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Short-term Coexisting Intracerebral Hemorrhage and Cerebral Infarctions

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Objective : Short-term coexisting intracerebral hemorrhage and cerebral infarctions defined as the recurrent stroke presented with different type within three weeks. Despite the high recurrence rate of stroke, little attention and insufficient clinical data had been given to short-term coexisting intracerebral hemorrhage and cerebral infarction's features. This study aims to estimate the risk factors and present the clinical features of short-term coexisting intracerebral hemorrhage and cerebral infarctions.

Methods : We investigated 18 patients with short-term coexisting intracerebral hemorrhage and cerebral infarctions who were admitted to our hospital between January 1995 and January 2005. They were subdivided by the recurrence interval such as a group of within one week and another of between one and three weeks as hyperacute and acute respectively.

Results : The mean interval between strokes was 6.64 days. Lesional analysis showed that short-term coexisting intracerebral hemorrhage and cerebral infarctions in this study occurred at the other side in 12 cases (66.7%). The abnormality on the electrocardiographic feature (23.5%) and long-term history of hypertension (20.5%) were the most common risk factors. However, short-term history of diabetes was more common in hyperacute group than in acute group ($P<0.05$). The mean number of risk factors was three in acute group. It is larger than that of hyperacute group ($P<0.05$).

Conclusion : If the patients who experienced cerebrovascular attack have many risk factors, they tend to be the cases of acute coexisting intracerebral hemorrhage and cerebral infarctions than hyperacute. Therefore, that cases are required to be vigilant to the change of patients' state up to three weeks in the treatment.

KEY WORDS : Intracerebral hemorrhage · Cerebral infarction · Recurrent stroke.

Introduction

Strokes, in general, have been treated as a single disease called palsy, a laymen's term, regardless of their causes. It is clear, however, that strokes are classified into cerebral infarction and intracerebral hemorrhage according to their generating causes. Therefore, the different strokes require different treatments. The former has a higher frequency than the latter does[13,18].

Short-term coexisting intracerebral hemorrhage and cerebral infarctions are rare. While studies on medical treatments over the recurrence of each stroke have been reported several times[4,13,23,25,34,36], there has been a few studies reported on the case of coexisting intracerebral hemorrhage and cerebral infarctions[17,28]. Even no study of short-term coexisting intracerebral hemorrhage and cerebral infarctions on the acute period simultaneously holding both acute cerebral infarction and intracerebral hemorrhage has been reported so far.

For the reason, the authors want to identify associated factors and to prevent from the first attack or the second recurrence of strokes by analysing the features of short-term coexisting intracerebral hemorrhage and cerebral infarctions, and are presenting this study with the literature review.

Materials and Methods

Eighteen short-term coexisting intracerebral hemorrhage and cerebral infarctions patients simultaneously developed with both their acute intracerebral hemorrhage and cerebral infarction were treated from January 1995 to January 2005. The authors retrospectively analysed with patient's records and radiologic findings.

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Fig. 1. Initial brain computed tomography revealing an intracerebral hemorrhage in the left thalamus.

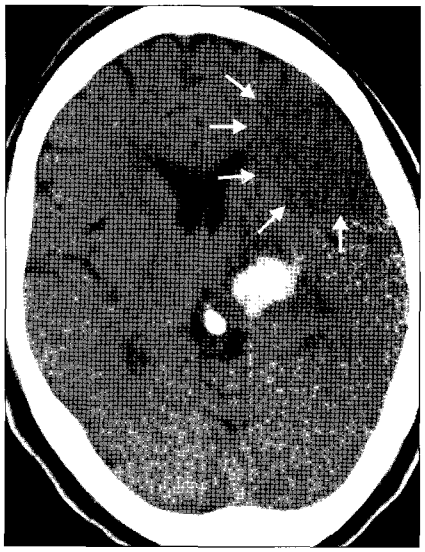

Fig. 2. After hospital 4day, follow up brain computed tomography revealing an cerebral infarction at the left middle cerebral artery territory (white arrows).

The authors selected cases within three weeks after the first attack and with the diagnosis of cerebral infarction and intracerebral hemorrhage confirmed with the CT and MRI (Fig. 1, 2, 3). The blood pressures were measured at the time of the first and second attack. The total cholesterol, blood glucose, electrocardiography (EKG), serum triglyceride, high density lipoprotein are checked at admission.

Of the patients with intracerebral hemorrhage, those with arteriovenous malformation(AVM), aneurysm rupture, blood dyscrasias, moyamoya disease, and traumatic cerebral hemorrhage were excluded as well as those prescribed with anticoagulant for this present study. Of those with cerebral infarction, cases of small vessel diseases without medical symptoms, hemorrhagic infarction, and cerebral infarction derived from the blood vessel after surgery are excluded, while overt acute cerebral infarction was included as subjects.

