Very Early Hemorrhagic Transformation of A Subcortical Infarction

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Abstract- Hemorrhagic transformation (HT) of an ischemic stroke within 6 hours has never been documented. We reported a case of 65-year-old female experiencing sudden onset of slurred speech and right side weakness. Her past history disclosed rheumatic heart disease and atrial fibrillation. The National Institutes of Health stroke scale (NIHSS) score was 20. The brain computed tomography one hour after symptom onset revealed a faint hypodense lesion in the left striatum. The lesion, however, was transformed spontaneously into a large hematoma within 3 hours of symptom onset. This case thus developed a very early HT of a subcortical infarct of possible cardioembolic origin and high initial NIHSS score. Though rare, very early spontaneous HT does happen.

Key Words: Hemorrhagic transformation, Cardiogenic embolic infarction, Ischemic stroke

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INTRODUCTION

Hemorrhagic transformation (HT) of ischemic cerebral infarcts is regarded as a consequence of arterial recanalization and reperfusion. It occurs chiefly in the cardioembolic patients (90%). Most HT of cerebral infarcts occurred within the first 48 hours[1,2]. In some of the reported cases, HT happened rather early, from the 6th to the 12th hours after the onset of the infarct[2,3]. HT that occurred within 6 hours of symptom onset, however, has not been reported yet.

Recent guidelines for acute stroke thrombolytic treatment recommend that intravenous tissue plasminogen activator (rt-PA) be given within 3 hours after symptom onset in order to reduce the risk of thrombolysis-related HT, which may have variable time courses, clinical presentations and outcomes[4,5]. In cases with cardioembolic cerebral infarction (CI) with high initial NIHSS score, there is no evidence that administration of intravenous tissue plasminogen activator (rt-PA) may precipitate or aggravate the bleeding from HT. However, the possibility remains and may obscure the true mecha-

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nism underlying the hemorrhage. Here we report a 65-year-old woman with a cardioembolic subcortical infarction that was transformed spontaneously into a large hematoma within 3 hours of symptom onset.

CASE REPORT

A right-handed 65-year-old woman was found to have rheumatic heart disease (RHD) and paroxysmal atrial fibrillation (Af) in recent 2 months due to exertional dyspnea. The medications given by cardiologists at the outpatient department was Digoxin (0.25 mg) 1# qd, Amiodarone (200 mg) 1# bid, and Benzyl hydrochlorothiazide (4mg) 1# qd. No antiplatelet or anticoagulant agent was prescribed. She was found to have slurred speech and weakness in the right limbs around 6:00 am April 19, 2001 at home. Her family recollected that she was rather well when she got up at 5 am that morning. Also, she was doing mild exercise without any difficulty about 30 minutes before symptom onset. She was sent to the emergency department of our hospital at 6:50 am The initial Glasgow coma scale (GCS) score was E3V3M5 and the National Institutes of Health stroke scale (NIHSS) score was 20 (detailed score listed in Table). Her heart rate was 70 beats per minute, and blood pressure was 130/70 mmHg. Irregularly irregular heart beats with midsystolic murmur of grade 3/6 at right upper sternal border was noted on auscultation. No eyeballs deviation or limitation of eyes movement was observed. Dysarthria, dysphagia, right central-type facial palsy and right hemiparesis with muscle power of 2/5 were noted. The deep tendon reflexes were symmetrical and plantar response was extensor on the right side. Right visual field defect was detected by threatening test. The other sensory modalities could not be reliably checked due to poor cooperation of patient. There was no past history of hypertension, diabetes mellitus, smoking, habitual drinking or drug abuse.

