Cerebral Blood Flow and Magnetic Resonance Imaging in Locked-in Syndrome

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The cerebral blood flow (CBF) of a patient suffering from locked-in syndrome (LiS) was examined before and after the onset using ^{99m}Tc-hexamethylpropyleneamine oxime single-photon emission computed tomography (SPECT) and the intravenous ^{133}Xe injection method. The mean CBF during the locked-in state was 32.2 ml/100 g/min, a 42% reduction from the asymptomatic stage. SPECT showed profound reductions of perfusion in the bilateral cerebral cortices, subcortical regions and in the cerebellum, with a less marked reduction in the frontal cortices. On Day 49, the patient showed some minimal voluntary return with a moderate increase in mean CBF of 40.2 ml/100 g/min. The relative CBF values in the cerebral cortices and subcortical regions were restored, but the bilateral cerebellar hypoperfusion remained unchanged. SPECT and CBF are useful for a better characterization of the brain pathophysiology in LiS.

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The term locked-in syndrome (LiS) has been used to described quadriplegia and a mute but alert state in patients with pathologic lesions in the ventral pons (*1,2*). Computed tomography (CT) and magnetic resonance imaging (MRI) studies have suggested that lesions which produce the LiS involve the corticospinal and corticobulbar tracts as they pass through the basis pontis (*3,4*). However, the time course of cerebral blood flow (CBF) in the presence of LiS has not been evaluated.

We report here on a LiS patient who underwent ^{99m}Tc-hexamethylpropyleneamine oxime (HMPAO) single-photon emission computed tomography (SPECT) and CBF measurement with the intravenous ^{133}Xe injection method before and after the disease.

CBF MEASUREMENTS

The mean CBF was measured prior to the HMPAO-SPECT using the intravenous ^{133}Xe injection technique based on the initial slope index (ISI) (*5*) with a 32-detector system.

Image acquisition for ^{99m}Tc-HMPAO was started 5 min after a tracer injection of 740 MBq with a single-head rotating gamma camera equipped with a low-energy, high-resolution parallel-hole collimator. Sixty-four views, 30-sec frames collected over 360°, were recorded in a 128 x 128 matrix format. Transaxial slices were reconstructed from the prefiltered raw data with the aid of filtered backprojection algorithms using a ramp filter. Sorenson's technique (*6*) (μ = 0.095 cm^{-1}) was used for attenuation collection. No scatter correction was performed. Transaxial sections at 2.7 mm intervals were used to reconstruct 8.1-mm thick computed images in planes parallel to the orbitomeatal line. The SPECT images were analyzed without linearization. Circular regions of interest (ROIs) of 7 pixels (18.9 mm) in diameter were drawn to obtain a rate of uptake normalized to the whole brain. The ROIs were set to cover 15 regions of the brain with reference to the CT images. The average counts per pixel of each ROI were normalized using average counts per pixel of the whole brain obtained from six contiguous slices, beginning with the lowest slice containing the basal ganglia.

CASE REPORT

A 72-yr-old man had been under treatment for hypertension and asymptomatic lacunar infarction for 3 yr in our neurologic department. MRI 9 mo before the onset showed a small infarct in the left basal ganglia. SPECT revealed no hypoperfused area with a mean CBF of 55.2 ml/100 g/min (Figs. 1 and 2).

On the night of January 19, 1992, the patient experienced headache, difficulty in speaking and heaviness of the left arm. Two hours later, he became confused and was unable to swallow or move his limbs. He was then transferred to our emergency room.

On arrival, his blood pressure was 150/88 mmHg and his heart rate was 86 bpm. Neurologic examinations showed a lethargic but awakable state with quadriplegia: the pronator drift test in the upper extremity and Barre's sign in the lower extremity were positive; DTRs were 1+ throughout; Babinski signs were absent; abdominal reflexes were absent; pinprick response was intact; facial movements were severely affected bilaterally; gag and palatal reflexes were abolished; eye movements were present only in the vertical plane; the pupils were slightly constricted but reactive to light and corneal reflexes were present. On Day 2, the patient became comatose, but on Day 3 he again appeared to be awake and blink his eyes to questions.