We used Glasgow outcome scale(GOS) in assessing the prognosis of the patients through neurological examinations; cases without deficit were graded as 'excellent', and cases of being capable of routines with mild deficit as 'good', cases of severe deficit leading not to manage routines without others' help as 'fair', cases of a state of coma leading to lay down on bed as 'poor', cases of decease as 'expire'.

The authors compared with and analyzed risk factors to strokes such as hypertension, diabetes, ischemic heart diseases, serum cholesterol, alcohol, cigarette smoking and age[8-10,12,16,18,23,35,37]. The diagnostic criteria of hypertension were determined by factors as follows : the past history of hypertension, and the history of antihypertensive medication, or more than 160/95mmHg of blood pressure[1,5,7]. Speaking of diabetes, determining factors to the diagnosis were as follows : the past history, more than 126mg/dl blood sugar after eight hours' fast, more than 200mg/dl blood sugar at two hours after meal, having typical symptoms and more than 200mg/dl blood sugar when randomly measured[12]. For the diagnosis of ischemic heart diseases, determining factors were as follows : the history of angina, cardiac infarction, more than 1mV of ST drop on the electrocardiogram, or the observation of coronary arterial diseases such as abnormal Q wave. The diagnosis of hyperlipidemia was determined in a case of more than 220mg/dl of the total fasting cholesterol[17].

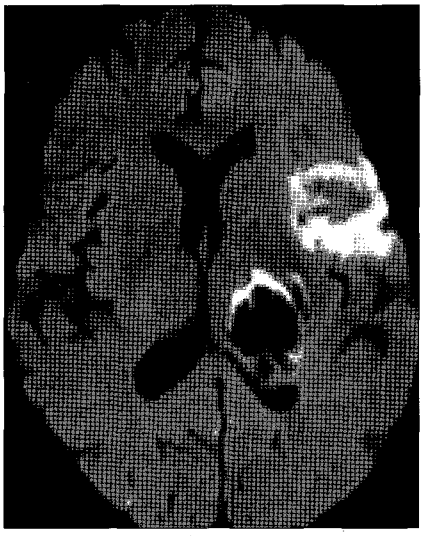

Fig. 3. At 5th hospital day, brain diffusion magnetic resonance image showing that there are intracerebral hemorrhage in the left thalamus and acute cerebral infarction in the left middle cerebral artery territory.

The risk factors and prognosis were divided into two groups according to the development period as follows : a group of hyperacute coexisting intracerebral hemorrhage and cerebral infarctions with one week after the first attack, and another group of acute stroke with the period from one to three weeks.

For statistical analysis, we used Statical Package of Social Science (Korean version 12) software. The mean analysis was adopted for quantitative data, while cross-tabulation analysis was used for qualitative data. We used t-test for the mean analysis and chi-square test for cross-tabulation analysis as test statistic value. A p-value of less than 0.05 was considered significant.

Results

The characteristics of patients were identified as follows (Table 1).

Table 1. Characteristics of short-term coexisting intracerebral hemorrhage and cerebral infarctions

Case	Sex	Age	Blood Pressure		Interval	ICH		Infarction	Glucose (mg/dl)	Cholesterol (mg/dl)	EKG abnormality	HTN	DM	GCS	GOS
			First attack	Second attack		Location	Volume (ml)								
1	M	66	140/100	160/90	1-3 weeks	Lt O	24	Stem	203	203	+	+	-	15	5
2	F	64	170/90	140/90	1 week	Rt Th	5	Stem	181	198	+	+	-	15	4
3	F	49	200/120	140/100	1 week	Rt BG	104	Rt MCA	184	172	-	-	-	5	1
4	M	61	170/100	120/80	1 week	Rt BG	70	Lt T	87	133	-	-	-	12	5
5	M	68	170/100	180/100	1-3 weeks	Stem	20	Stem	283	210	+	+	+	8	1
6	F	81	200/110	200/110	1 week	Rt BG	3	Lt MCA	161	233	-	-	-	11	2
7	F	58	150/90	130/80	1 week	Rt F	5	Lt Th	100	167	+	+	-	15	5
8	M	50	160/100	140/80	1 week	Rt Th	3	Stem	87	168	+	-	-	15	2
9	F	21	120/75	130/80	1 week	Lt F	30	Lt ICA	109	133	-	-	-	9	1
10	F	46	100/80	190/120	1-3 weeks	Lt BG	80	Cbll	89	215	-	+	+	13	1
11	F	70	170/120	170/120	1 week	Rt BG	4	Lt Th	103	163	-	-	-	14	5
12	F	81	170/60	160/60	1-3 weeks	Rt T	5	Rt T	66	109	-	-	-	14	2
13	M	53	150/90	260/130	1-3 weeks	Stem	15	Rt MCA	89	368	+	+	+	7	1
14	F	63	170/100	110/60	1 week	Lt BG	5	Rt MCA	125	202	+	-	-	14	3
15	M	58	180/100	150/90	1 week	Rt BG	40	Rt MCA	191	244	+	-	-	9	1
16	M	46	140/90	140/90	1-3 weeks	Lt BG	25	Rt BG	377	206	-	-	+	13	3
17	F	52	220/180	160/80	1 week	Cbll	32	Rt MCA	236	183	-	+	+	13	1
18	F	76	150/70	160/70	1 week	Lt Th	10	Lt MCA	131	177	-	-	-	14	4

