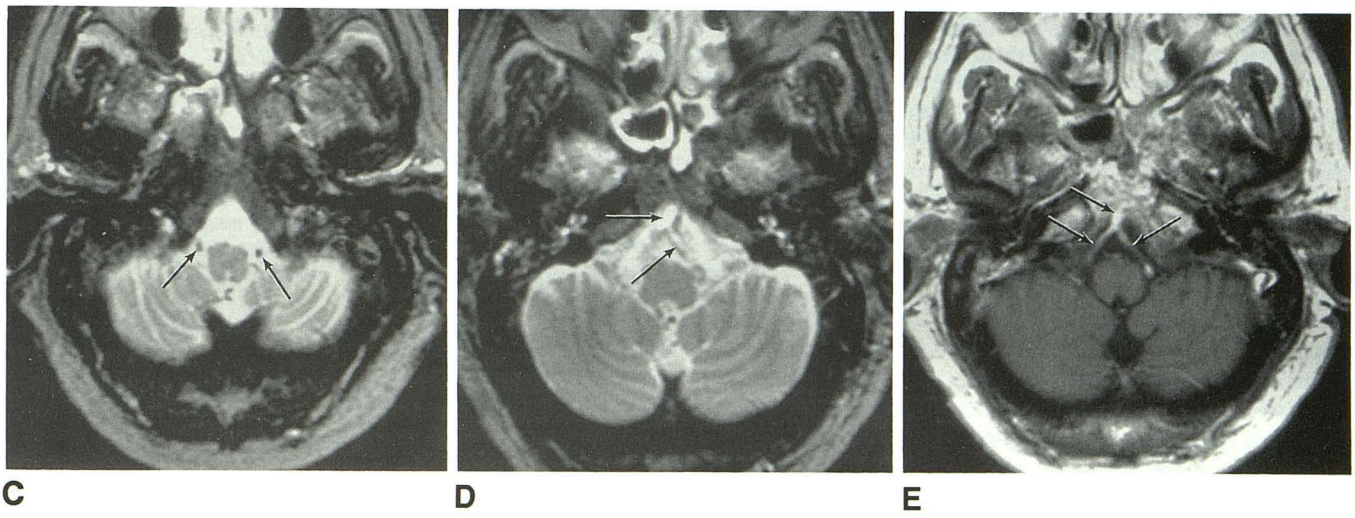




**Fig. 4.—Intravascular enhancement sign inferior to a 4-day-old pontine infarction. The patient is a 57-year-old woman with nystagmus, lower extremity weakness, and right-sided internuclear ophthalmoplegia.**

***A*, High signal is seen in right upper pons on this T2-weighted (2500/80) image. Note flow void in adjacent basilar artery (*arrow*).**

***B*, Postcontrast T1-weighted image (600/20) at same level as *A* shows no enhancement.**

***C*, T2-weighted image (2500/80) at foramen magnum shows flow voids in both vertebral arteries (*arrows*).**

***D*, At level of upper medulla, high signal from slowly flowing blood is refocused (and obliquely misregistered) by gradient moment nulling (*arrows*).**

***E*, Intravascular enhancement sign (*arrows*) is noted in both vertebral arteries and lower basilar artery on this postcontrast T1-weighted (600/20) image.**

