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Clinical Article

Time to Recover Consciousness in Patients with Diffuse Axonal Injury : Assessment with Reference to Magnetic Resonance Grading

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Objective : This study was conducted to investigate the correlation between the degrees of injury on brain magnetic resonance imaging (MRI) and the time interval to recovery of consciousness in patients with diffuse axonal injury.
Methods : From January 2004 to December 2008, 25 patients with diffuse axonal injury were treated at our hospital. We retrospectively investigated the patients' medical records and radiological findings. We divided the patients into three groups according to the grade of MRI finding : grade I, small scattered lesions on the white matter of the cerebral hemisphere; grade II, focal lesions on the corpus callosum; and grade III, additional focal lesions on the brain stem.
Result : Seven patients belonged to the grade I group; 10 to the grade II group; and 8 to the grade III group. The mean Glasgow Coma Scale (GCS) score of all patients at the time of admission was 7.28. Recovery of consciousness was observed in 23 of the 25 patients; the remaining two patients never regained consciousness. The time interval to recovery of consciousness (awake status) ranged from 1 day to 125 days (mean 22.1 days) : grade I group patients, within approximately 1 week (mean 3.7 days); grade II group patients, within approximately 2 weeks (mean 12.5 days); and grade III group patients, within approximately 2 months (mean 59.5 days).
Conclusion : Our study results suggest a correlation between the mean time interval to recovery of consciousness in patients with diffuse axonal injuries and the degrees of brain injuries seen on MRI. Patients with grade I and II diffuse axonal injuries recovered consciousness within 2 weeks, while patients with grade III injuries required approximately 2 months.

KEY WORDS : Brain stem · Consciousness · Diffuse axonal injury · MRI.

INTRODUCTION

Diffuse axonal injury is caused from widespread tearing of axons and small vessels by shearing forces and is defined as prolonged post-traumatic coma over 6 hours following injury without demonstrable mass lesion[3-5]. "Diffuse degeneration of the cerebral white matter" was first defined by Strich[17] in a study of patients with severe post-traumatic dementia in 1956. The time course of the pathological changes was established by Adams et al.[1] Diffuse axonal injury can be diagnosed using clinical signs and radiological evidence. Brain magnetic resonance imaging (MRI) is known to be the most sensitive method to diagnose diffuse axonal injury, especially in gradient echo image[9,10,15].

Numerous studies have been performed on the outcome of and the searching for the prognostic factors of diffuse axonal injury. This study aimed to investigate the correlation between the degrees of injuries based on MRI findings and the mean time intervals to recovery of consciousness in patients with diffuse axonal injuries.

MATERIALS AND METHODS

Twenty-five patients who had been diagnosed with diffuse axonal injury and underwent MRI at our hospital from January 2004 to December 2008 were included in this study. We had excluded patients with secondary hypoxic brain damage on admission or who had undergone cranial

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operation during treatment from this study. All the medical records and radiographic findings were reviewed retrospectively. Patients were divided into three groups according to the location of lesions on MRI findings (grade I, II, and III) as classified by Gennarelli et al.[7] An MRI finding of scattered small hemorrhagic lesions on hemispheric white matter was classified as grade I, a finding of additional focal lesions on the corpus callosum was classified as grade II, and a finding of additional focal lesions on the brain stem was classified as grade III (Fig. 1). Various clinical parameters such as sex, age, initial Glasgow Coma Scale (GCS) score, follow-up GCS score, time interval from injury to