MRI on Day 4 (Fig. 3) showed hypersignals in the bilateral ventral and tegmental portion of the pons, and in the right cerebral peduncle on T2-weighted images. SPECT on Day 5 (Figs. 1 and 2) showed a generalized flow reduction in the parietal cortex, temporal cortex, visual cortex, thalamus, hippocampus and the cerebellum, whereas the flow in the frontal cortex was relatively increased. The mean CBF was 32.2 ml/100 g/min, a 42% decrease from the asymptomatic stage.

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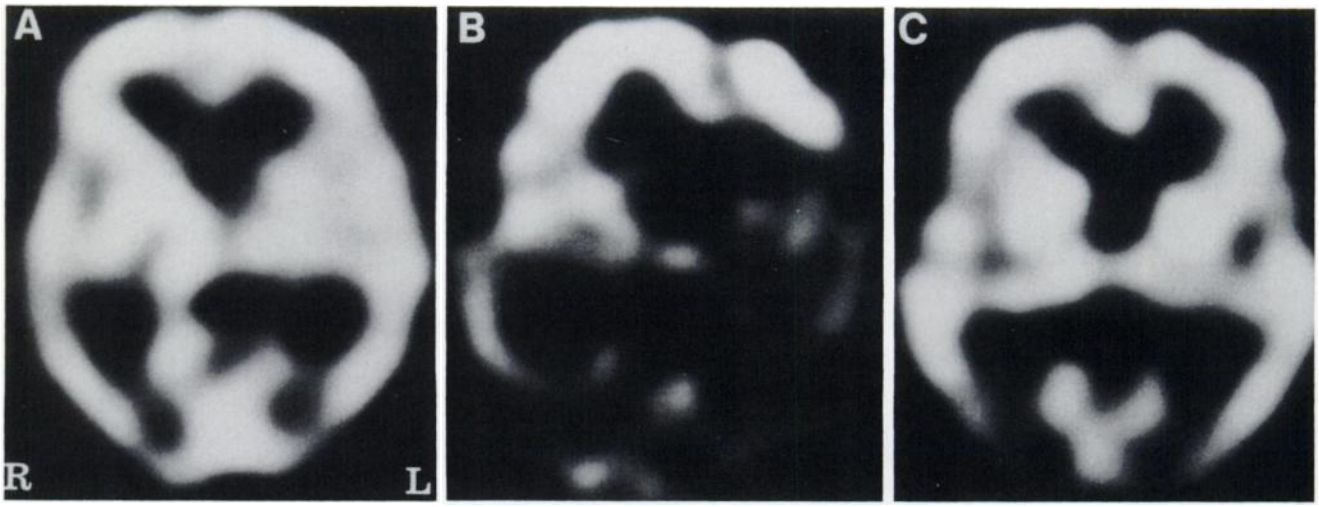

FIGURE 1. (A) SPECT image before the onset of symptoms shows no abnormality. (B) SPECT image on Day 5 after the onset of the disease shows generalized rCBF reduction on both sides of the parietal cortex, temporal cortex, visual cortex, basal ganglia and thalamus, and a preserved flow in the bilateral frontal cortices. (C) SPECT image on Day 49 shows partially restored flow on both sides of the parietal and visual cortices and normalized flow in the temporal cortex, thalamus and basal ganglia. The relative flow in the frontal cortices shows a modest decrease from that of the acute stage. Images are displayed at the level containing the thalamus and the basal ganglia with a gray scale from 15% to 100% of the maximum counts.

