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Clinical Article

Detection of Traumatic Cerebral Microbleeds by Susceptibility-Weighted Image of MRI

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Objective : Susceptibility-weighted image (SWI) is a sensitive magnetic resonance image (MRI) technique to detect cerebral microbleeds (MBLs), which would not be detected by conventional MRI. We performed SWI to detect MBLs and investigated its usefulness in the evaluation of mild traumatic brain injury (MTBI) patients.

Methods : From December 2006 to June 2007, twenty-one MTBI patients without any parenchymal hemorrhage on conventional MRI were selected. Forty-two patients without trauma were selected for control group. According to the presence of MBLs, we divided the MTBI group into MBLs positive [SWI (+)] and negative [SWI (-)] group. Regional distribution of MBLs and clinical factors were compared between groups.

Results : Fifty-one MBLs appeared in 16 patients of SWI (+) group and 16 MBLs in 10 patients of control group [control (+)], respectively. In SWI (+) group, MBLs were located more frequently in white matters than in deep nucleus different from the control (+) group ($p < 0.05$). Nine patients (56.3%) of SWI (+) group had various neurological deficits (disorientation in 4, visual field defect in 2, hearing difficulty in 2 and Parkinson syndrome in 1). Initial Glasgow Coma Scale (GCS)/mean Glasgow Outcome Scale (GOS) were 13.9 ± 1.5 / 4.7 ± 0.8 and 15.0 ± 0.0 / 5.0 ± 0.0 in SWI (+) and SWI (-) groups, respectively ($p < 0.05$).

Conclusion : Traumatic cerebral MBLs showed characteristic regional distribution, and seemed to have an importance on the initial neurological status and the prognosis. SWI is useful for detection of traumatic cerebral MBLs, and can provide etiologic evidences for some post-traumatic neurologic deficits which were unexplainable with conventional MRI.

KEY WORDS : Traumatic brain injury · Susceptibility-weighted image · Microbleeds.

INTRODUCTION

Patients with traumatic brain injury (TBI) sometimes show significant neuropsychological dysfunction without any abnormalities on conventional neuroradiological examinations. It is well established that severe head trauma can cause identifiable brain injury with corresponding symptoms or signs[16]. But, the pathophysiology of various symptoms and signs after mild TBI (MTBI) still remains poorly understood. MTBI can be defined as Glasgow Coma Scale (GCS) score of 13 to 15 on admission, loss of consciousness (LOC) for less than 20 minutes, and required hospital stay less than 48 hours[15]. Symptoms such as persistent headache, nausea, cognitive decline, and personality changes may be identified in the MTBI patients, but conventional neuroimaging studies rarely reveal pathologic findings in the brain to explain these problems[10]. Evaluation of MTBI is complicated by the limited predictive power of injury-severity indicators such as GCS score, duration of impaired consciousness, post-traumatic amnesia, and brain imaging tests.

Cerebral microbleeds (MBLs) were known to be related to GCS and neurologic deficits in the patients with diffuse axonal injury (DAI)[17]. Hemorrhagic lesions less than 5 mm in diameter without connection to the brain surface or ventricular system on computed tomography (CT) or magnetic resonance image (MRI) were defined as cerebral MBLs[17]. Despite the usefulness of CT and conventional MRI in the evaluation of TBI patients, they have not been sufficiently sensitive to detect MBLs[17,18]. Accordingly, we defined radiologically MTBI as head trauma without any

