Paradoxical hyperfixation of hexamethylpropyleneamine oxime in cerebral infarction.

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Paradoxical Hyperfixation of Hexamethylpropyleneamine Oxime in Cerebral Infarction

Shuzo Shintani, Shin Tsuruoka, and Tatsuo Shiigai

Summary: We describe four patients with cerebral infarction and ^{99m}Tc-hexamethylpropyleneamine oxime (HMPAO) hyperfixation in distributions corresponding to the infarctions seen at CT and/or MR imaging. Increased HMPAO extraction due to hyperpermeability across the blood-brain barrier and increased retention due to reduced back diffusion of the tracer probably accounted for the increased fractional fixation in infarcts seen in our patients.

Index terms: Brain, infarction; Single-photon emission computed tomography

Brain imaging using ^{99m}Tc-hexamethylpropyleneamine oxime (HMPAO) single-photon emission computed tomography (SPECT) reflects regional cerebral flow (1, 2). Sperling and Lassen (3) reported that HMPAO SPECT can overestimate reflow hyperemia after spontaneous reperfusion in patients with subacute ischemic stroke (2 to 3 weeks). We previously described one patient with spurious hyperfixation of HMPAO in cerebral infarction (4), and we now describe an additional three patients with HMPAO hyperfixation in stroke. The findings in these patients demonstrate that hyperfixation can occur in all stages of infarction and does not appear to depend on recanalization.

Case Reports

Case 1

Left-sided hemiplegia suddenly developed in a 71-year-old man with atrial fibrillation (This patient was the subject of a previous report [4]). CT of the brain 2 hours after onset of symptoms showed normal findings, but HMPAO SPECT at 4 hours showed marked hyperfixation of HMPAO in the right frontotemporoparietal region (Fig 1A and B). Radiotracer counts in the region of interest in the area of HMPAO hyperfixation and in the corresponding region of the contralateral hemisphere averaged 195.3 ± 17.6 versus 42.7 ± 1.4 (Fig 1A) and 145.3 ± 10.0 versus 41.3 ± 3.0, respectively (Fig 1B).

Intravenous administration of 2400×10^4 U of tissue plasminogen activator was initiated at the time of the SPECT study and was completed in 1 hour. At 6[½] hours after the onset of symptoms, neurologic examination showed complete recovery.

Contrast-enhanced CT scans obtained the day after the event showed low-density lesions in the striatocapsular region and in the white matter of the right hemisphere (Fig 1C), but there were no neurologic deficits. The area of HMPAO hyperfixation on the SPECT study performed 1 day earlier corresponded to the area of infarction seen on the CT study.

Case 2

A 70-year-old man with atrial fibrillation was admitted with sudden onset of seizure and right hemiplegia. Neurologic examination revealed nonfluent aphasia and right-sided hemiplegia, including facial droop; Babinski's sign was present on the right side. Findings on CT scans of the brain on admission were normal.

Two days after the stroke, a ^{99m}Tc-HMPAO SPECT scan showed marked hyperfixation in the left frontal, temporal, and occipital lobes (Fig 2A and B). Radiotracer counts in the region of interest in the area of HMPAO hyperfixation and in the corresponding region of the contralateral hemisphere averaged 72.9 ± 2.1 versus 38.6 ± 2.0 (Fig 2A), and 80.2 ± 1.4 versus 52.5 ± 1.0, respectively (Fig 2B). On day 4, a CT scan of the brain showed a faint low-density lesion in the left temporal lobe adjacent to the sylvian fissure. Magnetic resonance (MR) imaging of the brain on day 6 showed high-intensity lesions in the left frontal, temporal, and parietal lobes on T2-weighted images (2000/100/1 [repetition time/echo time/excitations]). On day 7, a SPECT study was repeated and also showed marked hyperfixation of HMPAO in the left frontal, temporal, and parietal lobes; on day 10, 9 days after the onset of stroke, a CT scan of the brain showed infarction in

