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# Clinical Features of Relative Focal Hyperperfusion in Patients with Intracerebral Hemorrhage Detected by Contrast-Enhanced Xenon CT

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***BACKGROUND AND PURPOSE:*** **The prevalence and clinical features of relative focal hyperperfusion were investigated in 165 consecutive patients with intracerebral hemorrhage.**

***METHODS:*** **Contrast-enhanced xenon CT was used to observe regional cerebral blood flow in all patients (86 men and 79 women ranging in age from 25 to 89 years; mean age, 66 years). The clinical data of patients with and without relative focal hyperperfusion were compared to define distinguishing characteristics.**

***RESULTS:*** **Relative focal hyperperfusion was observed in 24 (23.5%) of 102 patients in the acute stage but in no patient in the subacute or chronic stages. Relative focal hyperperfusion was associated significantly more often with putaminal and subcortical hemorrhage than with thalamic and cerebellar hemorrhage. We found that patients with relative focal hyperperfusion had a lower mean age than those without it; a male dominance; and a more common history of intracerebral hemorrhage.**

***CONCLUSION:*** **Relative focal hyperperfusion occurs in the acute stage after intracerebral hemorrhage and does not persist for more than 30 days. The most common locations are the putamen and subcortical areas. Risk factors include male sex and previous bleeding in the same area.**

Hyperperfusion in the areas of the brain surrounding intracerebral hemorrhage (ICH) has been described as luxury perfusion, focal hyperemia, or relative focal hyperperfusion (1–4). Positron emission tomography (PET), single-photon emission computed tomography (SPECT), and contrast-enhanced xenon CT have all detected this phenomenon, but in relatively small numbers of patients and without establishing its precise clinical features (1–12). We investigated the clinical features of relative focal hyperperfusion in 165 consecutive patients with ICH who underwent contrast-enhanced xenon CT studies.

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## Methods

Between December 1992 and November 1996, contrast-enhanced xenon CT was performed in 165 consecutive patients with spontaneous ICH. The study group included 86 men and 79 women who ranged in age from 25 to 89 years (mean age, 66 years). Examinations of eight patients were excluded because of inadequate imaging due to motion artifacts. The location of the ICH and the delay from onset to imaging are shown in Table 1. The xenon CT studies were divided into three groups depending on the stage in which they were performed: acute stage (within 1 week from onset), subacute stage (between 1 week to 1 month), and chronic stage (after 1 month). Hematoma volume was calculated by using the following formula: $\pi/6 \times$ longitudinal length $\times$ transverse length $\times$ thickness of hematoma on CT scans at the time of admission. The xenon CT studies were performed with a Toshiba Xpeed CT system (Toshiba, Tokyo, Japan).

Patients inhaled a mixture of 30% xenon gas in oxygen for 4 minutes, followed by a wash-out time of 4 minutes. During inhalation of xenon gas, a series of 8-second CT scans were obtained at 60-second intervals. Cerebral blood flow (CBF) values were analyzed with an Az-7000 image processing system (Anzai, Tokyo, Japan). Confidential images and filters ($4 \times 4$, $6 \times 6$) were also used to analyze the images. Arterial blood

**TABLE 1: Location of intracerebral hematoma and timing of xenon CT**

| | Stage* | | | Total (%) |
|---|---|---|---|---|
| | Acute | Subacute | Chronic | |
| Putamen | 45 | 12 | 31 | 88 (53.3) |
| Thalamus | 24 | 4 | 9 | 37 (22.4) |
| Subcortical | 21 | 2 | 4 | 27 (16.4) |
| Cerebellum | 8 | 1 | 0 | 9 (5.5) |
| Brain stem | 4 | 0 | 0 | 4 (2.4) |
| Total | 102 (61.8%) | 19 (11.5%) | 44 (26.7%) | 165 (100) |

* Xenon CT was performed within 1 week (acute stage), between 1 week to 1 month (subacute stage), and later than 1 month (chronic stage) after onset.

