Delayed Ischemic Hyperintensity on T1-Weighted MRI in the Caudoputamen and Cerebral Cortex of Humans After Spectacular Shrinking Deficit

Masayuki Fujioka, MD; Toshiaki Taoka, MD; Ken-Ichiro Hiramatsu, MD; Syouji Sakaguchi, MD; Toshisuke Sakaki, MD

Background and Purpose—Transient internal carotid artery (ICA)–middle cerebral artery (MCA) occlusion caused by cardiogenic embolus can lead to spectacular shrinking deficit (SSD): sudden hemispheric stroke syndrome followed by rapid improvement. The aim of this study was to investigate sequential neuroradiological changes in the brains of patients after SSD compared with those after brief cardiac arrest and hypoglycemia, which we previously studied with the same methods.

Methods—We serially studied CT scans and MR images obtained at 1.5 T in 4 patients with SSD. All 4 patients suffered from transient neurological deficits due to cardiogenic embolus in ICA-MCA. The symptoms began to disappear from 25 to 50 minutes after onset.

Results—Repeated CT scans demonstrated no abnormal findings in the affected cerebral hemisphere in 3 of the 4 patients and a small cortical infarct in the remaining 1. In each patient, repeated MRI between day 7 and month 23 after stroke showed basal ganglionic and cortical lesions. These lesions were hyperintense on T1-weighted and relatively hypointense on T2-weighted imaging. These ischemic lesions of hyperintensity on T1-weighted MRI subsided with time.

Conclusions—Transient ICA-MCA occlusion leading to SSD produces a specific ischemic change with delayed onset in the basal ganglia and cerebral cortex in humans on MRI but not CT scans. We speculate that the lesions represent incomplete ischemic injury, including selective neuronal death, proliferation of glial cells, paramagnetic substance deposition, and/or lipid accumulation. Unlike brief cardiac arrest or hypoglycemia, the localized lesions on MRI of patients after SSD seem to be incomplete and to differ from infarction or hemorrhage. (Stroke. 1999;30:1038–1042.)

Key Words: carotid arteries ■ cerebral ischemia, transient ■ magnetic resonance imaging ■ neuronal death

Transient internal carotid artery (ICA)–middle cerebral artery (MCA) occlusion due to cardiogenic embolus can lead to spectacular shrinking deficit (SSD) in patients with various heart diseases. SSD refers to a sudden major hemispheric stroke syndrome followed by rapid improvement within a few hours after stroke, leaving mild or no deficits. Experimentally, brief MCA occlusion (MCAO) causes selective neuronal necrosis and apoptosis with intact glial cells and microvessels in the caudoputamen and cerebral cortex. In these ischemic lesions, the brain tissue framework is preserved and no cavitation develops. This ischemic lesion with selective neuronal death and gliosis has been termed “incomplete infarction.” Nakano et al reported that selective neuronal damage slowly progressed in the dorsolateral striatum of rats for 4 weeks after 15 minutes’ MCAO and that microvacuolation never occurred in the ischemic area. However, very few reports are available on the serial changes in the human brain after transient hemispheric ischemia leading to SSD, which represent the clinical equivalent of the experimental conditions described above.

In humans, we previously investigated the serial changes on CT scans and MRI in the brains of patients after cardiac arrest and hypoglycemic coma. In the present study, we focused on the sequential neuroradiological changes in the basal ganglia and cerebral cortex of the brains of patients after brief cerebral hemispheric ischemia leading to SSD and compared the results with those of patients after transient global brain ischemia or profound hypoglycemia previously studied using the same methods.

Subjects and Methods

We repeatedly studied CT scans and MRI obtained at 1.5 T in 4 patients after SSD. This study included subjects satisfying the following criteria: (1) no apparent history of neurological disease diagnosed clinically and neuroradiologically; (2) persons were hospitalized due to heart diseases; (3) persons suffering from SSD were observed by medical staff from the onset of the neurological

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Clinical Features of Four Patients With SSD

<table>
<thead>
<tr>
<th>Pt No./Age, y/Sex</th>
<th>Type of Heart Disease</th>
<th>Neurological Findings</th>
<th>Low Density on CT</th>
<th>Onset of Recovery, min*</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/73/M</td>
<td>AMI, AF</td>
<td>R hemiparesis</td>
<td>L F Cor</td>
<td>50</td>
<td>Mild motor aphasia</td>
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<tr>
<td>Post CABG</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2/56/M</td>
<td>RHD with MS</td>
<td>L hemiparesis</td>
<td>N</td>
<td>45</td>
<td>Total recovery</td>
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<tr>
<td>AF</td>
<td></td>
<td>Anosognosia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3/44/M</td>
<td>AMI, AF</td>
<td>R apraxia</td>
<td>N</td>
<td>25</td>
<td>Total recovery</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Motor aphasia</td>
<td></td>
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</tr>
<tr>
<td>4/53/M</td>
<td>AF</td>
<td>R hemiparesis</td>
<td>N</td>
<td>30</td>
<td>Total recovery</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Global aphasia</td>
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</tbody>
</table>

SSD indicates spectacular shrinking deficit; Pt, patient; GCS, Glasgow Coma Scale (score); AMI, acute myocardial infarction; AF, atrial fibrillation; CABG, coronary artery bypass graft; RHD, rheumatic heart disease; MS, mitral valve stenosis; F, frontal; Cor, cerebral cortex; and N, no low density.