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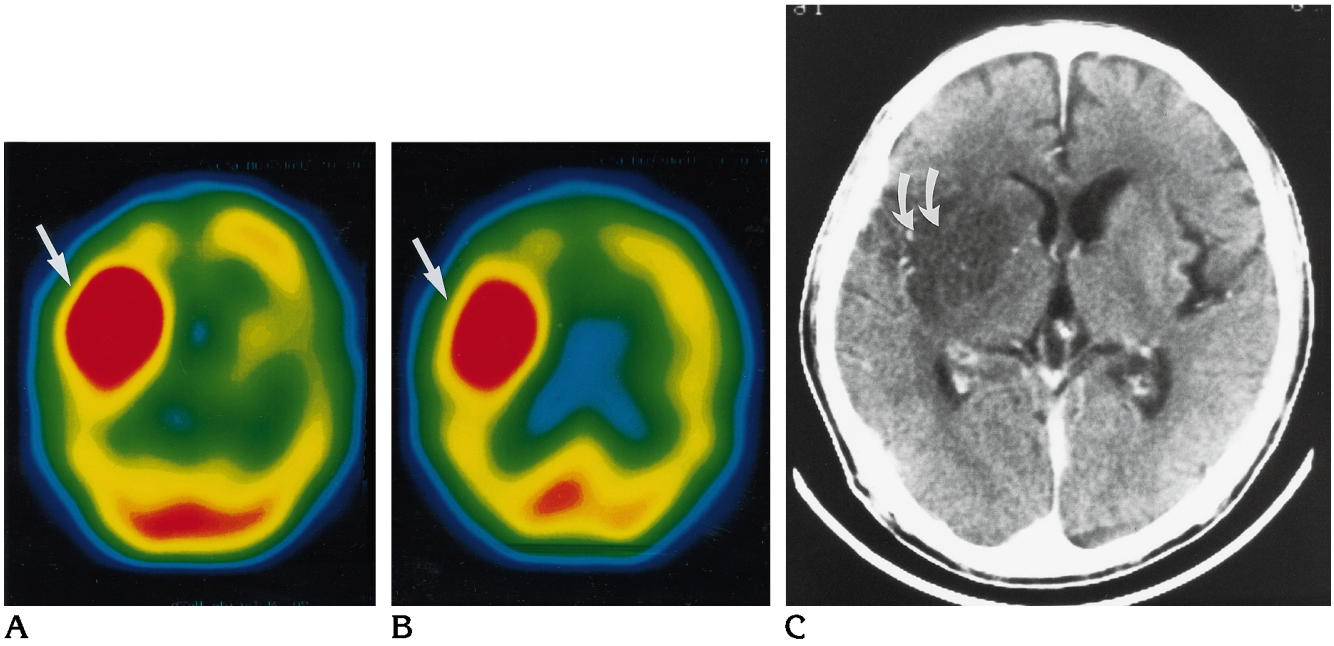

Fig 1. Case 1: 71-year-old man with atrial fibrillation and sudden onset of left-sided hemiplegia.

A and *B*, HMPAO SPECT scans 4 hours after the onset of stroke show marked elevation of ^{99m}Tc-HMPAO uptake (*arrows*) in the right frontal, temporal, and parietal lobes, including the striatocapsular region.

C, Contrast-enhanced CT scan the day after onset of stroke shows a low-density lesion (*arrows*) in the striatocapsular region and in the white matter of the right hemisphere. This area of low density corresponds to the area of hyperfixation on the HMPAO SPECT study.