pressure and arterial carbon dioxide tension ($PaCO_2$) were monitored during CT examination. CBF values were calculated by fitting the Kety equations (Equations 1 and 2) to the time-attenuation curves of brain CT number [Ci(t)] and arterial CT number (Ca) using the least-squares method:

$$1) \qquad Ci(t) = \kappa\lambda \int_0^t e^{k(s-t)} Ca(s)ds$$

where Ca(s) = xenon density in arterial blood at time s, Ci(t) = attenuation in the region of interest at time t, $\kappa$ = build-up constant, and $\lambda$ = blood-partition coefficient, and

$$2) \qquad f = 100\kappa\lambda$$

where f = blood flow, measured in milliliters of blood flow per 100 mL of brain tissue per minute. Follow-up xenon CT was performed from 6 to 30 days after the initial study in the 25 patients who showed relative focal hyperperfusion, which was ascertained visually by two neurosurgeons. Statistical analysis was performed with Student's *t*-test and the $\chi^2$-test.

## Results

There was no significant difference in mean arterial blood pressure or $PaCO_2$ during xenon CT in the various stages (Table 2). Relative focal hyperperfusion was observed in 24 patients in the acute stage (23.5%) but in no patients in the subacute and chronic stages. The delay from onset to imaging in these 24 patients ranged from 1 to 6 days (mean, 2.7 days).

Relative focal hyperperfusion was significantly ($P < .01$) more common in patients with putaminal hematoma and subcortical hematoma than in patients with cerebellar hematoma and thalamic hematoma (Table 3, Figs 1 and 2). No relative focal hyperperfusion was found in patients with brain stem hematoma.

Patients with relative focal hyperperfusion were 25 to 79 years old (mean age, 58 years), which was significantly younger than patients without relative focal hyperperfusion ($P < .05$), and there was a significant male dominance ($P < .01$) (Table 4). Nine of the 24 patients with relative focal hyperperfusion had a history of ICH in the same location, which was significantly more common ($P < .01$) than in patients without relative focal hyperperfusion. The hematoma volumes were not significantly different (Table 4). CBF values in the core of the area of relative focal hyperperfusion ranged from 77 mL/100 g per minute to 106 mL/100 g per minute (mean, 91.3 mL/100 g per minute), and there was no significant difference according to location of hematoma. The area of relative focal hyperperfusion was located lateral to the hematoma in 16 patients, anterior in 14 patients, and posterior in 20 patients. No sagittal or coronal scans were obtained, so the proximal or distal relationship between the blood supply to the territory of the hematoma and the area of relative focal hyperperfusion is unknown. Follow-up xenon CT showed the relative focal hyperperfusion had disappeared in all 24 patients.

**TABLE 2: Physiological parameters at xenon CT in each stage**

| Parameters | Stage | | |
|---|---|---|---|
| | Acute (n = 82) | Subacute (n = 10) | Chronic (n = 30) |
| MABP | 109 ± 8 | 104 ± 11 | 103 ± 10 |
| $PaCO_2$ | 38.4 ± 3.9 | 37.3 ± 4.4 | 37.6 ± 4.1 |

Note.—Values are mean ± standard deviation. There is no statistically significant difference among the stages. MABP indicates mean arterial blood pressure; $PaCO_2$, arterial carbon dioxide tension.

## Discussion

Relative cerebral hyperemia was first identified as luxury-perfusion syndrome by Lassen (13), who believed that the cause was metabolic acidosis. Hyperemia has since been observed in association with various cerebrovascular diseases. Hoedt-Rasmussen et al (14) measured CBF in six patients with acute apoplexy using the $^{133}Xe$ injection method and re-

**TABLE 3: Location of intracerebral hematoma (ICH) and prevalence of relative focal hyperperfusion (RFH)**

| Location of ICH | RFH No. (%) | Non-RFH | Total |
|---|---|---|---|
| Putamen | 15 (33.3)* | 30 | 45 |
| Thalamus | 2 (8.3) | 22 | 24 |
| Subcortical | 6 (28.6)* | 15 | 21 |
| Cerebellum | 1 (12.5) | 7 | 8 |
| Brain stem | 0 (0) | 4 | 4 |
| Total | 24 (23.5) | 78 (76.5) | 102 (100) |

* $P < .01$ versus thalamus and cerebellum.