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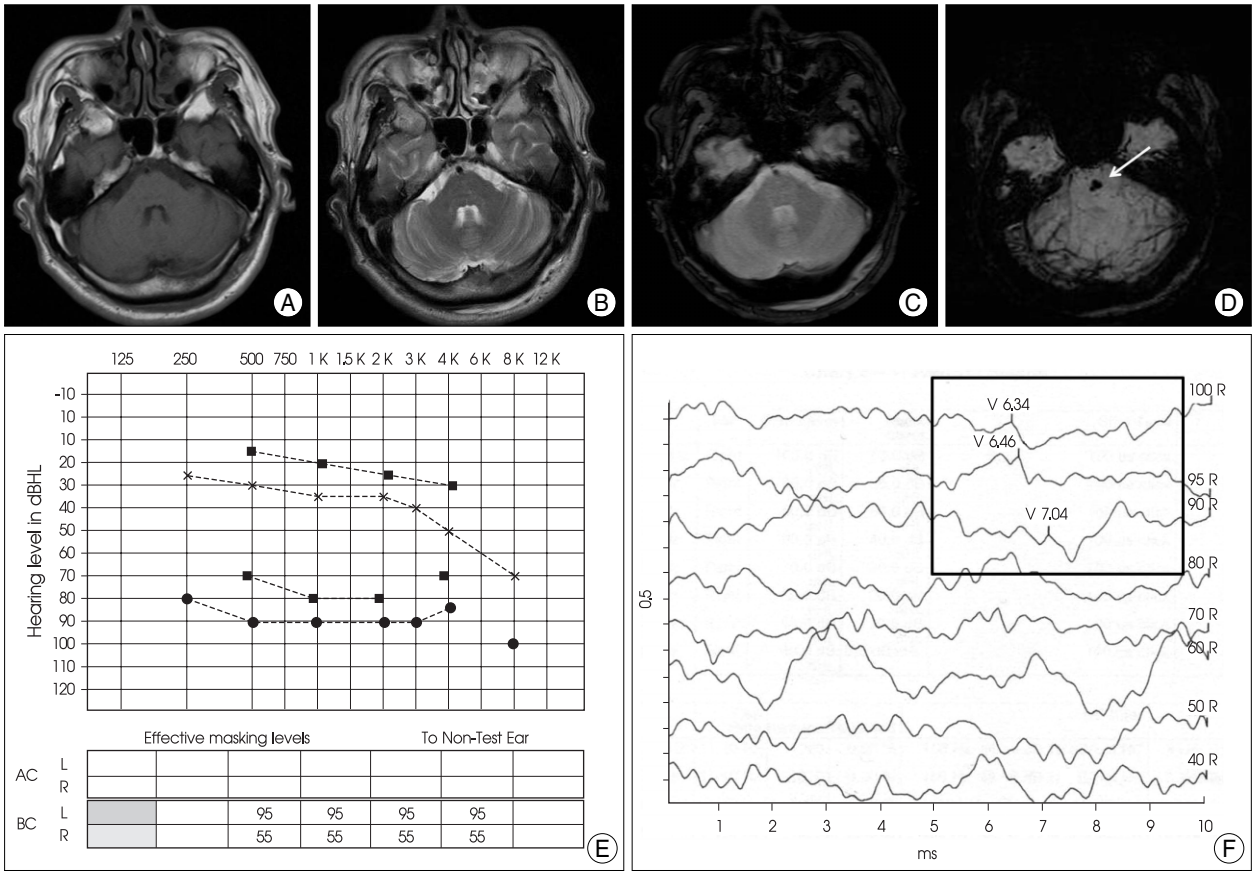

Fig. 1. Brain MRI of a 50-year-old man (patient number 7) who complained of left side hearing difficulty after head trauma by traffic accident. (A), (B) and (C) demonstrating no visible hemorrhagic spot at the level of lower pons on T1-weighted magnetic resonance image (MRI) (A), T2-weighted MRI (B), T2-weighted gradient recalled echo MRI (C) , respectively. (D) susceptibility-weighted image presenting a hemorrhagic lesion at the same level of pons containing the lateral lemniscus fibers. This pontine hemorrhage seems to be related with left side hearing difficulty in this patient. (E) Pure tone audiometry shows abnormal finding on the left side. (F) In the box, V wave is detected in 90 dB. Result of auditory brainstem response shows profound hearing loss owing to brainstem lesion.

evidences of parenchymal hemorrhage on CT or conventional MRI in this study.

Before the development of SWI, T2-weighted gradient recalled echo (GRE) MRI was known to be the most sensitive one for detecting hemorrhage[17]. SWI is a modified T2-weighted 3-D GRE MRI with unique post-processing that allows improved detection of paramagnetic hemorrhagic blood products, extravascular deoxyhemoglobin and methemoglobin, based on their magnetic susceptibility effects[6,14,17]. Recently, this SWI has been added to our routine brain MRI protocol and we could find MBLs in some MTBI patients. We investigated the characteristics and clinical usefulness of traumatic MBLs detected by SWI especially in the MTBI patients.