GCS : Glasgow Coma Scale, Glasgow Outcome Scale(GOS) : excellent(5), good(4), fair(3), poor(2), expire(1), HTN : have hypertension more than 5years (+), less than 5years(-), DM : have DM more than 5years (+), less than 5year (-), BG : basal ganglia, Th : thalamus, Cbll : cerebellum, F : frontal, T : temporal, O : occipital, Stem : pons and midbrain

Demography

Eighteen subjects were comprised here in the study : 7 men and 11 women. For the age of occurrence, the median was 59.5 year-old ranging from 21 to 81 (mean 59.05 year-old). The mean was 57.4 year-old for the men and 60.0 year-old for the women.

Period of development

The interval between intracerebral hemorrhage and cerebral infarction was 6.64 days in average, and the most frequent case was the one that developed within one week, which was 11 patients (66.7%).

The location of the lesion

In the sequential relation between intracerebral hemorrhage and cerebral infarction, the occurrence of the cerebral infarction after intracerebral hemorrhage had the higher frequency, which was 16 cases. In the cases of intracerebral hemorrhage, the amount of blood volume varied and the locations of hemorrhage were orderly basal ganglia as well as thalamus (61.1%), subcortex (22.2%), brain stem (11.1%), and cerebellum (6%). In the cases of cerebral infarction, the occurrence rate of the infarction at middle cerebral artery territories had the highest frequency (38.9%). The other ones such as infarction at brain stem and perforating arteries of basal ganglia were 22.2% and 16.7% respectively. In the locational analysis, cases that recurred at different cerebral hemisphere (12 cases, 66.7%) were more frequent than cases at the same hemisphere.

Risk factors

Short-term coexisting intracerebral hemorrhage and cerebral infarctions patients had 1.83 risk factors in average. Risk factors showing the highest frequency were firstly an EKG abnormality (23.5%), and secondly, more than five year-old history (20.5%) of hypertension (Table 2).

The blood pressure at first attack measured immediately after the patients arrived at the hospital was high (mean systolic blood pressure 162.77mmHg), which was statistically significant ($p<0.01$). However, the systolic blood pressure measured at the time of the second occurrence was not higher than first attack measured systolic blood pressure (mean sys-

Table 2. Frequency of risk factors in short-term coexisting intracerebral hemorrhage and cerebral infarctions

Factors	Group A(n=12)	Group B(n=6)	Total
Over 65 years old	3 (18.8%)	3 (16.7%)	6 (17.6%)
Glucose > 200mg/dl	1 (6.2%)	3 (16.6%)	4 (11.8%)
Cholesterol > 220mg/dl	2 (12.5%)	1 (5.55%)	3 (8.8%)
EKG abnormality	5 (31.3%)	3 (16.6%)	8 (23.5%)
Smoking	1 (6.2%)	0 (0%)	1 (2.9%)
Previous HTN > 5 years	3 (18.8%)	4 (22.2%)	7 (20.5%)
Previous DM > 5 years	1 (6.2%)	4 (22.2%)	5 (14.7%)
Total	16	18	34

Group A : Patients of hyperacute group, Group B : Patients of acute group

tolic blood pressure 157.78mmHg). This is not statistically significant ($p>0.05$).

Progress and prognosis

At the time of admission, the state of consciousness were graded as follows : 11 patients of Glasgow coma scale(GCS) 13-15, 4 ones of GCS 9-12, and 3 ones of less than GCS 8 (Table 1). The overall clinical outcome was as follows : 6 patients were favorable (GOS≥4). 5 patients were the fair or poor (GOS 2-3). And 7 patients expired (GOS 1) (Table 1).