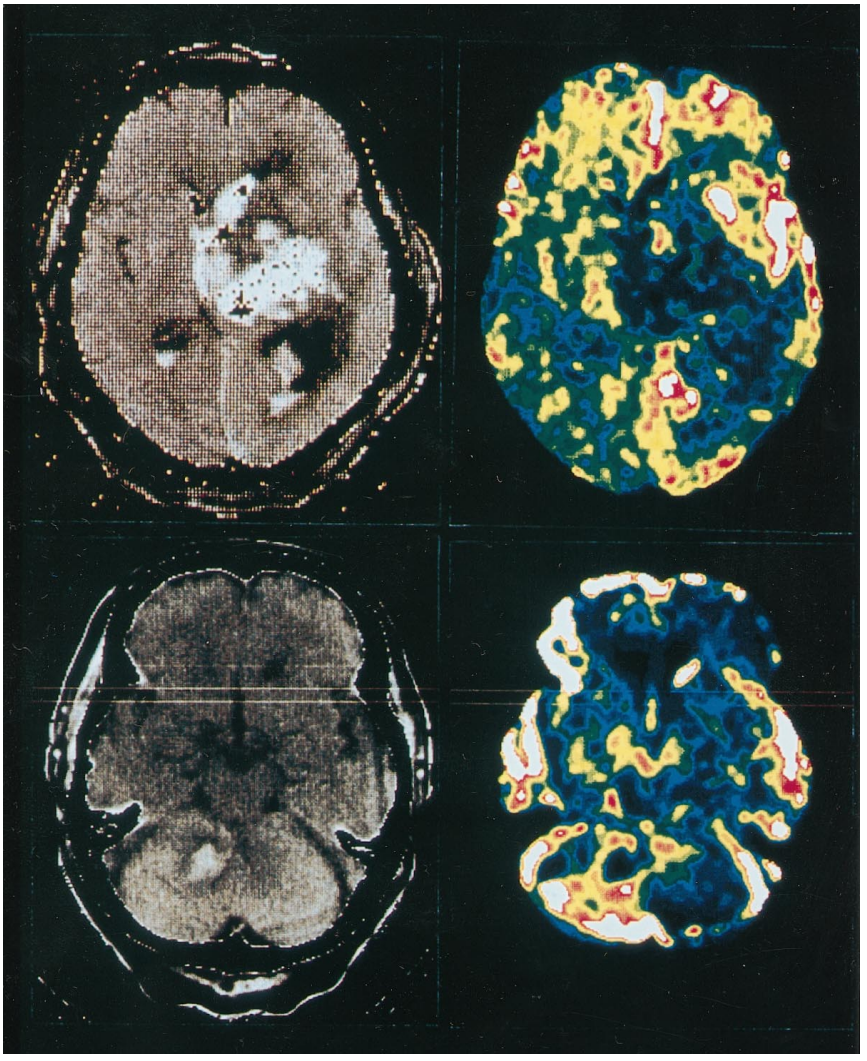

FIG 1. CT scans (*left*) and regional cerebral blood flow (rCBF) maps (*right*) 2 days after the onset of putaminal hemorrhage (*above*) and 3 days after the onset of cerebellar hemorrhage (*below*). The rCBF maps show the defect in the hematoma surrounded by areas of hyperemia lateral, anterior, and posterior to the hematoma (*above*) and the defect in the hematoma surrounded by areas of hyperemia posterior to the hematoma (*below*).