MATERIALS AND METHODS

From December 2006 to June 2007, 21 MTBI patients[10,15] without any parenchymal hemorrhage on conventional MRI, who underwent SWI at the same time, were selected for MTBI group. Another group of 42 patients without TBI history who complained of headache and received brain MRI study including SWI during the same period were selected for control group. All patients received brain MRI study including SWI within a week after admission. Mean age, sex ratio, regional distribution of MBLs, number of MBLs, and the relationship between symptoms and MBLs were analyzed. Spatial distribution and number of MBLs were checked at eight brain areas, frontal lobe, temporal lobe, parietal lobe, occipital lobe, basal ganglia, thalamus, cerebellum, and brain stem.

According to the presence of MBLs, we divided the MTBI group into MBLs positive [SWI (+)] (n = 16) and negative [SWI (-)] (n = 5) groups to compare their clinical courses, GCS and Glasgow Outcome Scale (GOS). GCS was checked on trauma day. GOS was checked at 1 year after trauma. The patients with MBLs in the control group were selected as control (+) group (n = 10). We also compared mean age, sex ratio, the regional distribution of traumatic MBLs in SWI (+) group with that of spontaneous

MBLs in the control group.

SWI was performed with a 1.5-T whole body MRI system (Magnetom Vision®, Simens, Germany) (Table 1). Student t-test and chi-squaretest were used for statistical analysis considering *p*-value less than 0.05 to be statistically significant.

Table 1. Imaging parameters of T2-weighted, T2-weighted GRE, and SWI sequence

Parameters	T2	T2-GRE	SWI
TR/TE/excitation	4000/99/1	800/26/1	49/40.3/1
Flip angle (˚)	150	20	15
Section thickness (mm)	5	5	2
Slice gap (mm)	2	2	0
Acquisition type (dimensions)	2	2	3

GRE : Gradient recalled echo, SWI : Susceptibility weighted image

Table 2. Demography and results of comparisons between SWI (+) group and SWI (-) group

Variable	MTBI	SWI (+)	SWI (-)	*p*-value*
Number	21	16	5	
Age (years)	37.2 ± 21.5	39.1 ± 26.8	35.2 ± 15.5	> 0.05
Sex (M : F)	3.2 : 1	4.3 : 1	1.5 : 1	< 0.05
Initial GCS	14.1 ± 4. 7	13.9 ± 1.5	15.0 ± 0.0	< 0.05
GOS	4.7 ± 0.7	4.7 ± 0.8	5.0 ± 0.0	< 0.05

*Comparisons between SWI (+) group and SWI (-) group. MTBI : mild traumatic brain injury, SWI (+) : parenchymal lesion positive at Susceptibility weighted image of brain, SWI (-) : parenchymal lesion negative at Susceptibility weighted image of brain, M : male, F : female, GCS : Glasgow Coma Scale, GOS : Glasgow Outcome Scale

Table 3. Regional distribution and number of MBLs in SWI (+) and control (+) groups

Location	SWI (+) (%)	Control (%)	*p*-value
Frontal	13 (25.5)	0 (0)	
Parietal	6 (11.8)	1 (6.3)	
Temporal	10 (19.6)	1 (6.3)	
Occipital	6 (11.8)	0	
Basal ganglia	2 (3.9)	7 (44)	
Thalamus	5 (9.8)	5 (31)	
Cerebellum	5 (9.8)	2 (12.5)	
Brain stem	4 (7.8)	0	
Total	51	16	< 0.05

MBLs : Cerebral microbleeds, SWI (+) : parenchymal lesion positive at Susceptibility weighted image of brain, control (+) : parenchymal lesion positive at Susceptibility weighted image of brain among control group

RESULTS

Mean age and sex ratios were 37.2 ± 21.5 and 3.2 : 1 in MTBI group, 39.1 ± 26.8 and 4.3 : 1 in SWI (+) group, 35.2 ± 15.5 and 1.5 : 1 in SWI (-) group. In the cases of control group and control (+) group, mean age and sex ratios were 47.2 ± 15.7 and 2.6 : 1, and 51.3 ± 12.9 and 2.3 : 1, respectively (Table 2). The hemorrhagic groups, SWI (+) and control (+) groups, showed male predominance. There was no statistically significant difference in the mean age among the groups.

Mean GCS of SWI (+) and SWI (-) groups were 13.9 ± 1.5 and 15.0 ± 0.0, respectively ($p < 0.05$). Mean GOS of SWI (+) and SWI (-) group were 4.7 ± 0.8 and 5.0 ± 0.0, respectively ($p < 0.05$) (Table 2).