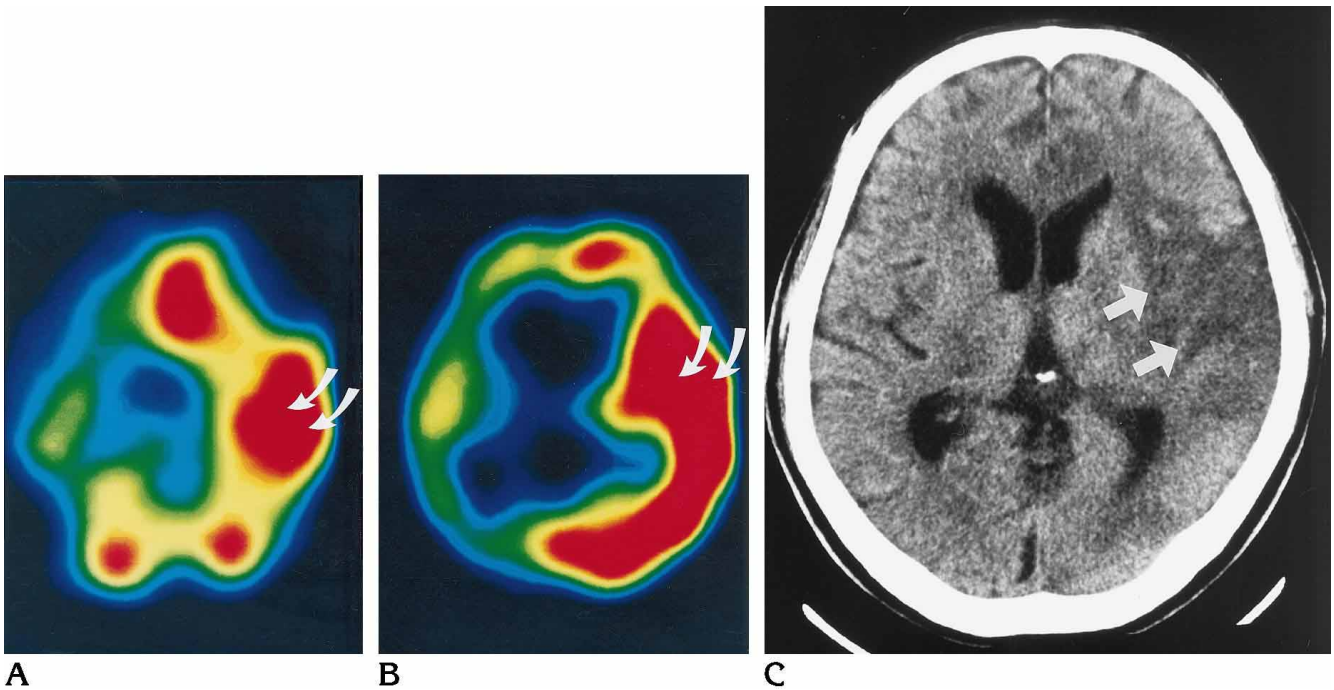

Fig 2. Case 2: 70-year-old man with atrial fibrillation and sudden onset of seizure and right-sided hemiplegia.

A and *B*, HMPAO SPECT scans 2 days after the onset of stroke show marked elevation of ^{99m}Tc-HMPAO uptake (*arrows*) in the left frontal, temporal, parietal, and occipital lobes.

C, Noncontrast CT scan on day 10, 9 days after the onset of stroke, shows infarction (*arrows*) in the left frontal, temporal, and parietal lobes.