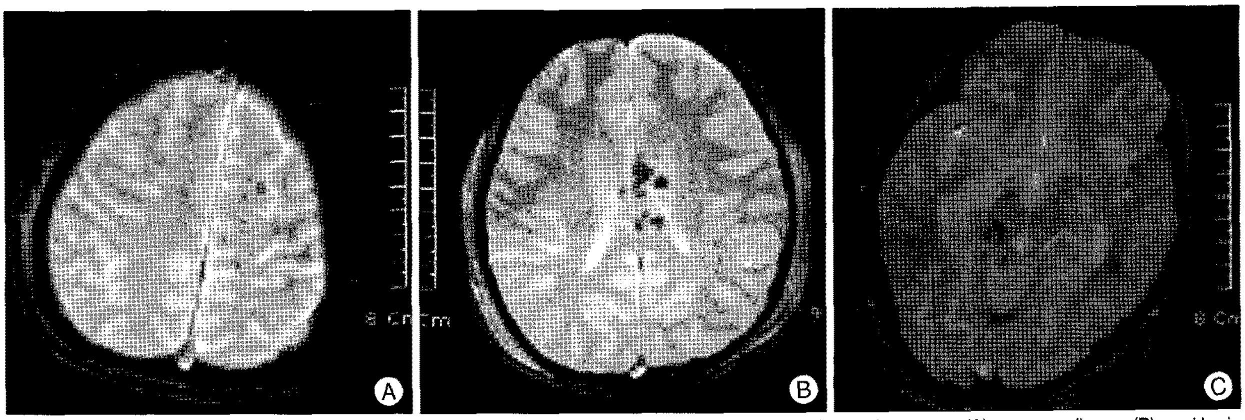

Fig. 1. Gradient-echo magnetic resonance images show multiple small hemorrhagic foci on the hemispheric white matter (A), corpus callosum (B), and brain stem (C).

Table 1. Summary of the total cases (n = 25)*

Case number	Sex/ Age	GCS score on admission	MRI grade	Time interval to awake (days)	Follow-up period (months)	GOS	Coincidental lesions	Kind of trauma
1	M/57	9	I	3	38	MD	Rib and humerus fx.	Fall
2	F/22	9	I	2	21	GR	Humerus fx.	Driver's TA
3	F/41	8	I	5	3	MD	SDH	Pedestrian TA
4	M/19	6	I	7	19	GR	SDH	Pedestrian TA
5	M/17	3	I	6	16	MD	Tibio fibular fx.	Pedestrian TA
6	M/9	9	I	2	12	GR	SDH	Pedestrian TA
7	F/14	8	I	1	1	GR	None	Pedestrian TA
8	M/20	11	II	1	1	GR	Skull fx., SAH	Driver's TA
9	F/7	8	II	5	8	GR	Skull fx.	Pedestrian TA
10	F/18	8	II	10	12	GR	SAH	Pedestrian TA
11	M/17	6	II	21	6	GR	Cerebral contusion	Mmotorbike TA
12	M/20	10	II	2	1	GR	Ankle fx.	Motorbike TA
13	M/48	8	II	20	13	GR	Facial bone fx.	Pedestrian TA
14	F/5	7	II	26	24	GR	IVH	Pedestrian TA
15	F/51	8	II	5	1	MD	Cerebral contusion	Pedestrian TA
16	M/26	6	II	30	1	MD	None	Driver's TA
17	M/53	4	II	5	2	SD	None	Fall
18	M/32	4	III	N/A	2	PVS	IVH	Fall
19	M/59	7	III	N/A	9	PVS	None	Driver's TA
20	M/46	6	III	45	15	MD	Fibular fx.	Pedestrian TA
21	M/35	6	III	60	11	SD	Iliac bone fx. SDH	Fall pedestrian TA
22	F/5	10	III	2	3	GR	Cerebral contusion	Driver's TA
23	M/19	7	III	51	16	GR	None	Pedestrian TA
24	F/32	7	III	125	12	SD	Cerebral contusion	Pedestrian TA
25	F/11	7	III	74	10	MD		

F : female, fx : fracture, GCS : Glasgow Coma Scale, GOS : Glasgow Outcome Scale, GR : good recovery, IVH: intraventricular hemorrhage, M : male, MD : mild disability, MRI : magnetic resonance imaging, N/A : not available, PVS : persistent vegetative state, SAH : subarachnoid hemorrhage, SD : severe disability, SDH : subdural hemorrhage, TA : traffic accident recovery of consciousness (awake status), and Glasgow Outcome Scale (GOS) were investigated. Recovery of consciousness was defined as opening eyes to verbal stimulus and obedience to command. Outcome was assessed by GOS as GR (good recovery), MD (mild disability), SD (severe disability), PVS (persistent vegetative state), and death. Statistical analysis was conducted with the SPSS program (version 12.0) (SPSS Inc., Chicago, IL, USA). The correlation between the MRI grade and the mean time interval to recovery of consciousness was evaluated by one-way analysis of variance (ANOVA). Statistical significance was defined as $p < 0.05$.

