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Cerebral perfusion changes in traumatic diffuse brain injury; IMP SPECT studies

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Diffuse brain injury (DBI) is characterized by axonal degeneration and neuronal damage which cause diffuse brain atrophy. We have investigated the time course of abnormalities in cerebral perfusion distribution in cases of DBI by using Iodine-123-IMP SPECT, and the relationship to the appearance of diffuse brain atrophy. SPECT scans were performed on eight patients with diffuse brain injury due to closed cranial trauma in acute and chronic stages. All patients showed abnormalities in cerebral perfusion with decreases in perfusion, even in non-depicted regions on MRI, and the affected areas varied throughout the period of observation. Diffuse brain atrophy appeared in all patients. In some patients, diffuse brain atrophy was observed at or just after the time when the maximum number of lesions on SPECT were seen. The abnormalities in cerebral perfusion in cases of DBI might therefore be related to axonal degeneration and neuronal damage which causes diffuse brain atrophy.

Key words: diffuse brain injury, cerebral perfusion, brain atrophy, IMP, SPECT

INTRODUCTION

HEAD INJURIES are classified into two groups, focal brain injury and diffuse brain injury (DBI).[1,2] DBI is characterized by axonal degeneration and demyelination evident on pathological assessment, and it has been proposed that neuronal damage also occurs.[1,3,4] DBI presents as small lesions in the white matter, corpus callosum or brain stem without space occupying lesions on X-ray CT (CT) or magnetic resonance imaging (MRI).[5–8] Nevertheless, it includes many cases with poor outcome.[9,10] Furthermore, it is known that DBI is often linked to diffuse brain atrophy caused by axonal degeneration and neuronal damage.[3,4]

There are many descriptions of changes in cerebral perfusion in brain injury including both focal and diffuse types, detected by single photon emission computed tomography (SPECT) and positron emission computed tomography (PET).[11–19] It has been reported that SPECT is more sensitive than CT or MRI and particularly useful for predicting the clinical outcome, and the application of SPECT for cases of head injury has built up a relatively large database in terms of detection and prognosis.[20] In addition, cerebral hemodynamics in patients with cerebral contusion or DBI have been investigated, and hyperemia which may be due to vasoparalysis, was observed in the acute stage after injury.[21–25]

In the present study, we investigated the time course of abnormalities in cerebral perfusion distribution in cases of DBI by using SPECT and assessed the relation to the appearance of diffuse brain atrophy on MRI.

MATERIALS AND METHODS

Subjects

Eight patients (16–31 years, 8 males) with diffuse brain injury due to closed cranial trauma, hospitalized within 6

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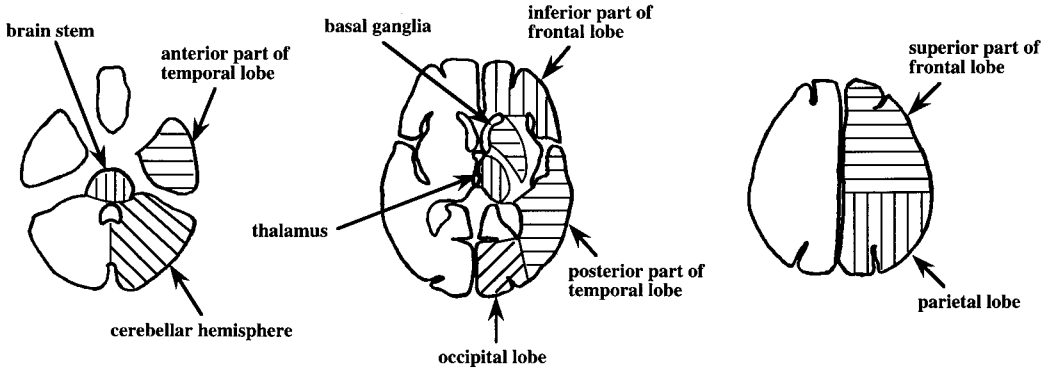

Fig. 1 Partitioning of regions for analyses of SPECT and MRI images (total 19 regions). Abnormalities of cerebral perfusion were noted and the MRI findings, i.e., brain injuries confirmed their presence.