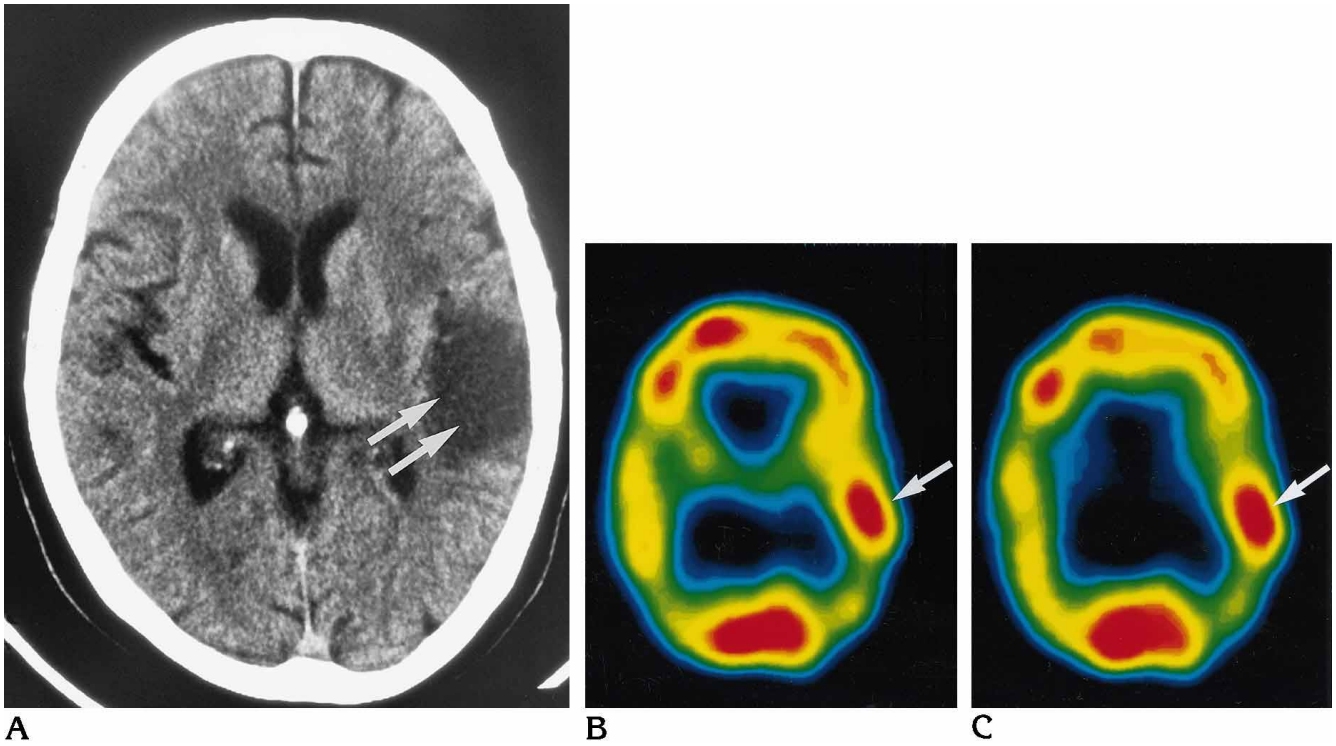

Fig 3. Case 3: 72-year-old woman with sudden onset of nonfluent aphasia.

A, Noncontrast CT scan 3 days after the onset of stroke shows a low-density lesion (*arrows*) in the left temporoparietal region.

B and *C*, HMPAO SPECT scans 17 days after the onset of stroke show marked elevation of ^{99m}Tc-HMPAO uptake in the left temporoparietal lobes (*arrows*). This area of HMPAO hyperfixation corresponded to the area of infarction seen on a former CT scan.

the same area (Fig 2C). On day 20, a third SPECT study also revealed marked hyperfixation of HMPAO in the left frontotemporal region.

Case 3

A 72-year-old woman had sudden onset of nonfluent aphasia. A CT study of the brain on admission, 3 days after the onset of stroke, showed a low-density lesion in the left temporal and parietal lobes (Fig 3A). ^{99m}Tc-HMPAO SPECT was performed 17 days after the onset of symptoms, and showed marked hyperfixation of HMPAO in the left temporoparietal region (Fig 3B and C). Radiotracer counts in the region of interest in the area of HMPAO hyperfixation and in the corresponding region of the contralateral hemisphere averaged 64.3 ± 6.7 versus 54.8 ± 3.4 (Fig 3B) and 65.1 ± 3.2 versus 54.5 ± 1.4, respectively (Fig 3C). This area of HMPAO hyperfixation corresponded to the area of infarction seen on the CT study.

Case 4

A 68-year-old woman suddenly experienced dysarthria. On admission, she was alert, and neurologic examination revealed only dysarthria. CT of the brain on the day after onset of stroke showed a low-density lesion in the right temporal lobe (Fig 4A). Five days after the onset of symptoms, a SPECT scan revealed hyperfixation of HMPAO in the right temporal lobe (Fig 4B). Radiotracer counts in the region of interest in the area of HMPAO hyperfixation and in the corresponding region of the contralateral hemisphere averaged 52.0 ± 2.3 and 43.0 ± 1.8, respectively (Fig 4B). A subsequent SPECT study, performed 16 days after the onset of symptoms, also revealed marked hyperfixation of HMPAO in the right temporal lobe. This area of HMPAO hyperfixation corresponded to the area of infarction seen at CT.