The initial computed tomography (CT) of brain was obtained at 7:10 am and revealed a faint hypodense area in the left striatum (Fig. 1). The initial condition of this patient met the criteria of thrombolytic treatment based on the current guidelines issued by Taiwan Stroke Society. Intravenous rt-PA or intra-arterial urokinase administration was suggested but the patient's family refused. At 8:50 am, Rapid deterioration of consciousness with the GCS score down to E2V1M5 was noted. The blood pressure at that particular moment was 139/97. Follow-up CT at 9:00 am revealed left striatal hemorrhage with rupture into ventricles (Fig. 2). The hematoma had irregular contour and heterogeneous content. Mild hydrocephalus and midline shift to the right side were also evident on the CT image. Mannitol (75 mg q6h IV infusion) was given to the patient.

Electrocardiogram showed atrial fibrillation rhythm. Transthoracic echocardiography revealed moderate calcified aortic stenosis, mild mitral regurgitation, mild calcified mitral stenosis, and aortic as well as tricuspid regurgitation. Electroencephalography displayed diffuse slow waves in both hemispheres. The hemoglobin, prothrombin time/normal control, and activated plasma thromboplastin time/normal control were 12.2, 10.6/12.2, and 29.6/30.8 respectively. Color-coded duplex sonography

Table. *The initial NIHSS score*

Items	Neurological deficit	score
1a. LOC	Stuporous	2
1b. LOC questions	Both incorrect	2
1c. LOC command	Both incorrect	2
2. Best gaze	Normal	0
3. Visual field	Complete hemianopia	2
4. Facial palsy	Partial paralysis	2
5a. Motor arm left	No drift	0
5b. Motor arm right	No effort against gravity	3
6a. Motor leg left	No drift	0
6b. Motor leg right	No effort against gravity	3
7. Limb ataxia	Absent	0
8. Sensory	Mild to moderate sensory loss	1
9. Best language	Severe aphasia	2
10. Dysarthria	Mild to moderate dysarthria	1
11. Extinction and inattention	No abnormality	0
Total score		20

* NIHSS: National Institutes of Health stroke scale; LOC: level of consciousness

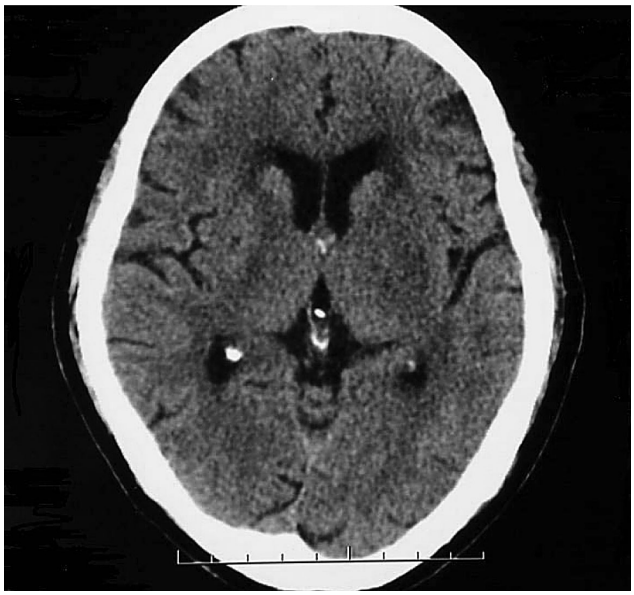

Figure 1. The initial brain CT shows low densities in the left subcortical area.

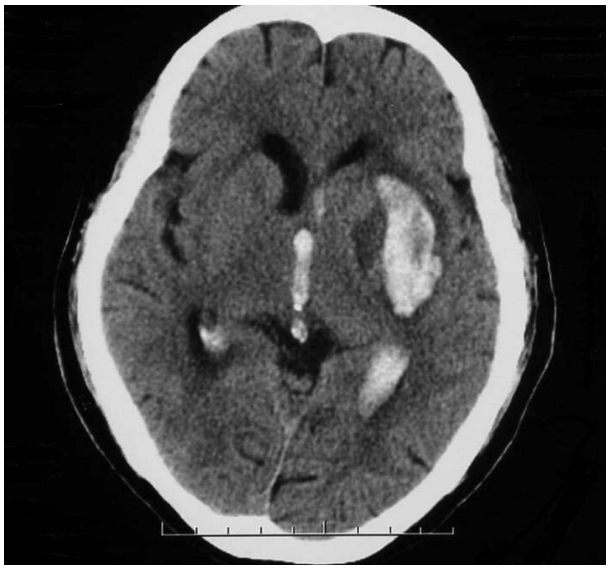

Figure 2. The following brain CT in 3 hours shows hemorrhagic transformation.