Table 1 Subject profiles

Patient No.	Age/Sex*	GCS†	GOS‡
1	16/M	7	SD
2	18/M	5	SD
3	20/M	7	MD
4	19/M	8	MD
5	31/M	7	MD
6	20/M	7	GR
7	25/M	8	GR
8	17/M	5	GR

*M: male, †GCS: Glasgow coma scale, ‡GOS: Glasgow outcome scale (GR: good recovery, MD: moderate disability, SD: severe disability)

hours after the injury were studied (Table 1). Glasgow Coma Scale (GCS) values[26] of all subjects were equal to or less than 8. Clinical diagnosis of diffuse brain injury was made by neurosurgeons by using MRI with both T_1- and T_2-weighted images.[3–8] The MRI examinations revealed injury of corpus callosum and the white matter in all patients which must be caused by shearing injury, indicating diffuse brain injury.[5–8] Space occupying lesions were not observed in any of the patients. None of the patients had any cerebrovascular risk factors (i.e., hypertension, diabetes or ischemic heart disease). Exclusion criteria were a past history of cranial trauma, neurological or psychiatric diseases, and drug and/or alcohol abuse. The patient's outcome at 3 months after the injury was evaluated with the Glasgow Outcome Scale (GOS).[27]

All patients underwent SPECT studies at least twice, within 1 wk (1–8 days) of the injury and after 1 mo (22–46 days). MRI studies were performed at the same time as SPECT studies. Some patients also underwent SPECT studies after 3–6 mo (Nos. 1, 2 and 5).

SPECT study

SPECT scans were performed at a mid-scan time of 40 min after intravenous infusion of 222 MBq of N-isopropyl-p-[^{123}I]iodoamphetamine (IMP) lasting 1 min.[28,29] The applied SPECT scanner was a Neurocam (Yokogawa Medical Systems Corp., Tokyo, Japan),[30] a three-head rotating gamma camera with an in-plane resolution of 9 mm FWHM and an axial resolution of 10 mm FWHM. The SPECT scan protocol acquired 64 projections at 50 sec per projection with 120° rotation of the camera. Reconstruction was performed by filtered back projection with a Butterworth filter and attenuation correction was made numerically by assuming the object shape to be an ellipse[31] and the attenuation coefficient to be uniform (0.12 cm^{-1}). Scattered photons were not corrected. Image slices were set up parallel to the orbito-meatal (OM) line and obtained for 8 mm intervals through the whole brain.

MRI study

The MRI unit used was a Magnetom Impact, 1.0 tesla (Siemens Corp.). Both T_1-weighted (transaxial) and T_2-weighted (transaxial and coronal) images were acquired with spin-echo (SE) pulse sequences (T_1: SE method, TR 450 msec, TE 15 msec, averaging 2; T_2: Fast SE method, TR 4000 msec, TE 90 msec, averaging 1). Slice thickness was 5 mm with a slice gap of 1 mm. The field of view was 26 cm, and image matrix size was 256 × 256.

Image analysis

All SPECT images were visually evaluated by two nuclear medicine radiologists without any knowledge of the clinical data. SPECT images were evaluated on both rainbow color photographs and monochrome films of transaxial section parallel to the OM line. The upper level of the radioactivity scale was set at the maximum value for the SPECT image for each subject. The lower level of the radioactivity scale was set at 20% of the upper level. Abnormalities in cerebral perfusion were confirmed by agreement of findings between rainbow color photographs and monochrome films. Abnormalities in cerebral perfusion were confirmed by referring to SPECT images of age-matched normal subjects for each region as follows: the superior and inferior parts of the frontal lobe, the anterior and posterior parts of the temporal lobe, parietal lobe, occipital lobe, cerebellar hemisphere, basal ganglia, thalamus and brain stem (total 19 regions, Fig. 1). The