Analysis on the period

There was not statistical significance ($p>0.05$) in factors such as gender, age, serum cholesterol, EKG, and prognosis to both the hyperacute and acute group of short-term coexisting intracerebral hemorrhage and cerebral infarctions patients.

Table 3. Comparison of possible risk factors between hyperacute and acute groups

Factors	Subgroup		x^2-value or t-value*	P-value
	Group A(n=12)	Group B(n=6)		
Sex				
M	3	4	2.92	0.09
F	9	2		
Age(years)				
20~30	1	0		
31~40	0	0		
41~50	1	2		
51~60	4	1	3.75	0.59
61~70	3	2		
71~80	2	0		
81~	1	1		
EKG				
+	5	3	0.11	0.74
−	7	3		
HTN				
> 5 years	3	3	1.13	0.29
< 5 years	9	3		
DM				
> 5 years	1	4	6.79	0.01**
< 5 years	11	2		
Glucose	141.25±48.35	184.50±126.00	−0.81*	0.45
Cholesterol	181.08±34.11	218.50±83.45	−1.37*	0.19
Outcome	2.92±1.78	2.17±1.60	0.87*	0.40
Number of Risk factor	1.33	3.0		0.02

** : p-value<0.01, Group A : Patients of hyperacute group, Group B : Patients of acute group, EKG +/− : evidence of ischemic heart disease/no evidence

Only the history of less than five years of diabetes appeared statistically significant in the former group ($p<0.01$). In particular, to the latter group, the number of average risk factors was three, which was more than the former group's (Table 3, 4).

Discussion

The mortality and morbidity rate from the strokes in Korea have been increasing due to the change of diet and the lengthening of life span by economic growth. According to the cause of death by the report of the Korea National Statistical Office in 2003, the death rate of strokes was the second highest next to the circulating disease, which was 75.5 death over the 100,000 patients[29]. The population of old age in Korea has been being increasing according to the definition of the old age for over 65 years olds[16]. According to the report of the Korea National Statistical Office, the rate of old population was 7.2% in 2000 and may be increasing to more than 15.7% in 2020. In Korea, an aging society has already begun. Therefore, it is very important to identify the pathophysiology of the stroke.

According to reports on the recurrence of strokes, the majority cases of features were of the same type diseases, for example, cerebral infarction from cerebral infarction, or intracerebral hemorrhage from intracerebral hemorrhage[13,36]. In this study, we selected the cases of the recurrence developed into a different type, which is rare so that a few studies on coexisting intracerebral hemorrhage and cerebral infarctions has been reported[17,20]. This study seems to be unique, to our knowledge, to deal with coexisting intracerebral hemorrhage and cerebral infarctions, especially, within 3 weeks.

According to reports on the recurrence age of strokes, the highest rate of hypertensive intracerebral hemorrhage occurrence is in the fifties[3,30], while the case of infarction is more frequent in the sixties and seventies[10,12]. In this study, we noticed that short-term coexisting intracerebral hemorrhage and cerebral infarctions tend to occur in the fifties, which is lower than in the case of infarction and similar as that of hypertensive intracerebral hemorrhage. In this study, there were more cases in the recurring features of short-term coexisting intracerebral hemorrhage and cerebral infarctions showing a pattern, cerebral infarction after intracerebral hemorrhage. This trait is the same as the case of coexisting intracerebral hemorrhage and cerebral infarctions with more than three weeks after the first attack[17,27], thus we could not conclude that cerebral infarction after intracerebral hemorrhage is the distinctive feature of short-term coexisting intracerebral

Table 4. Number and type of risk factors for interval of short-term coexisting intracerebral hemorrhage and cerebral infarctions

Case	Age (>65 years)	Glucose (>200mg/dl)	Cholesterol (>220mg/dl)	EKG abnormality	Smoking	HTN (>5years)	DM (>5years)
Group A(n=12)	3	1	2	5	1	3	1
Group B(n= 6)	3	3	1	3	0	4	4
Total	6	4	3	10	1	7	5

Group A : Patients of hyperacute group, Group B : Patients of acute group

hemorrhage and cerebral infarctions depending on the period.

Several studies on the recurrence of strokes so far can be summarized. Despite the slightly different findings and opinions, the average period of recurrence is 35 months, and the recurrence rate of the cerebral infarction (88%) was more than that of intracerebral hemorrhage[27]. However, in the analysis on the recurrence periods of hypertensive intracerebral hemorrhage, the probability of recurrence within one year was 34% to 55.8%, and the probability of recurrence from one year to two years is 14% to 32.1%. In particular, the case of within 6 months had the highest frequency[3,30,31]. Differently from this, in the recurrence of cerebral infarction, the probability of recurrence within one month was 6%, 12% in the case of within one year, and 21% in the case of within 5 years, which indicates that the longer the period, the higher the probability[34]. We realized that it was very rare to see the recurrence period of within three weeks. Also, there has not been a study on recurred strokes of within three weeks so far.