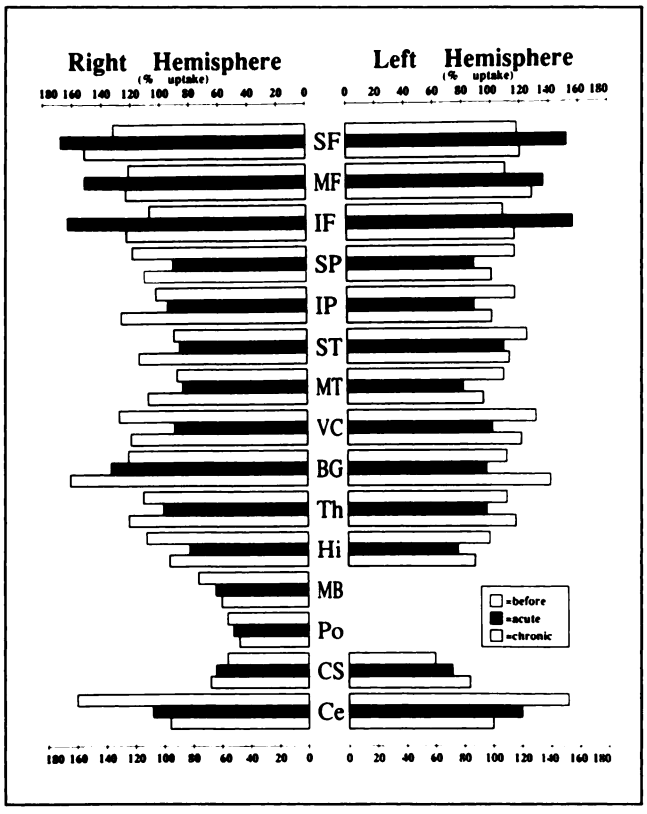

FIGURE 2. Relative CBF distribution in different brain regions measured before admission (before), at 5 days (acute) and at 49 days (chronic) after admission. The uptake rates for the whole midbrain and pons are shown in the right hemispheric side. SF = superior frontal; MF = middle frontal; IF = inferior frontal; SP = superior parietal; IP = inferior parietal; ST = superior temporal, MT = middle temporal; VC = visual cortex; BG = basal ganglia; Th = thalamus; Hi = hippocampus; MB = midbrain; Po = pons; Cs = centrum semiovale and Ce = cerebellum.

On Day 17, he was able to move his right hand slightly on command, and 3 days later, he could move both legs slightly. On Day 29, he could shake his head in response to questions.

Repeated SPECT on Day 49 showed a partially restored flow in the parietal and visual cortices and a normalized flow in the temporal cortex, thalamus and the basal ganglia on both sides. In contrast, the hypoperfusion in the bilateral cerebellum remained unchanged compared to that of the acute stage (Figs. 1 and 2). The mean CBF was 40.2 ml/100 g/min, a 27% decrease from the asymptomatic stage.

He is now alive and neurologically stable.

DISCUSSION

The classical LiS involves patients with total immobility except for vertical eye movements and blinking (*1*). When any other voluntary movement is present, the patient is categorized as having incomplete LiS (*3*). Our patient fulfilled the diagnostic criteria of classical LiS at the time of the first SPECT after the disease, and of incomplete LiS at the time of repeated SPECT.

Only one report has addressed rCBF alterations in LiS. Levy et al. (*7*), using positron emission tomography, found that the LiS, 5 mo after the onset of illness, had a cortical gray flow of 31.9 ml/100 g/min, a 26% reduction from normal values. The rCBF changes involved not only the cerebral cortex but also the basal ganglia and the cerebellum. In accordance with their results, under the condition of incomplete LiS, our patient showed a 27% reduction in mean CBF from the asymptomatic stage. The CBF in our case varied with the severity of the neurologic deficit and with the period of time after the ictus at which measurements were made.

Diffuse cerebral malfunction or postomesencephalic reticular formation malfunction has been thought to cause