Regarding MBLs, SWI (+) group showed total of 51 MBLs in 16 patients (76%) among 21 MTBI patients, but control (+) group did only 16 MBLs in 10 patients (23%) among 42 patients ($p < 0.05$). In SWI (+) group, MBLs were located more frequently in white matter (44, 86.3%) than in deep nucleus (basal ganglia and thalamus) (7, 13.7%) ($p < 0.05$), but in control group, more frequently in deep nucleus (14, 87.5%) than in white matter (2, 12.5%) ($p < 0.05$). Interestingly, we found the MBLs in frontal lobe, occipital lobe, and brain stem only in the SWI (+) group. However, we could not find MBLs at frontal lobe, occipital lobe, and brain stem in control group (Table 3).

The patients of SWI (+) group were divided into two groups according to the number of MBLs, 6 and less [SWI (≤ 6)] group, patient number #1 - 7) and more than 6 [SWI (> 7)] group, patient number #8 - 16) (Table 4). Initial GCS scores were 14.7 ± 0.5 and 13.1 ± 1.7 in SWI (≤ 6) and SWI (> 7) groups, respectively ($p < 0.05$). GOS scores at 1 year were 5.0 ± 0.0 and 4.1 ± 0.9 in SWI (≤ 6) and SWI (> 7) groups, respectively ($p < 0.05$).

Whereas there was no symptomatic patient in SWI (-) group, 56.3% (9/16) of SWI (+) group showed various symptoms ($p < 0.05$). Their symptoms were abnormal behavior in 4, visual field defect in 2, hearing difficulty in 2, and Parkinson syndrome in 1.

DISCUSSION

Although CT is still useful in the evaluation of skull fracture and cerebral hemorrhage, MRI seems to be superior to CT in the evaluation of small hemorrhagic lesions of brain. Owing to its excellent tissue contrast, MRI can define small parenchymal abnormalities with T2-weighted GRE MRI. Although, sT2-weighted GRE MRI allow better detection of intracranial hemorrhage compared to conventional MRI, recent studies have shown that SWI is more sensitive for MBLs than T2-weighted GRE MRI[17]. SWI is an imaging technique that was developed in 2004 by Haacke et al.[4] using a basic physical phenomenon, the phase and change

Table 4. List of patients including locations, numbers of MBLs, and presenting symptoms in the SWI (+) group

No	Sex	Age	GCS	GOS	Numbers of MBLs on SWI	Site (numbers) on SWI	MBLs related symptoms at admission
#1	M	27	14	5	1	F (1)	None
#2	M	17	15	5	2	F (2)	None
#3	F	29	15	5	2	T (2)	None
#4	M	25	15	5	3	T (3)	Hearing difficulty, dizziness
#5	M	27	15	5	3	F (3)	None
#6	M	26	14	5	5	F (2), T (3)	Confusion, irritability
#7	M	50	15	5	5	Th (2), Cbl (2), BS (1)	Hearing difficulty, dizziness
#8	M	49	15	5	7	F (2), T (4), O (1)	None
#9	M	50	15	5	7	F (3), O (2), Th (1), Cbl (1)	None
#10	M	29	13	4	9	F (5), T (1), P (3)	None
#11	F	68	12	3	12	F (7), T (5)	Confusion, irritability
#12	M	73	11	3	14	F (2), T (3), P (6), O (3)	Visual field defect
#13	M	21	14	5	16	F (4), T (6), P (1), O (1), Th (3), BS (1)	Visual field defect
#14	M	55	11	3	17	F (4), T (2), P (4), O (4), BG (3)	Confusion, irritability
#15	M	77	15	5	24	F (7), T (1), O (5), Th (4), Cbl (3), BS (4)	Parkinson syndrome
#16	M	29	12	4	31	F (7), T (3), P (3), O (4), BG (5), Th (3), Cbl (4), BS (2)	Confusion, irritability