RESULTS

All cases are presented in Table 1. All patients were transferred to our hospital within one day from injury. Among these, the cause of hospitalization was pedestrian traffic accident (TA) in fourteen patients, driver's TA in 5 patients, fall from heights in 4 patients, and motorbike TA in 2 patients. The male/female ratio was 1.5 : 1, and the mean age was 27.32 years. The patients had several coincidental injuries such as rib fracture, long bone fracture, and scanty amount of intracranial hemorrhage (subdural hematoma, contusion, subarachnoid hemorrhage, and intraventricular hemorrhage). But, the scanty amount of intracranial hemorrhage did not require decompressive cranial operation. Specific intracranial complication did not occur in all patients. Tracheostomy had been performed in 7 patients because of pneumonia.

The average GCS score of all patients on admission was 7.28, and the mean follow-up period was 10.28 months. By using the GOS to classify outcomes, 13 patients (52%) were assessed as GR, 7 patients (28%) were assessed as MD, 3 patients (12%) were assessed as SD, and 2 patients (8%) were assessed as PVS. None of the patients died. Among the 25 patients, 7 patients (28%) had grade I injuries, 10 patients (40%) had grade II injuries, and 8 patients (32%) had grade III injuries. In the grade I group, the mean GCS score on admission was 7.43, and the mean time interval to awake status was 3.7 days. All of their outcome were better than SD. In the grade II group, the mean GCS score was 7.6 and the mean time interval to awake status was 12.5 days. In the grade III group, the mean GCS score was 6.75, and the mean time interval to awake status was 59.5 days. Two patients in the grade III group did not regain consciousness and were excluded from the time interval to awake status estimates. Fig. 2 shows the sequential changes in the mean GCS scores of each grade over time. Patients' GCS scores in the grade I and II groups began to improve soon after admission; those in the grade III group did not improve until 1 month after injury. Statistical analysis was performed for comparison of the mean time interval to awake status of each grade (Table 2). The mean time interval to awake status between the grade I and II groups did not show significant difference; however, there were statistically significant differences between the grade I and III groups (p = 0.001) and the grade II and III groups (p = 0.002) (Table 2).

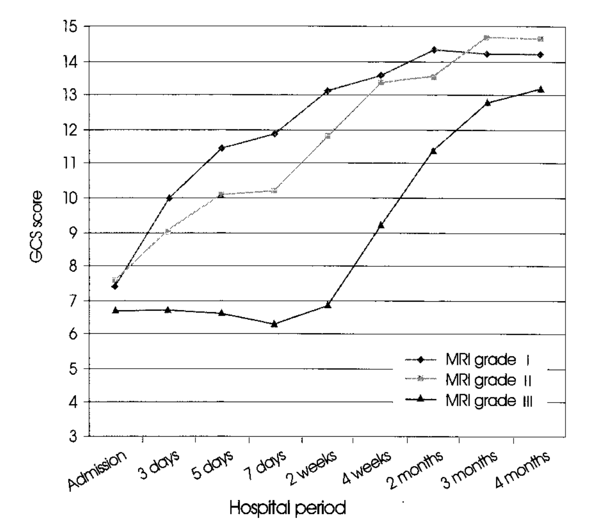

Fig. 2. Graph shows sequential changes in the mean Glasgow Coma Scale scores of each magnetic resonance imaging grade according to hospital period.

Table 2. Statistical analysis of the mean time interval to awake status between MRI grade

MRI grade*	Difference of mean time interval to awake(days)	p
I vs. II	-8.79	.711
I vs. III	-55.79	.001†
II vs. III	-47.00	.002‡

*Comparison between two grades of MRI using one-way analysis of variance (ANOVA), †Significant difference between MRI grade I and III, ‡ Significant difference between MRI grade II and III. MRI: magnetic resonance imaging

DISCUSSION

Diffuse axonal injury (i.e., widespread damage to axons in the white matter of the brain) is well recognized as a severe post-traumatic head injury[2]. It is defined as prolonged post-traumatic coma following injury without demonstrable intracranial mass lesion[3-5].

In 1956, Strich[17] defined the "diffuse degeneration of the cerebral white matter" in a series of patients with severe post-traumatic dementia.

