CASE REPORT

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"Brain Stunning" Atypical Feature of tPA Thrombolysis Following Aneurysm Embolization

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"Stunning" represents prolonged contractile depression of any muscular component after alleviation of severe ischemia, as shown in reperfusion following acute myocardial ischemia or ischemic stroke. Clinically, it presents with no or delayed recovery past to thrombolytic therapy but its pathogenic mechanism is not fully uncovered yet. We describe a unique case of a 63-year-old woman, who was undertaken endovascular coiling for the aneurysms, deteriorated several hours later without known cause, and showed delayed clinical improvement over the next 3 days following thrombolysis. Immediate post-thrombolysis magnetic resonance imaging scan showed no apparent abnormality except for high signal intensity within the corresponding hemisphere. Reversible, but delayed nature of "brain stunning" can be explained by these images and it seems to be caused by a certain type of reperfusion injury.

KEY WORDS : Acute ischemic stroke · Endovascular coiling · Magnetic resonance imaging · (Brain) Stunning · Thrombolytic therapy.

Introduction

Intravenous tissue plasminogen activator(tPA) thrombolysis can cope with the acute ischemic stroke(AIS) when selected cautiously, although its long-term outcome with regards to the relative efficacy is still questionable when comparing this to the intra-arterial route[4]. As reported earlier, some AIS patients treated with intravenous tPA showed early recanalization that was proved by transcranial Doppler(TCD), and they showed delayed clinical improvement. This phenomenon is newly termed as "brain stunning" and brain edema formation, no-reflow phenomenon with proximal or distal occlusion, and potential additional reperfusion injury were elicited as etiologic mechanisms[1,2]. Up to the present, there has been no single literature concerning magnetic resonance image(MRI) features for this peculiar condition in the very acute stage of stroke. We herein briefly summarize the case and try to implicate these findings.

Case Report

A 63-year-old woman with known multiple intracranial aneurysms came to our endovascular center for occlusion of the residual aneurysm at the left ophthalmic artery. On initial presentation, 13 months ago, the patient complained several episodes of visual loss in her left eye, characterized by "part of words disappearing" when she has been reading. Arteriogram demonstrated three aneurysms : the largest one at the left ophthalmic artery (13mm), at left clinoidal segment just proximal to the larger one (5mm), and at right internal carotid artery bifurcation (5mm) (Fig. 1A). Embolization by using Guglielmi detachable coils(GDC) (Target, Boston Scientific, Fremont, CA, USA) and Micrus coils (Micrus Endovascular, Sunnyvale, CA, USA) was performed to secure the ruptured left ophthalmic artery aneurysm. However, some residual filling of the anterolateral aspect of the aneurysm still remained at the conclusion of the procedure. She underwent uneventful microsurgical clipping for the right internal carotid artery bifurcation aneurysm, 3 months thereafter. Control arteriogram showed residual filling at the previously coiled aneurysm, measured 6mm in diameter. Two months prior to the present visit, endovascular coiling with stenting was tried to occlude 2 aneurysms on the left side under a general anesthesia. Before catheterization, systemic heparinization (5000 unit) and intra-arterial heparinization through the arterial sheath with

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pressurized flushing apparatus was done. Two Neuroform stents (Target, Boston Scientific, Fremont, CA, USA) measuring 4.5×20mm, 4.5×15mm were placed in correct position, and occlusion of the residual aneurysm was attempted. After stent deployment, Eptifibatide (Integrillin; Millennium Pharm., Cambridge, MA, USA) 15mg was systemically infused. But, coiling of the smaller superior hypophyseal artery aneurysm was only attained. She was discharged unremarkably.

At the present time, third embolization trial with 2mm ultrasoft GDC and 2mm MTI coils (Micro Therapeutics Inc., Irvine, CA, USA) were successfully carried out. The ophthalmic artery aneurysm was filled well at its base but slight coil protrusion into the carotid lumen occurred during the procedure. Protruded coil was removed with EXPRO Retrieval Microsnare (Radius Medical, Maynard, MA, USA) and Integrillin 15mg was injected intravenously in addition to the systemic heparin. Control arteriogram showed relatively well filled aneurysm (Fig. 1B). Postoperatively, the patient did well immediately, but she developed left hemispheric ischemic stroke 7 hours later and it became more clearly evident. She showed severe expressive aphasia and right hemiplegia. After taking normal computed tomography(CT) scan of head (Fig. 2A), she was consulted to the stroke team and intravenous tPA was given within 2 hours of her symptom onset together with coumadin and aspirin. An immediate post-thrombolysis MRI scan showed no definite evidence of stroke (Fig. 2B), however, repeated MRI was needed to clarify her unnoticeable clinical improvement the next day. Remarkably, T2 weighted fluid attenuation inversion recovery(FLAIR) images showed high signal intensity lesion filled with sulci and cisterns of the left hemisphere (Fig. 2C). Her hemispheric symptoms gradually resolved during the next 3 days to the baseline. Follow-up carotid angiogram disclosed no responsible or newly developed lesions and she was discharged with some instructions.