Abbreviations : MBLs : microbleeds, SWI (+) : parenchymal lesion positive at Susceptibility weighted image of brain, GCS : Glasgow Coma Scale, GOS : Glasgow Outcome Scale, SWI : Susceptibility-weighted image magnetic resonance image, F : frontal, T : temporal, P : parietal, O : occipital, BG : basal ganglia, Th : thalamus, Cbl : cerebellum, BS : brain stem

in the local magnetic field are proportional to each other if the echo time is constant[11]. In SWI, data is acquired using a sequence of 3-D GRE with flow compensation applied in 3 directions, and the image is then multiplied several times by filtering the phase image. With the complicated processing, SWI could dramatically improve the visualization of hemorrhage and ferrugination, permitting small hemorrhagic lesions to be readily depicted[11]. Our SWI consists of a strongly T2-weighted, low-bandwidth (80 Hz/pixel) 3-D fast low angle shot (FLASH) sequence (TR/TE = 49/40.3 msec, FA = 15°) (Table 1). Although larger hemorrhages are readily detectable with CT or conventional MRI, numerous small hemorrhagic shearing lesions can be visible by only using SWI. In MTBI group, SWI is useful to demonstrate hemorrhagic lesions which were not depicted on T2-weighted and T2-weighted GRE MRI. SWI detected six times more number of hemorrhagic lesions and two-fold greater volume of hemorrhage than T2-weighted GRE MRI. As a result, SWI could provide additional useful information that would improve the evaluation, treatment, and management of patients with traumatic brain injury and suspected diffuse axonal injury[17]. These are supporting our study showing higher sensitivity of SWI for MBLs than that of T2-weighted MRI in MTBI group. But, relatively long acquisition time is one of disadvantages of SWI, which may be modified and overcome by echo-planes imaging or parallel imaging method in the future[18].

In this study, 76.2% of patients in MTBI group showed MBLs on SWI and 56% of SWI (+) group presented with various symptoms. Definitive correlations between MBLs and symptom, four abnormal behaviors, two visual field defects, two hearing difficulties, and one Parkinson syndrome, were seen in 56.3% of Rm-TBI (+) group. We believe that the high correlation between MBLs and symptoms in this study is contributed by the improved sensitivity of SWI. Patients SWI (+) group showed poor GCS and GOS comparing to that of SWI (-) group. Our data support prior studies reporting positive relationship between increasing number of hemorrhagic lesions and poor prognosis and between MBLs and neuropsychiatric deficit[3,5,8,9,12,18].

Patients with confusion and irritability (patient #6, #11, #14 and #16) mostly improved after a month, but complained intermittent headache and decrease in concentration. Symptoms remained in patients with hearing difficulty (patient #4 and #7), with visual defect (patient #12 and #13), and with Parkinson syndrome (patient #15). It seems to have positive relationship between MBLs locations and specific symptoms. For examples, MBLs at occipital lobe, pons, and midbrain seemed to be accompanied with visual field defect, sensorineural hearing loss, and Parkinson syndrome, respectively (Table 4).

Neuropathological studies have reported that approximately 50% of DAI lesions occur in the deep white matter or corticomedullary junction of frontal and temporal lobes with small diameter (5-15 mm)[1]. Lobar white matter, corpus callosum, corona radiata, rostral midbrain, and cerebellum are commonly affected by TBI[1,2,9,13,18]. The presence of MBLs in TBI patients was also closely related with not only initial consciousness level but also clinical outcome (GOS). Tong et al.[17] reported that traumatic MBLs were mainly distributed lesions in frontal white matter or parieto-temporo-occipital gray or white matter[16], whereas spontaneous

MBLs were mainly distributed at basal ganglion and thalamus. These data were comparable to our results representing similar distribution patterns of traumatic and spontaneous MBLs. Spontaneous MBLs are seen with coagulopathy, vasculitis, some infections, cerebral neoplasm, vascular disorders such as Sturge-Weber syndrome, or certain types of vascular malformation. All the patients with 6 or less MBLs showed good outcomes, which was similar to the previous report presenting the patients with 7 or more MBLs were at risk of poor outcome[18]. GCS and GOS seemed to be closely related with not only the location of traumatic MBLs but also the number of MBLs.

Our study has several limitations. First, only a small number of TBI patients were enrolled. Second, spontaneous MBLs may have possibly been included in the MBLs of TBI patients. Third, the patient groups enrolled in the study showed wide range of age making it difficult to rule out age related bias.

CONCLUSION

SWI was superior to conventional MRI in the detection of small hemorrhagic lesions, MBLs. According to our results, traumatic MBLs seemed to occur more frequently in male patients, and also showed characteristic regional distribution, white matters predominance, comparing to those of spontaneous MLBs. The presence and number of traumatic MBLs were closely related with initial GCS and clinical outcome in TBI patients. Some of traumatic MBLs could also provide clues for symptoms or signs which might be unexplainable by conventional MRI.

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