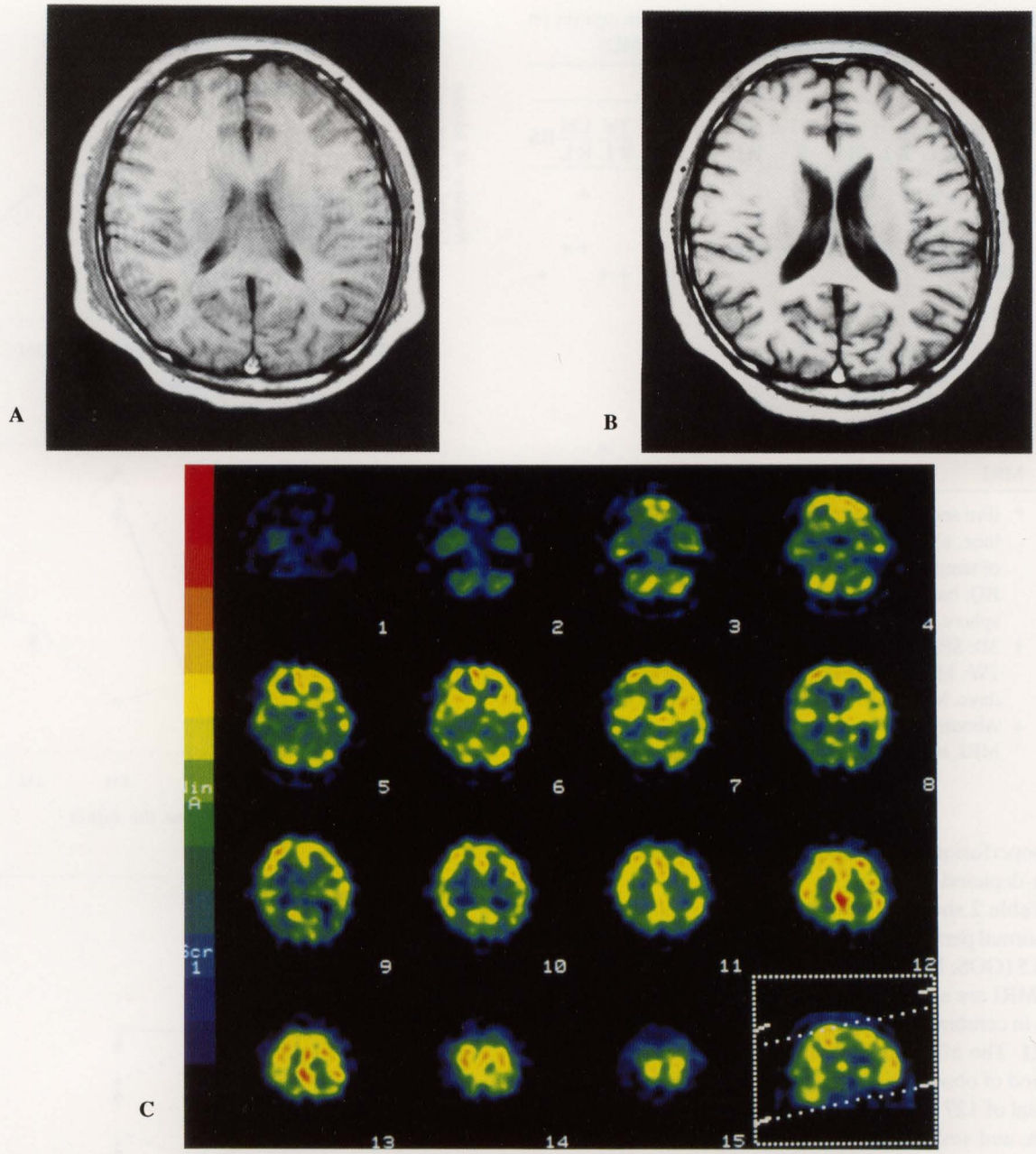

Fig. 2 MRI (T_1-weighted images) and SPECT images of a typical case (No. 3) (MRI: 1 wk (A) and 1 mo (B) after the injury, SPECT (C): 1 mo after the injury). There is no diffuse brain atrophy on MRI after 1 wk (A). Diffuse brain atrophy is observed after 1 mo (B). Widespread hypoperfusion is observed on SPECT including in non-depicted regions on MRI (C). In all images, the anterior is at the top of the image and the subject's right is on the left.

evaluation was agreed on after consensus between the two observers.

MRI findings in brain parenchyma injuries were also evaluated for each region corresponding to the regions on SPECT by two observers without any knowledge of the clinical data by using both T_1- and T_2-weighted images of transaxial (T_1, T_2) and coronal (T_2) sections. The appearance of diffuse brain atrophy was also evaluated on the sequence of MRI examinations, referring to MRI images of age-matched normal subjects. MRI images were evaluated on monochrome film. The evaluation was agreed on after consensus between the two observers.