of the carotid arteries was performed 1 week later and no atherosclerosis was found. Inaccessible temporal window was noted by transcranial Doppler study (TCD).

During hospitalization, the patient's consciousness gradually and then fully recovered in 2 weeks after admission. Three weeks after onset, she was still hemiparetic but the NIHSS score decreased to 8. Three months later, she could raise her right leg and walked with assistance.

DISCUSSION

Previous studies on hemorrhagic infarction have demonstrated that cardioembolic origin, M1 occlusion, hyperglycemia, early focal hypodensity in brain CT, absence of collateral flow are important predictors of HT[6-8]. Cardioembolic stroke and large infarction have a higher incidence of HT[9]. For cardioembolic stroke, Molina et al. proposed that an NIHSS scale >14 on baseline, proximal MCA occlusion, hypodensity >33% of MCA territory, and delayed recanalization >6 hours of onset were significantly associated with HT[2,3]. This patient had a highly probable embolic source from the heart because of RHD and Af. There was neither carotid artery stenosis nor history of diabetes mellitus or hypertension[9]. The initial NIHSS score was high. Therefore, the risk of developing HT in this patient is high. However, most studies have speculated that the development of HT is delayed for 6-12 hours after cardioembolic stroke[1], and no previous report had demonstrated spontaneous HT within 6 hours of stroke onset.

In cardioembolic infarcts, the mechanism of HT is postulated to occur when embolic fragment migrated distally from its initial site of obstruction, allowing reperfusion of the damaged vascular bed (recanalization)[1]. Although delayed recanalization occurring >6 hours has emerged as an independent predictor of HT[3], recanalization developed in 3 hours had never been reported. The exact timing of recanalization in this patient, regrettably, could not be evaluated by ultrasound due to inaccessible temporal windows.

Thrombolysis-related HT had also been studied recently. Large petechial hemorrhage (PH) is the only type of HT which was correlated with clinical deterioration[4]. Kidwell et al. reported that higher NIHSS score (NIHSS score 0-5/HT 0%; 6-10/13%; 11-15/33%; 16-20/55%; 21-25/53%; ≧26/67%), lower platelet count,

longer time to recanalization, and elevated sugar level were important predictors of thrombolysis-related HT[10]. On the other hand, PH could also be a marker of early successful recanalization and leads to reduced infarction size as well as improved clinical outcome[5].

Except for an obvious cardioembolic source and a high initial NIHSS score, this patient did not have additional predictors of HT proposed by Group[11]. Because the first brain CT showed <33% hypodensity of MCA territory, the patient was eligible for thrombolytic treatment according to the protocol developed by the National Institutes of Neurological Disorders (NINDS). Also, cardioembolic cerebral infarction with high initial NIHSS score is not a contra-indication based on current treatment guidelines of IV rt-PA for acute cerebral infarction. There is not enough evidence for a definite increase of poor outcome in these patients after rt-PA treatment, although possibilities of aggravation of hematoma do exist. In any case, if this patient had received rt-PA treatment, the mechanism of HT would have been obscure. We do not mean to depreciate the value of rt-PA treatment in patients with large cardioembolic infarction. However, very early spontaneous HT does happen, though rare.

CONCLUSION

Spontaneous HT within 3 hours of stroke onset is rare. In cardioembolic ischemic stroke patients with a high initial NIHSS score, very early spontaneous HT does happen.

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