Diffuse axonal injury is caused by acceleration-deceleration effects of the mechanical input to the head upon shaking of the brain within the skull[3,5-7]. This results in shearing or stretching of nerve fibers with consequential axonal damage. Mostly, this injury mechanism is caused by traffic accident that produce long acceleration comparatively. Determination of its severity is based on the direction, magnitude, and speed of the head motion during the injury sequence[5]. Gennarelli et al.[7] reported a high correlation between the direction of the head motion in acceleration and the duration of coma in an experimental animal model study. Although diffuse axonal injury could occasionally occur when the head was accelerated in a sagittal or oblique direction, it was most readily produced by coronal acceleration of the head[7]. In mild injury the lesions are localized within frontotemporal cerebral white matter, stronger injury of rotatory acceleration caused additional lesions on corpus callosum and upper brain stem. Gennarelli et al.[7] reported severe injury has a tendency to cause deeper lesions.

The time course of the pathological changes has been established by Adams et al.[1] In humans, instantaneous injury occurs to numerous axons in the white matter of the brain, manifested by axonal retraction balls visible on microscopic examination. Gross lesions associated with severe diffuse axonal injury in humans consist of hemorrhagic tears in the corpus callosum and in the dorsolateral quadrant of the rostral brain stem. Several days later, microglial clusters appear and the axonal retraction balls start to disappear. Months after the injury, the bulk of the white matter is reduced and long tract degeneration can be demonstrated[7].

Diffuse axonal injury can be diagnosed using clinical signs (level of consciousness and neurological deficits) and radiological findings. Zimmerman[19] reported the first study of radiological diagnosis of diffuse axonal injury that includes small hemorrhagic lesions on the corpus callosum, upper brain stem, corticomedullary junction, parasagittal area, and basal ganglia. Brain computed tomographic (CT) findings lack accuracy in the prediction of a patient's outcome and do not correspond well to the patient's GCS score or neurological state[10,20].

Brain MRI gradient echo imaging is far more sensitive than spin echo imaging on paramagnetic lesion such as hemorrhage or calcification for a long time. So, brain MRI gradient echo imaging is currently known to be the most sensitive method of confirming the presence of small hemorrhagic lesions on the white matter, corpus callosum, and brain stem in diffuse axonal injury[9,10,15].

Numerous clinical prognostic factors in patients with severe head injuries have been studied, including initial GCS, abnormal motor response, hypothalamic injury sign, duration of loss of consciousness, initial pupil size, associated hypotension or hypoxia, age, and sex[1,6,12,13,16,18].

Hypoxia and hypotension have been known to be among the most important associated medical conditions with regard to outcome in severely injured patients[3,12,13,18]. Initial GCS in patients with head injuries strongly correlates with outcome, especially a GCS score below 5, which is associated with a poorer outcome[6-8,12,16]. Pupillary abnormalities such as anisocoria or bilateral pupil dilatation due to herniation have also been reported to correlate with poor prognosis[11,14]. The duration of loss of consciousness has been shown to be strongly related with the outcome in some reports[16,18]. The correlation between outcome and MRI findings has been studied in several reports[9,10,15,16]. Kim et al.[9] reported an association between higher MRI grade and longer duration of loss of consciousness, but not statistically significant difference between MRI grade and outcome or clinical severity. Oh et al.[15] reported worse outcomes in patients with brain stem lesions shown on MRI but sizes of lesions were not consistent with outcomes. Kim et al.[10] reported more lesions on corpus callosum and brain stem in worse outcome in patients. And Park et al.[16] reported that 14.3% of patients with cerebral white matter lesions did not recover their consciousness and 50% of patients with corpus callosum lesions, 51.6% of patients with brain stem lesion did not recover their consciousness.

In our study, initial GCS scores of each MRI grade were similar, but sequential changes in GCS scores looked different : the mean GCS scores of the grade I and II groups tended to improve within 5 days, but GCS score improvement was not seen in the grade III group until after 1 month (Fig. 2). We investigated the mean time interval to awake status according to the MRI grade. Patients with grade I or II injury recovered their consciousness within 2 weeks. Patients with grade III injury recovered consciousness within 2 months. Although our relatively small number of cases was a limitation, our data were statistically significant. Therefore, in case of diffuse axonal injury except secondary hypoxic brain damage, patients with lesions on cerebral white matter and corpus callosum has a tendency to recover their consciousness earlier than patients with lesions on brain stem.

CONCLUSION

This study shows a correlation between the time interval to recovery of consciousness in patients with diffuse axonal injury and the degrees of brain injuries seen on MRI, despite the limitation of a small study population. Patients with diffuse axonal injuries with small hemorrhagic lesions on the hemispheric white matter or corpus callosum recovered consciousness within 2 weeks. In contrast, patients with additional lesions on the brain stem did not recover consciousness within 2 months.