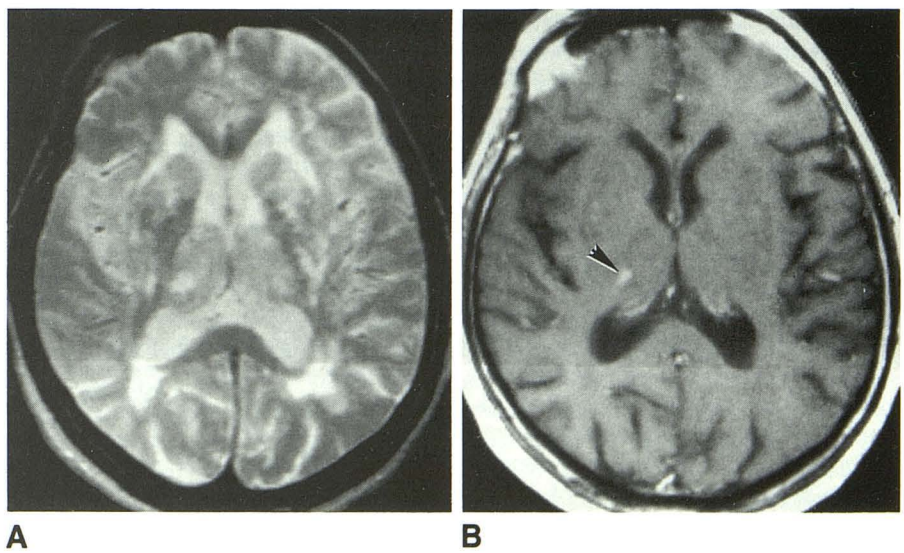



**Fig. 5.—79-year-old woman with multiple cardiovascular risk factors who experienced a right hemisphere transient ischemic attack with left-sided weakness 6 days before imaging.**

***A*, Precontrast T2-weighted image (2500/80) reveals multiple high-signal-intensity lesions in white matter, internal capsule, and thalamus, the ages of which are indeterminate.**

***B*, Postcontrast T1-weighted image (600/20) reveals enhancement of a right-sided lacuna (*arrowhead*), confirming its subacute age.**

our series the rate of occurrence of the intravascular enhancement sign might have been increased.

The complete absence of meningeal enhancement associated with brainstem and deep cerebral infarctions can also be reasonably explained. The meningeal enhancement sign has previously been reported only in association with large cortical infarctions. The relatively smaller size of most brainstem and deep cerebral infarctions, together with the fact that the

location of these infarctions is remote from the dural surface, may mean that engorgement of meningeal collaterals and subsequent meningeal enhancement would be unlikely.

Although intravascular and meningeal enhancement signs were uncommonly detected in this series, classic parenchymal enhancement was noted in nearly half the cases. The peak time for visualization of parenchymal contrast enhancement was from about 3 days to 3 weeks, when greater than 85% of strokes enhanced. No brainstem or deep cerebral infarction in our series older than 80 days demonstrated contrast enhancement.

Another interesting observation from this present series is that parenchymal contrast enhancement appears to be the exception rather than the rule for early (i.e., less than 3-day-old) brainstem and deep cerebral infarctions. Similar findings for cortical cerebral infarctions were also noted by Imakita et al. [15] and Elster and Moody [16]. This is in contradistinction to at least one previous animal study, in which MR contrast enhancement was said to be reliably detected within the first 24 hr [12]. It may very well be that by using T1-weighted spin-echo pulse sequences and a 0.1 mmol/kg dose of gadopentetate dimeglumine, parenchymal enhancement of cerebral infarction on MR will occur with a similar (or identical) time course to that expected for iodinated agents on CT.

The mechanism of parenchymal contrast enhancement in subacute stroke with iodinated contrast agents is reasonably well understood [22]. It is now almost universally accepted that extravasation of contrast material through a leaky blood-brain barrier can account for most features seen on CT scans [23]. Increase in blood volume and luxury perfusion likely produce only a small fraction of the increase in attenuation seen with iodinated contrast agents. Caution must be exercised in the extrapolation of an exact concordance in the behavior of CT and MR imaging contrast agents, however. For example, it is well known that CT enhancement and radionuclide uptake do not always occur simultaneously or match exactly [21]. The possibility that gadopentetate dimeglumine also behaves somewhat differently from CT contrast material warrants further research.

In most cases, contrast-enhanced images are not needed to diagnose an acute brainstem or deep cerebral infarction. Consideration of clinical history coupled with precontrast images will usually suffice. In many cases, however, the clinical and radiologic picture may not be nearly so clear-cut. Relatively large but clinically silent infarctions may occur in the basal ganglia and thalamus. Nonspecific white matter changes that may mimic a stroke are frequently encountered in the brainstems of elderly patients. Furthermore, some brainstem strokes occur in critically ill or nursing home patients, so that the precise time of clinical ictus may be in doubt. In these instances, knowledge of the expected time course of contrast enhancement on MR imaging may be both helpful and critical in arriving at the proper diagnosis.

In conclusion, MR contrast enhancement of brainstem and deep cerebral infarction appears to occur with a time course similar to that expected for iodinated CT agents—over a period of about 3 days to 3 months following ictus. Intravascular enhancement in the vertebrobasilar system is only occasionally noted, and meningeal enhancement is apparently never seen. Lack of both parenchymal and intravascular enhancement is thus to be expected for several days following a brainstem or deep cerebral infarction.

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