*Minutes after stroke onset.

Results

MR images of our patients illustrated noteworthy changes with time that did not appear on the CT scans in the caudoputamen and cerebral cortex of the affected cerebral hemisphere (Table; Figures 1 and 2).

Serial CT scans demonstrated no abnormal findings in the brain of 3 patients and a left frontal cortical infarct in patient 1 from a day after SSD (Table). In all patients after SSD, the first MRI obtained on days 2 or 3 showed normal findings (Figure 2, A and B), except for the left frontal cortical and external capsular infarcts in patient 1 (Figures 1 and 2).

However, serial MRI consistently revealed ischemic lesions of hyperintensity/relative hypointensity on T1W/T2W imaging, respectively, in the caudoputamen in all patients and in the cerebral cortex in 2 patients (patients 1 and 3) from day 7 after SSD (Figures 1 and 2). These ischemic lesions of hyperintensity on T1W MRI in the basal ganglia and cerebral cortex appeared most clearly between 1 and 3 weeks after SSD, and thereafter gradually faded away and disappeared (Figures 1 and 2). Additionally, the affected structures atrophied over time, resulting in widening of the neighboring ventricular and subarachnoid spaces in all patients (Figure 2).

Discussion

Delayed Ischemic Hyperintensity on T1W MRI After SSD

The present neuroradiological data can be interpreted as follows. First, specific ischemic lesions developed in the basal ganglia and cerebral cortex in the ischemic hemisphere of patients after brief ICA or MCA occlusion leading to SSD. Second, these lesions appeared on MRI but not on CT scans. Third, the lesions on MRI appeared after days 7 to 10 but not on days 2 to 3. Fourth, the localized ischemic lesions exhibited persistent hyperintensity/relative hypointensity on serial T1W/T2W MRI, respectively, with the hyperintensity on T1W MRI gradually subsiding with time. Last, the affected structures atrophied over time during the period of this study.

This specific ischemic change of delayed onset and of long-lasting hyperintensity/hypointensity on T1W/T2W MRI, respectively, and of isodensity on serial CT scans seems to differ from known ischemic changes such as the following 3 neuroradiological entities. (1) Ischemic edema and infarct appear hypointense and hyperintense on T1W and T2W MRI, respectively, relative to normal parenchyma.10 (2) The signal intensity of hemorrhagic brain tissue changes according to the process of hemoglobin degradation. Intracellular deoxyhemoglobin leads to hypointensity on T2W but little change on T1W imaging. In parallel with the oxidation of deoxyhemoglobin to methemoglobin inside red blood cells (RBC), the signal intensity increases on T1W imaging. After RBC lysis, extracellular methemoglobin appears hyperintense on both...
T1W and T2W imaging. With advancing hemoglobin degradation, hemosiderin inside macrophages causes selective shortening of the T2 relaxation time. These signal changes progress from the periphery to the center of a hemorrhage.\textsuperscript{11} (3) Ectopic calcifications can appear hyperintense and hypointense on T1W and T2W MRI, respectively, but as high-density lesions on CT scans.\textsuperscript{12} Therefore, the present study indicates a novel form of ischemic change on MRI. We designate this ischemic change “delayed ischemic hyperintensity on T1W MRI” (DIH).

We could not precisely elucidate what this DIH represented histologically. However, the present results may be partly explained by several experimental and clinical studies.\textsuperscript{2,3,6,7,13–16} In experimental animals, transient MCAO leads to selective neuronal death and various glial responses without necrosis of the brain tissue in the ischemic region when reperfusion is instituted within a short period of time.\textsuperscript{2,3,6,7} This selective neuronal loss advances from the striatum to the cerebral cortex in parallel with the prolongation of MCAO. In humans, several studies\textsuperscript{13–16} suggest the presence of incomplete brain infarction after ischemia of either short or moderate severity. The incomplete infarction signifies an ischemic change with selective loss of some neurons and relative preservation of the integrity of the brain tissue structure. Therefore, the DIH in the basal ganglia and cerebral cortex may neuroradiologically represent selective neuronal loss and gliosis without infarct or hemorrhage.