According to studies on the recurrent types of strokes, the recurred cases of cerebral infarction were associated with atrial fibrillation and the carotid artery stenosis[10,26], while the cases of intracerebral hemorrhage were associated with the failure of controlling hypertension[6,11,19,24]. However, it is not statistically significant in the blood pressure change between at the first attack and at second recurrence in short-term coexisting intracerebral hemorrhage and cerebral infarctions in this study. Furthermore, of the subjects, there was only one patient related to atrial fibrillation, which proves that the risk factors of the recurrences of cerebral infarction as well as intracerebral hemorrhage are different from those of short-term coexisting intracerebral hemorrhage and cerebral infarctions.

In the prognosis, it has been known that when the strokes recur, it is worse than the previous one[4,13,25,34,35], however, we could not reach a conclusion over the prognosis depending on the recurrence interval.

According to studies on hypertensive intracerebral hemorrhage, the highest frequent lesion is located on basal ganglia or thalamus, the second frequent location is subcortex[3,11,14,24,30,31,33], and when it is recurring, the location moves to the other areas[3,11,14,24,31,33]. In addition to, it is reported that the recurrence showed the same type of stroke and same location[13]. In this study, short-term coexisting intracerebral hemorrhage and cerebral infarctions patients showed the similar recurrence features in the location of hypertensive intracerebral hemorrhage, while the second lesions tend to appear in different areas rather than the original one.

In the analysis of risk factors, it is revealed that abnormality on the EKG as well as more than five year history of hypertension occupy the highest frequencies in cases of short-term coexisting intracerebral hemorrhage and cerebral infarctions. This findings support the study of Baker et al. that cardiac stroke occupied 30 to 40% as the highest mortality cause of patients with recurred strokes[4].

Cholesterol was not found to be significant in this study. It reflects that there has been the controversy among studies so far about whether there is connection between serum cholesterol and strokes. To explain, it is reported that hyperlipidemia is one of the most critical risk factors in the stroke, and the case of the recurred stroke patients with hyperlipidemia appears to have a significantly high frequency[12]. On the contrary, there is a report that the low serum cholesterol cannot play a role of decreasing the rate of development or mortality of the stroke[2,21]. Therefore, it is reasonable to say that the analysis with more data and the prospective research are required to figure out the relation between short-term coexisting intracerebral hemorrhage and cerebral infarctions and cholesterol.

In this study, it is intriguing to find that the number of risk factors for short-term coexisting intracerebral hemorrhage and cerebral infarctions patients is 1.83 in average, while those of the acute coexisting intracerebral hemorrhage and cerebral infarctions is three, which is more than that of hyperacute coexisting intracerebral hemorrhage and cerebral infarctions patient group. Accordingly, patients with many risk factors do not tend to be the cases of hyperacute coexisting intracerebral hemorrhage and cerebral infarctions, and moreover, it is required to be vigilant to the change of patients' state up to three weeks in the treatment.

In addition, it is interesting that hyperacute coexisting intracerebral hemorrhage and cerebral infarctions patients group have less than five years of the diabetic history.

Lee et al. have concluded that the features of coexisting intracerebral hemorrhage and cerebral infarctions have not only the similar pathophysiological characteristics of lacunar infarction rather than that of cortical infarction, but also that of small vascular disease[17]. In the recent literature, asymptomatic cerebral microbleeds, which is seen to multifocal signal loss lesion in gradient-echo T2*-weighted Brain MRI have correlation to risk factors to recurrence of hemorrhagic stroke or ischemic stroke in patients of hypertension[15,20-22,28,32].

Cerebral microbleeds is affiliated with small vascular disease entity, therefore it can explain pathogenesis of coexisting intracerebral hemorrhage and cerebral infarctions for small vascular disease. But, there are still a point of question about interval of stroke, expression to different characteristics of stroke which are not enough to get conclusion.

Conclusion

The patients of this study suffered from the recurrence of different type strokes in a short period although they were

appropriately treated according to the cause of primary diseases. Based on the clinical features, there was no difference in the prognosis between hyperacute group and acute group. However there were noticeable aspects : one thing is that there are more risk factors of strokes in acute group, and another is that hyperacute group tend to have less than five years history of diabetes. For now, it is recommended that prospective studies on short-term coexisting intracerebral hemorrhage and cerebral infarctions with more subject number generating adequate data in order to reach more clear and concrete natural history.

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