RESULTS

Figure 2 shows MRI and SPECT images of a typical case (No. 3) (MRI: 1 wk (A) and 1 mo (B) after the injury, SPECT (C): 1 mo after the injury). There was no diffuse brain atrophy on MRI after 1 wk (A). Diffuse brain atrophy was observed on MRI after 1 mo (B). Widespread

Table 2 Regions of abnormal perfusion and brain injuries on SPECT and MRI for patient Nos. 3 and 5 (GOS: MD)

No.	Exam†	region*																	
		iFrn		sFrn		aTm		pTm		Par		Occ		BG		Thl		Cbl		BS
		R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	
3	1W	+	+			+	+				+		+						+	
	2W						+													
	1M					+	+	+	+	+	+	+	+						+	+
	MRI						+									+	+			+
5	3D				+		+		+											
	1W				+		+		+											
	2W				+		+		+											
	1M		+				+													
	3M				+		+			+		+		+						
	6M				+		+			+		+		+			+			
	MRI				+		+				+									

* iFrn and sFrn: the inferior and the superior part of frontal lobe. aTm and pTm: the anterior and the posterior part of temporal lobe. Par: parietal lobe, Occ: occipital lobe. BG: basal ganglia, Thl: thalamus. Cbl: cerebellar hemisphere, BS: brain stem. R and L: the right and left.

† 3D: SPECT study on the day of the injury. 1W: 4–8 days, 2W: 13 days, 1M: 29–40 days, 3M: 92 days, 6M: 162 days. MRI: MRI study within 1 wk of the injury.

\+ Abnormal perfusion and brain injuries on SPECT and MRI, respectively.

hypoperfusion was observed on SPECT including in MRI non-depicted regions (C).

Table 2 shows representative data of time courses of abnormal perfusion regions on SPECT for patients Nos. 3 and 5 (GOS: MD (Table 1)). The regions of brain injuries on MRI are also shown. All patients showed abnormalities in cerebral perfusion even in non-depicted regions on MRI. The affected regions on SPECT varied over the period of observation. One hundred and twenty lesions of a total of 127 lesions showed decreases in cerebral perfusion, and seven lesions showed an increase in cerebral perfusion for all SPECT studies.

Figure 3 shows the time courses of changes in the number of abnormal perfusion regions on SPECT for all patients along with the time of the appearance of diffuse brain atrophy. The numbers of regions of brain injuries on MRI within 1–8 days from the injury were 3, 1, 4, 3, 3, 2, 2 and 1 for patients Nos. 1–8, respectively. The maximum numbers of lesions on SPECT were 6, 8, 10, 11, 5, 6, 7 and 3 for patients Nos. 1–8, respectively. Diffuse brain atrophy on MRI was observed in all patients. The appearance times of diffuse brain atrophy after the injury were 6 mo (151 days) for patient No. 1, 3 mo (90 days) for patient No. 5, and 1 mo (21–46 days) for patients Nos. 2–4 and 6–8. In some patients, diffuse brain atrophy was observed at or just after the time when the maximum number of lesions on SPECT were seen.