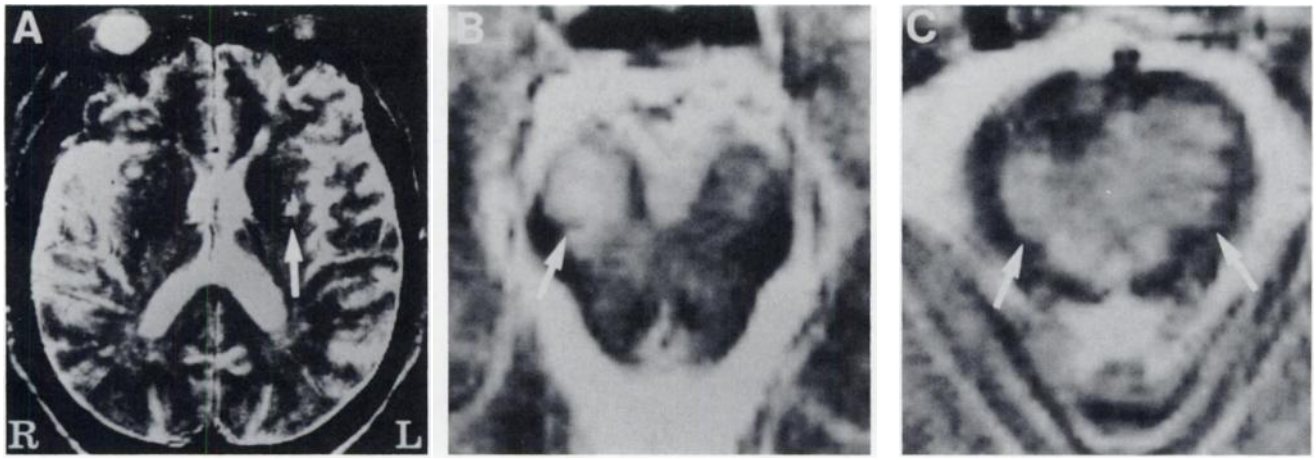

FIGURE 3. Axial T2-weighted MRI(TR 3000 ms/TE 90 ms) performed on Day 4 after the onset of symptoms. (A) At the level of the basal ganglia and thalamus, the arrow shows a hypersignal in the left basal ganglia. (B) At the level of the cerebral peduncle, the arrow shows a hypersignal in the right cerebral peduncle. (C) At the level of the mid-pons, the arrows show a bilobar hypersignal in the ventral and tegmental portions of the pons.

coma (*1*). The improvement of consciousness from coma to full alertness in our case could signify that the reticular activating system of the pons was not completely destroyed. Ascending pontine reticular fibers travel via the central tegmental fasciculus to the thalamic nuclei and then influence the electrical activity of broad areas of the cerebral cortex (*8*). Thus, from the viewpoint of the functional suppressions of the remote areas by deafferation of neural inputs from other neurons (*9*), it is not surprising that a CBF reduction was seen not only in the cerebral cortex but also in the subcortical regions. The pontine nuclei also constitute the most important relay for the conduction of impulses from the cerebral cortex to the cerebellum (*8*). This may explain the reason for the persistence of the reduction of flow in the cerebellum throughout the stages.

A previous study revealed a reduction of the frontal flow in comatose patients (*10*). The frontal flow typically increases during cognitive activation and is related to the level of consciousness (*11*). We believe that, in our case, relative preservation of the frontal flow implies the presence of an inner monologue and an awareness of external and internal stimuli.

In conclusion, although MRI is essential for the confirmation of the anatomical location of clinically responsible lesions in LiS, a quantitative approach with CBF and SPECT may have greater clinical use for the investigation of the progression of the disease, and the establishment of the relationships with the neurologic signs.

REFERENCES

1. Plum F, Posner JB. The *Diagnosis of stupor and coma*, 2nd edition. Philadelphia: FA Davis Company; 1972:24–25.
2. Bryant J, Plum F. Persistent vegetative state after brain damage. *Lancet* 1972;1:734–737.
3. Baurer G, Gerstebrand F, Rumpel F. Varieties of the locked in syndrome. *J Neurol* 1979;221:77–91.
4. Zapella EJ, Dunvall ER, Langford KH. Computed tomography and magnetic resonance imaging in traumatic locked-in syndrome. *Neurosurg* 1988;22:591–593.
5. Risberg J, Ali Z, Wilson EM, Willis EL, Hasley JH. Regional cerebral blood flow by ^{133}Xe inhalation: preliminary evaluation of an initial slope index in patients with unstable flow compartments. *Stroke* 1975;6:142–148.
6. Sorenson JA. Qualitative measurement of radioactivity in vivo by whole body counting. In: Hine GJ, Sorenson JA, eds. *Instrumentation in nuclear medicine, volume 2*. New York: Academic Press; 1977:311–324.
7. Levy DE, Sidtis JJ, Rottenberg DA, Jarden JO, et al. Differences in cerebral blood flow and glucose utilization in vegetative versus locked-in syndrome. *Ann Neurol* 1987;22:673–682.
8. Carpenter MB. Pons, cerebellum. In: Carpenter MB, ed. *Core text of neuroanatomy*. Baltimore: Williams & Wilkins; 1985: p 133–168, 198–220.
9. Meyer JS, Hata T, Imai A. Clinical and experimental studies of diaschisis. In: Wood JH, ed. *Cerebral blood flow*. New York: McGraw-Hill; 1987:481–502.
10. Deutsch GD, Eisenberg HM. Frontal blood flow changes in recovery from coma. *J Cereb Blood Flow Metab* 1987;7:29–34.
11. Risberg J. Regional cerebral blood flow measurements by ^{133}Xe-inhalation: methodology and applications in neuropsychology and psychiatry. *Brain Lang* 1980;9:9–34.