However, only selective neuronal loss with gross preservation of brain tissue in incomplete infarct has been considered unlikely to affect x-ray transmission on CT scans and magnetic field in MRI. The evidence of incomplete infarct has been estimated neuroradiologically using single-photon emission computed tomography only by measurement of the neuronal benzodiazepine receptor bound by the specific radioligand.\textsuperscript{5,13,16,17} Therefore, the delayed ischemic change of hyperintensity/hypointensity on T1W/T2W MRI in our patients could involve biochemical changes that shorten the T1 and T2 relaxation times. These biochemical factors include paramagnetic compounds\textsuperscript{18} such as iron and manganese ions, and free radicals produced by macrophages.\textsuperscript{19} Lipid accumulation also appears hyperintense on T1W MRI.\textsuperscript{20}

Recently, neuropathological and neurochemical changes at late perfusion periods after brief brain ischemia have drawn attention in experimental studies.\textsuperscript{21–23} These suggest that neuronal cell death matures slowly in the course of several weeks after a mild ischemia and that the glial reactions and apoptotic brain cell death play a role in the life and death of neurons. Kondo et al\textsuperscript{24} reported that iron deposits gradually increased and formed clusters, with increasing glial reactions, in the hippocampal CA1 region from 4 weeks after 30-minute forebrain ischemia in rats. However, very few studies have addressed whether long-term ischemic changes could occur in human brains in the setting of both global and focal ischemia. Our present study using serial MRI demonstrates that very slowly progressive neuroradiological changes can occur in human brains in the chronic stage (>1 week) after focal ischemia leading to SSD.

Comparison With Basal Ganglia Injuries After Cardiac Arrest or Hypoglycemic Coma

We compared sequential neuroradiological changes in the basal ganglia of patients after SSD with those after brief

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure1.png}
\caption{Specific changes with time on MRI in patients after SSD. These specific changes of hyperintensity and relative hypointensity on T1W and T2W MRI, respectively, in the basal ganglia and cerebral cortex are considered to reflect incomplete ischemic injury, including selective neuronal death, gliosis, paramagnetic substance deposition, and/or lipid accumulation but not infarction or hemorrhage. T1WI indicates T1-weighted imaging; T2WI, T2-weighted imaging.}
\end{figure}
On the other hand, in the patients after hypoglycemic coma, repeated MRI showed bilateral lesions of persistent hyperintensity and hypointensity on both initial and second T1W and T2W imaging, respectively, in the basal ganglia, cerebral cortex, substantia nigra, and hippocampus from day 8 after hypoglycemic injury. The changes of increased intensity on T1W and decreased intensity on T2W imaging seem common to both patients after SSD and hypoglycemia. These changes are neuroradiologically interpreted as lesions devoid of infarct or hemorrhage. We speculate that this signal change on MRI is the final result of an unknown common pathway in the brain lesion produced by incomplete or brief energy failure, such as brief focal cerebral ischemia or hypoglycemia. However, the hypoglycemic brain injury persisted on MRI within about 1 year after hypoglycemic coma. In this sense, the DIH after SSD appears to be incomplete and not to be identical to hypoglycemic brain injury.

The present study lacks histological confirmation, this being the weakest point of our study. Therefore, we have started an experimental study with rat SSD models. We are now investigating by MR imaging and histological studies whether “delayed ischemic hyperintensity on T1W MRI” can be reproduced in rats and what the neuroradiological change represents histologically.

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**References**


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**Figure 2. Temporal profile of delayed ischemic hyperintensity on T1W MRI after brief hemispheric ischemia. In patient 1, serial MRI reveals no marked change in the basal ganglia 3 days after brief hemispheric ischemia (A and B) but hyperintensity on T1W imaging (C, E, G, and I) and relative hypointensity on T2W imaging (D, F, H, J, and L) in the basal ganglia and cerebral cortex (C; arrow) at 7 days after the insult. The T1 hyperintensity subsided with time and disappeared 23 months after ischemia (K). (T1W and T2W imaging: day 3, A and B; day 7, C and D; day 22, E and F; 3 months, G and H; 8 months, I and J; and 23 months, K and L.)**

cardiac arrest and hypoglycemia previously studied by us with the same methods. In the patients after cardiac arrest, MRI, but not CT scans, revealed symmetrical changes suggestive of minor hemorrhages in the basal ganglia, thalami, and/or substantia nigra. We suggested that these hemorrhages resulted from diapedesis of RBC through the cerebrovascular endothelium damaged by severe ischemia-reperfusion injury. In SSD patients, the DIH appears unlikely to represent infarcts or hemorrhages on MRI. We think that this difference results partly from the difference in severity of ischemia per se between focal cerebral ischemia leading to SSD and global brain ischemia caused by cardiac arrest.
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