ported that four of the six had focal hyperemia. Paulson (15) found that the $^{133}$Xe injection method showed the perifocal hyperemic area in four patients with middle cerebral artery occlusion within the first 3 days of onset, and one patient had hyperemia persisting until 30 days after onset. Fieschi et al (16) investigated the regional CBF in 18 ischemic lesions and in three hemorrhagic lesions using the $^{85}$Kr regional clearance method and encountered five cases of hyperemia associated with ischemia but none associated with hemorrhage. Agnoli et al (5) measured the regional hyperemia in four of seven patients with ICH using the $^{85}$Kr clearance technique within 2 days of stroke and found that focal hyperemia was never observed in the area of the lesion but rather in the surrounding areas, such as the frontal, parietal, and occipital lobes.

Relative focal hyperperfusion has been investigated in patients with ICH using several methods, but the information is incomplete, preventing comparison of these studies. Therefore, we summarized previous reports to identify any differences with the present study. The prevalence of relative focal hyperperfusion varied widely (Table 5), with an overall frequency of 23%. The $^{133}$Xe injection method showed hyperperfusion with a frequency of 36% to 57%, which seemed to be higher than that found by using PET, SPECT, and xenon CT. The $^{133}$Xe injection method cannot easily verify complex changes in small areas or eliminate artifacts that affect the calculated CBF, because the detector unit has only six probes with large crystals. SPECT has some difficulty in detecting abnormalities in deep structures, like the basal ganglia or cerebellum, because of the limitations of spatial resolution. In contrast, PET and xenon CT have excellent spatial resolution for detecting small or deep lesions. PET provides a great deal of information about relative focal hyperperfusion, because both the CBF and the metabolism around the ICH can be measured, but it has disadvantages in both time and cost requirements. Therefore, xenon CT is presently the most practical method for measuring CBF.

The prevalence of relative focal hyperperfusion measured by xenon CT ranged from 4% to 100%, and the present study found 23.5% in the acute stage. These differences seem to depend largely on the timing of the measurement. In the chronic period, relative focal hyperperfusion was found in only 8% of all