Discussion

In a previous report, we described a patient with cerebral infarction and paradoxical hyperfixation of ^{99m}Tc-HMPAO on SPECT studies (4). This report describes four patients (including the one from the previous article) with the same finding on HMPAO SPECT studies obtained 4 hours to 19 days after the onset of symptoms. The regions of HMPAO hyperfixation corresponded to areas of infarction seen on CT and MR studies. The paradoxical hyperfixations of HMPAO appeared at every stage of the cerebral infarction, from the extremely acute to the subacute stage.

Sperling and Lassen (3) reported that SPECT with HMPAO can overestimate reflow hyper-

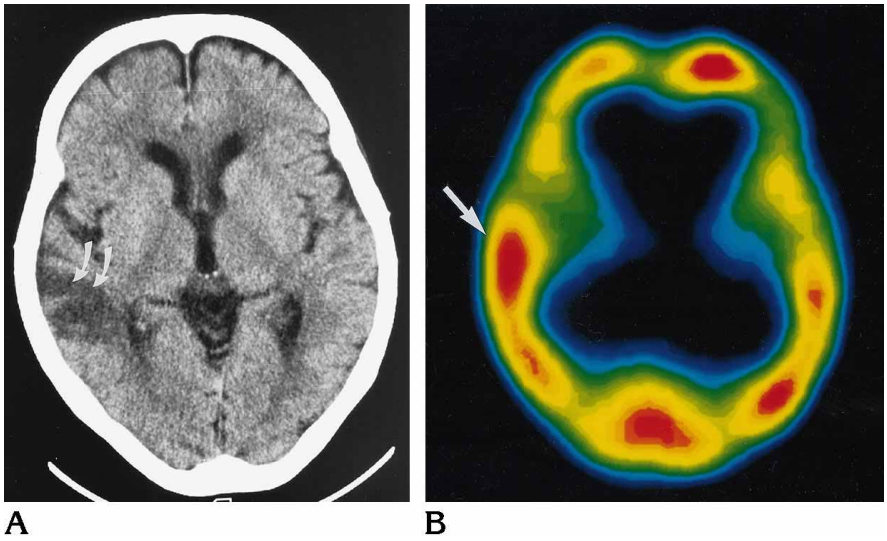

Fig 4. Case 4: 68-year-old woman with sudden onset of dysarthria.

A, Noncontrast CT scan the day after onset of stroke shows a low-density lesion (*arrows*) in the right temporal lobe.

B, SPECT study 5 days after the onset of stroke shows hyperfixation of HMPAO in the right temporal lobe (*arrow*).

emia after "spontaneous reperfusion" in patients with "subacute" ischemic stroke (2 to 3 weeks). In our patients, SPECT with HMPAO appeared to overestimate cerebral blood flow in all stages of infarction. On the basis of the imaging findings and clinical evolution of our patients, we believe that paradoxical hyperfixation of HMPAO does not depend on spontaneous recanalization.

Interpretation of ^{99m}Tc-HMPAO scans in terms of cerebral blood flow distribution assumes that a similar fraction of locally supplied tracer is fixed in the various regions, healthy as well as diseased, at the time imaging is performed. This fixation is due to extraction across the blood-brain barrier and to retention of the extracted tracer molecules resulting from chemical conversion to a hydrophilic metabolite that is unable to cross cell membranes or the blood-brain barrier (3). A constant degree of fractional fixation in all brain regions of 40% to 50% has been found in humans (1). However, our findings indicate that fractional fixation of ^{99m}Tc-HMPAO in infarction is not constant and probably exceeds the normal level of 40% to 50%. The increased extraction due to hyperpermeability across the blood-brain barrier and increased retention due to reduced back diffusion of tracer probably accounts for the increased fractional fixation in infarcts.

In all our patients, the lesions on final CT or MR studies were smaller and fainter than on previous studies. This reduction in size corresponds to the increased fractional fixation on the SPECT study and implies that initial abnormalities may have been due to vasogenic rather than cytotoxic edema. Cytotoxic edema breaks the blood-brain barrier and increases the back diffusion of the extracted tracer molecules across the cell membranes and blood-brain barrier. The reduced retention results in decreased fractional fixation. On the other hand, vasogenic edema retains the blood-brain barrier, and may have increased fractional fixation by the reduced back diffusion. The radiologic reduction of lesion size on final CT or MR studies was probably caused by the abnormal vasogenic edema.

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