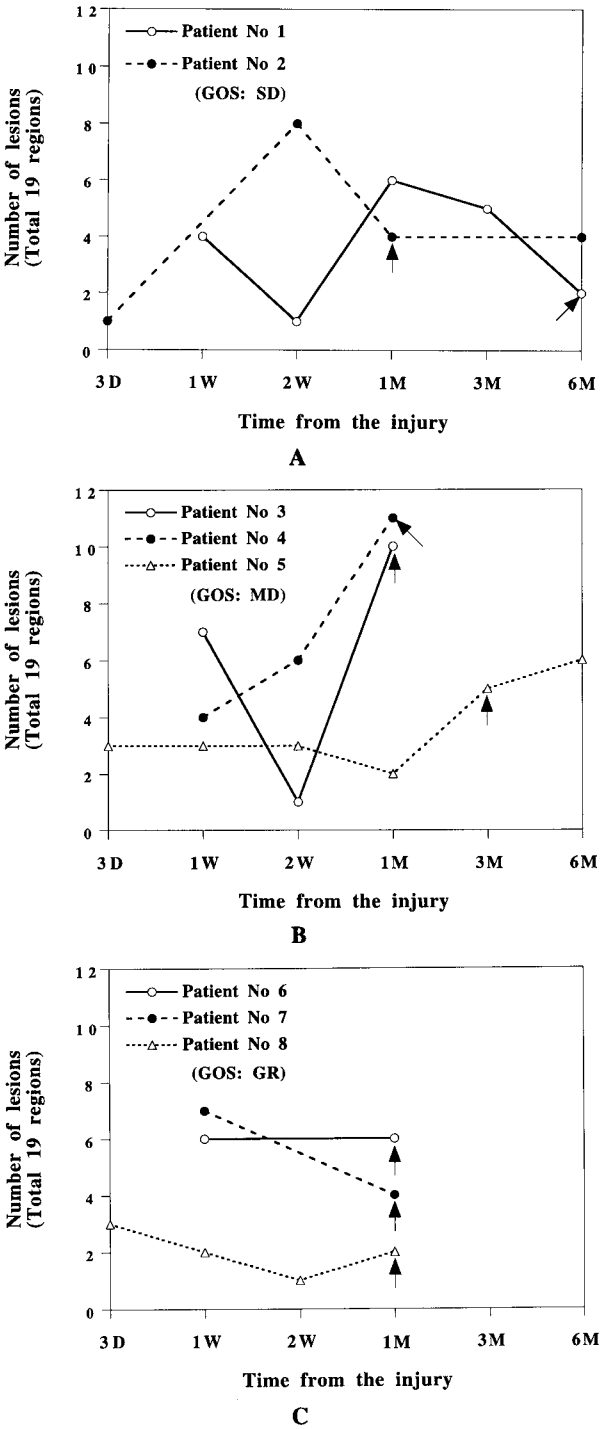

Fig. 3 Time courses of changes in number of abnormal perfusion regions on SPECT with the time of appearance of diffuse brain atrophy for all patients (A: Nos. 1–2 (GOS: SD); B: Nos. 3–5 (GOS: MD); C: Nos. 6–8 (GOS: GR)). The arrows indicate the time of appearance of diffuse brain atrophy. 3D, 1W, 2W, 1M, 3M and 6M correspond to 1–3 days, 4–8 days, 11–17 days, 22–46 days, 76–92 days and 162–189 days from the injury, respectively.

DISCUSSION

DBI is characterized by axonal degeneration and demyelination on histopathology, and it has been proposed that neuronal damage occurs in DBI.[3,4] It is also known that DBI is often associated with diffuse brain atrophy caused by axonal degeneration and neuronal damage.[1,3,4] In the present study, diffuse brain atrophy was observed in all patients. In all patients, many lesions on SPECT were observed even in areas which were not depicted on MRI, and the affected regions varied throughout the period of observation (Table 2, Figs. 2 and 3). This indicates that the abnormalities in cerebral perfusion in DBI might be related to the axonal degeneration and neuronal damage which precedes diffuse brain atrophy. In addition, the diaschisis through the nerve fiber connection, e.g., cerebral cortex — contralateral cerebellum,[32,33] thalamus — cerebral cortex,[33,34] etc., might also play a role, but the fact of inconstancy of affected regions suggests that the results cannot be affected mainly by the diaschisis.

It has been reported that hyperemia due to vasoparalysis is observed in the acute stage after DBI,[21–25] and this factor could have exerted an influence in the present cases. But in the present study abnormalities in cerebral perfusion distribution were also observed in the chronic stage, i.e., more than 1–6 mo after the injury and thus it is unlikely that hyperemia due to vasoparalysis is responsible. In addition, the brain edema which was often observed in the acute stage after DBI might affect cerebral perfusion. But in the chronic stage the brain edema was not observed in any of the patients.

In some patients, traumatic subarachnoid hemorrhage (t-SAH), epidural hematoma (EDH) and subdural hematoma (SDH) were observed. It was considered that these lesions might affect cerebral perfusion,[35,36] but in the present study, t-SAH, EDH and SDH were small, and therefore our results would not be affected.

It has been reported that SPECT is more sensitive than CT or MRI and particularly useful for predicting the patients' clinical outcome.[12–19] This is supported by the present findings of many lesions on SPECT which were located in regions not depicted on MRI. In addition, in some patients, diffuse brain atrophy appeared at or just after the time when the maximum number of lesions on SPECT were observed (Fig. 3). SPECT might therefore be useful for predicting the appearance of diffuse brain atrophy, but in order to confirm this, further studies on a large patient group with more frequent SPECT and MRI examinations will be required. It has been reported that closed head injury causes behavioral and psychosocial sequelae.[37] Since diffuse brain atrophy in DBI is potentially related to these sequelae, SPECT might also be able to assist in these predictions. In the present study, the number of lesions on SPECT was not correlated with the Glasgow Outcome Scale (GOS).

CONCLUSION

The present investigation of the time course of abnormalities in cerebral perfusion distribution in cases of DBI by using SPECT revealed many lesions on SPECT in all patients, even in non-depicted regions on MRI, and the affected areas varied throughout the period of observation. Diffuse brain atrophy was observed in all patients. In some patients, diffuse brain atrophy was observed at or just after the time when the maximum number of lesions were seen on SPECT. These findings indicate that abnormalities in cerebral perfusion in DBI might be related to the axonal degeneration and neuronal damage which cause diffuse brain atrophy.

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