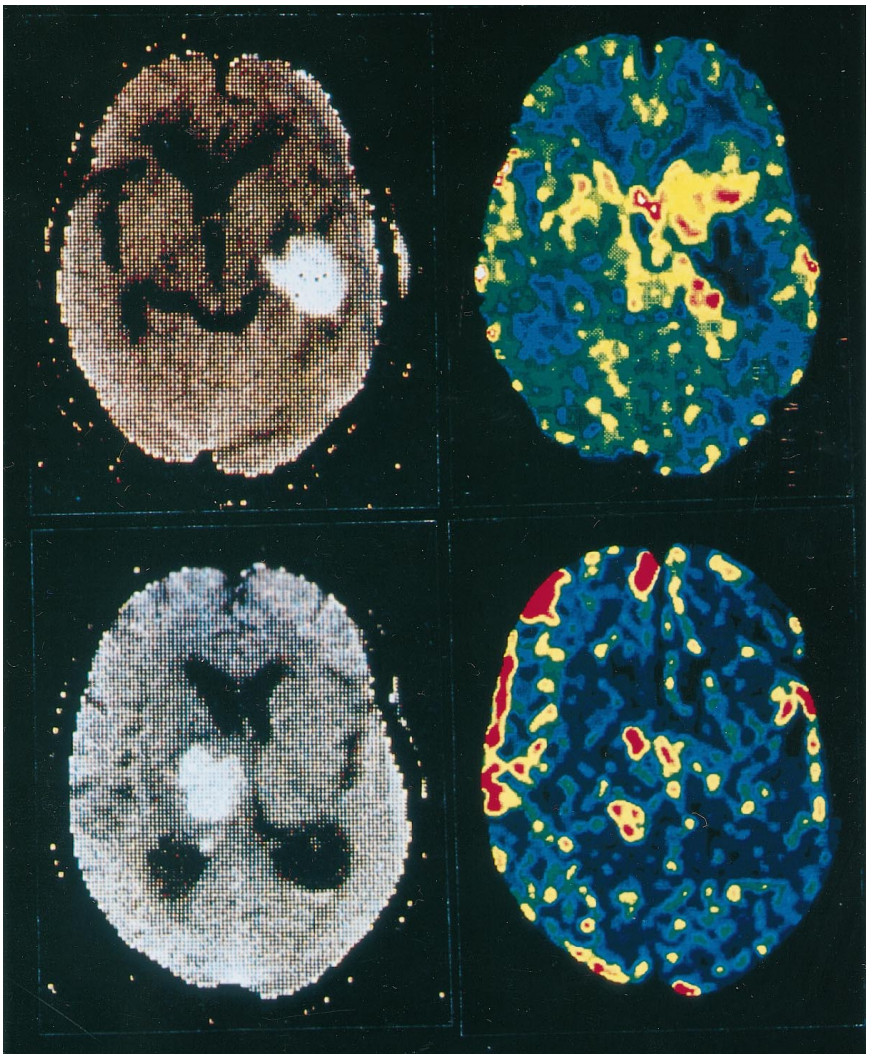

FIG 2. CT scans (*left*) and regional cerebral blood flow (rCBF) maps (*right*) 1 day after onset of subcortical hemorrhage (*above*) and 5 days after onset of thalamic hemorrhage (upper portion of the hematoma) (*below*). The rCBF maps show hyperemia anterior to the hematoma (*above*) and hyperemia lateral and posterior to the hematoma (*below*).

patients (11), but in all patients in the acute period (4). Thus, relative focal hyperperfusion is likely to be recognized in the acute or subacute stage. Such findings support the proposal that the mechanism of relative focal hyperperfusion depends on metabolic acidosis, which leads to vasoparalysis in the early stage of cerebral ischemia.

Table 6 summarizes the clinical data of the patients with relative focal hyperperfusion from the previous and present studies. The age distribution was not different. Male dominance was clear in the present study but not obvious in previously reported cases. The site of ICH associated with relative focal hyperperfusion was the putamen (18 cases) and the subcortical areas (nine cases) when described. We found a similar association, but also recognized relative focal hyperperfusion in one case of cerebellar hematoma and in two of thalamic hematoma. The putamen is the most common site for ICH associated with relative focal hyperperfusion in the surrounding area, but hyperperfusion could also be detected in deep structures, probably because of the high spatial resolution of the xenon CT method. The low prevalence of hyperperfusion associated with ICH in the cerebellum and brain stem may be due to the small number of cases or to the lower sensitivity of CT in the parenchyma of the posterior fossa caused by beam-hardening effects in this area. Hematoma volume was reported in only six previous cases, with a mean volume of 49.5 mL compared to our value of 21.1 mL. There was no significant difference between the studies, but this observation possibly indicates that relative focal hyperperfusion can be associated even with a small ICH. The reaction of luxury perfusion can occur not only in the entire brain but also in a limited area (13). Hyperperfusion was located mainly on the lateral side of the ICH in previous studies but was

**TABLE 4: Clinical data for patients with and without relative focal hyperperfusion (RFH)**

| | RFH | Non-RFH |
|---|---|---|
| Age, y (mean) | 25–79 (58.1)* | 41–89 (65.4) |
| Sex | M: 18, F: 6† | M: 45, F: 33 |
| History of ICH | 9/24 (37.5%)† | 5/78 (6.4%) |
| Hematoma volume, mL (mean) | 3.5–65.4 (21.1) | 2–131 (17.4) |

* $P < .05$.

† $P < .01$ vs non-RFH group.

Note.—ICH indicates intracerebral hematoma.