References

1. Adams H, Mitchell DE, Graham DI, Doyle D : Diffuse brain damage of immediate impact type. Its relationship to "primary brain stem damage" in head injury. **Brain 100** : 489-502, 1977
2. Adams JH, Graham DI, Murray LS, Scott G : Diffuse axonal injury due to nonmissile head injury in humans : an analysis of 45 cases. **Ann Neurol 12** : 557-563, 1982
3. Alberico AM, Ward JD, Choi SC, Marmarou A, Young HF : Outcome after severe head injury : relationship to mass lesions, diffuse injury, and ICP course in pediatric and adult patients. **J Neurosurg 67** : 648-656, 1987
4. Eisenberg HM, Gary HE Jr, Aldrich EF, Saydjari C, Turner B, Foulkes MA et al. : Initial CT findings in 753 patients with severe head injury. A report from the NIH Traumatic Coma Data Bank. **J Neurosurg 73** : 688-698, 1990
5. Eum SW, Lim DJ, Kim BR, Cho TH, Park JY, Suh JK, et al. : Prognostic factors in patients with diffuse axonal injury. **J Korean Neurosurg Soc 27** : 1668-1674, 1998
6. Gennarelli TA, Spielman GM, Langfitt TW, Gildenberg PL, Harrington T, Jane JA, et al. : Influence of the type of intracranial lesion on outcome from severe head injury. **J Neurosurg 56** : 26-32, 1982
7. Gennarelli TA, Thibault LE, Adams JH, Graham DI, Thompson CJ, Marcincin RP : Diffuse axonal injury and traumatic coma in the primate. **Ann Neurol 12** : 564-574, 1982
8. Kalff R, Kocks W, Pospiech J, Grote W : Clinical outcome after head injury in children. **Childs Nerv Syst 5** : 156-159, 1989
9. Kim CH, Lee HK, Koh YC, Hwang DY : Clinical analysis of diffuse axonal injury (DAI) diagnosed with magnetic resonance image (MRI). **J Korean Neurosurg Soc 26** : 241-248, 1997
10. Kim HJ, Park IS, Kim JH, Kim KJ, Hwang SH, Kim ES, et al. : Clinical analysis of the prognosis of the patients with cerebral diffuse axonal injuries, based on gradient-echo MR imaging. **J Korean Neurosurg Soc 30** : 168-172, 2001
11. Lee HS, Lee KS, Bae HG, Yun IG, Lee IS : Systemic insults in the early death after head injury. **J Korean Neurosurg Soc 19** : 1101-1106, 1990
12. Levati A, Farina ML, Vecchi G, Rossanda M, Marrubini MB : Prognosis of severe head injuries. **J Neurosurg 57** : 779-783, 1982
13. Levi L, Guilburd JN, Lemberger A, Soustiel JF, Feinsod M : Diffuse axonal injury : analysis of 100 patients with radiological signs. **Neurosurgery 27** : 429-432, 1990
14. Miller JD, Butterworth JF, Gudeman SK, Faulkner JE, Choi SC, Selhorst JB, et al. : Further experience in the management of severe head injury. **J Neurosurg 54** : 289-299, 1981
15. Oh KS, Ha SI, Suh BS, Lee HS, Lee JS : The correlation of MRI findings to outcome in diffuse axonal injury patients. **J Korean Neurosurg Soc (Suppl I) 30** : S20-S24, 2001
16. Park SW, Park K, Kim YB, Min BK, Hwang SN, Suk JS, et al. : Prognostic factors in diffuse axonal injuries of brain. **J Korean Neurosurg Soc 20** : 983-990,1991
17. Strich SJ : Diffuse degeneration of the cerebral white matter in severe dementia following head injury. **J Neurol Neurosurg Psychiatry 19** : 163-185, 1956
18. Williams JM, Gomes F, Drudge OW, Kessler M : Predicting outcome from closed head injury by early assessment of trauma severity. **J Neurosurg 61** : 581-585, 1984
19. Zimmerman RA, Bilaniuk LT, Genneralli T : Computed tomography of shearing injuries of the cerebral white matter. **Radiology 127** : 393-396, 1978
20. Zimmerman RA, Bilaniuk LT, Hackney DB, Goldberg HI, Grossman RI : Head injury : early results of comparing CT and high-field MR. **AJR Am Roentgenol 147** : 1215-1222, 1986