**TABLE 5: Frequency of relative focal hyperperfusion (RFH) in reported studies**

| Methods | Author | Year | RFH/Total (%) |
|---|---|---|---|
| $^{133}$Xe-CT | Agnoli et al (5) | 1970 | 4/7 (57.1) |
| | Uemura et al (6) | 1973 | 14/33 (42.4) |
| | Kawakami et al (7) | 1974 | 16/44 (36.4) |
| PET | Ackerman et al (1) | 1983 | 1/5 (20.0) |
| | Uemura et al (2) | 1986 | 2/22 (9.1) |
| SPECT | Imao et al (3) | 1989 | 6/15 (40.0) |
| | Sasadaira et al (8) | 1989 | 1/33 (3.0) |
| | Ueda and Ohgawara (10) | 1990 | 5/46 (10.9) |
| | Sunada et al (9) | 1992 | 10/36 (27.8) |
| Contrast-enhanced xenon CT | Suzuki et al (4) | 1988 | 5/5 (100) |
| | Yoshinaga et al (11) | 1990 | 1/12 (8.3) |
| | Yoshinaga (12) | 1994 | 1/28 (3.6) |
| Total | | 1970–1994 | 66/286 (23.1) |

Note.—PET indicates positron emission tomography; SPECT, single-photon emission computed tomography.

**TABLE 6: Clinical characteristics of patients with relative focal hyperperfusion (RFH) in reported and present studies**

| | Reported Studies | Present Study (n = 24) |
|---|---|---|
| Age, y (mean) | 48–86 (62.9) (n = 20) | 25–79 (58.1) |
| Sex | M: 10, F: 6 (n = 16) | M: 18, F: 6 |
| Location of ICH | | |
| Putamen | 18 | 15 |
| Thalamus | 0 | 2 |
| Subcortical | 9 | 6 |
| Cerebellum | 0 | 1 |
| Hematoma volume, mL (mean) | 10–88 (49.5) (n = 6) | 3.5–65.4 (21.1) |
| Time to examination, d (mean) | 1–15 (6.6) (n = 20) | 1–6 (2.7) |
| Site of RFH | | |
| Lateral | 14 | 16 |
| Anterior | 5 | 14 |
| Posterior | 1 | 20 |
| History of ICH | None | 9/24 (37.5%) |

Note.—ICH indicates intracerebral hematoma.

equally distributed on the posterior, lateral, and anterior sides of the ICH in the present study. This observation may be related to the different characteristics of the detector units.

The duration from appearance to disappearance of relative focal hyperperfusion is an important topic, but is difficult to investigate with the xenon CT method because of the limitations of repeated examination. We found that all areas of hyperperfusion had disappeared at the time of the follow-up xenon CT study performed between 6 and 30 days after the initial study. Previous studies have reported disappearance after 4 to 25 days, or 21 to 29 days, so that relative focal hyperperfusion is unlikely to persist for more than 31 days. Unfortunately, no follow-up neuroimaging studies to assess the outcome of these areas are available for these patients.

The difference in clinical features between patients with and without relative focal hyperperfusion has been investigated in only a few studies. Ueda and Ohgawara (10) compared such patient groups and found no difference in the CT classification of ICH, hematoma volume, or clinical neurologic grading. Similarly, our study found no characteristic differences between the two groups in neurologic grading or hematoma volume; however, the mean age of the patients with relative focal hyperperfusion was lower and the ratio of males to females was apparently male dominant (Table 4). A similar age distribution and a tendency to male dominance were found in the previous studies, but the reasons are not known (Table 6). Investigation of the history of the patients revealed that those with relative focal hyperperfusion were more likely to have a history of bleeding at the same location (Table 4).

## Conclusion

The present study observed relative focal hyperperfusion in 24 (23.5%) of 102 patients with ICH in the acute stage, most commonly associated with ICH in the putamen and subcortical areas. Hyperperfusion appeared in the acute stage and did not persist for more than 30 days. Further clinical studies to clarify the mechanisms and outcome of relative focal hyperperfusion associated with ICH are necessary.

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