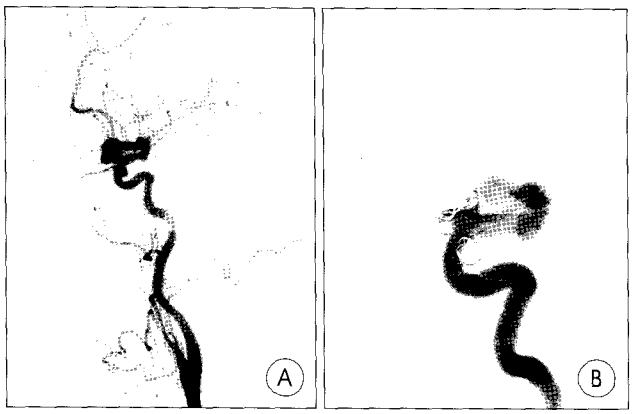

Fig. 1. A : Initial left carotid arteriogram demonstrates two aneurysms located at the ophthalmic artery and at the clinoidal segment. B : On complication of the third coiling, arteriogram shows that two neuroform stents (4.5×20mm, 4.5×15mm) are placed correctly, and the ophthalmic artery aneurysm is filled well at its base.

Discussion

The term "stunning" or "hibernation" is originally used to explain pathophysiologic process of the myocardial ischemia (reversible ventricular dysfunction) and either of two forms may be involved to produce this condition. The former is defined as prolonged contractile depression after alleviation of severe ischemia (i.e. reperfusion after coronary occlusion), whereas the latter represents reversible dysfunction during severe chronic ischemia. Some biochemical mechanisms, such as alteration of cyclic adenosine monophosphate(cAMP), heat shock protein, and regulatory protein in cardiac Ca^{2+}-cycling, were found to be responsible for this temporary cardiac shut down. Repetitive stunning is supposed to be the principle mechanism of hibernation, but exact differentiation between the two is not always possible in clinical ground[6].

With regard to the brain tissue, similar phenomenon (brain stunning) was already described in clinical situations that AIS patients treated with intravenous tPA. Either persistence of arterial occlusion or emergence of early reocclusion appears to be the most common cause of early clinical fluctuation and worsening after thrombolytic therapy for ischemic stroke. Several potential mechanisms may predispose brain tissue to ischemic stunning. They are edema formation without hypoattenuation, no-reflow phenomenon with or without persistent distal occlusion, proximal reocclusion, and possibly additional reperfusion injury that may be targeted by different combination therapies with thrombolysis[1,2].

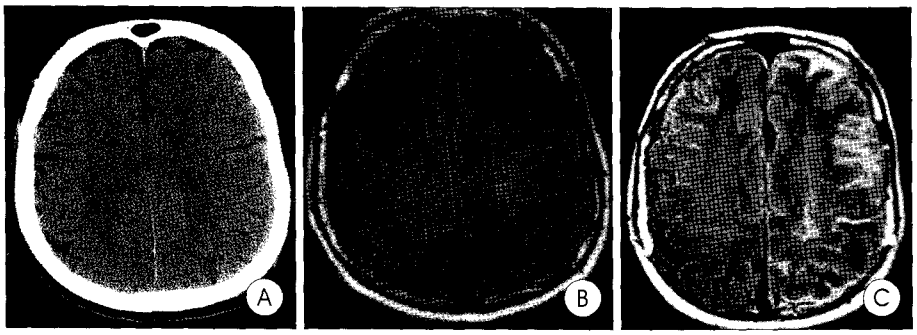

Fig. 2. A : Computed tomography scan obtained immediately following clinical deterioration shows normal finding except lacunar infarcts. B : Immediate post-rescue magnetic resonance image scan also shows no definite evidence of stroke. C : Repeated magnetic resonance image scan, 1 day following thrombolytic therapy. Axial T2 weighted fluid attenuation inversion recovery image shows high signal intensity filled with the entire sulcal spaces of the left hemisphere.

Until now, as for the surveillance and imaging of the AIS patients

involved, only TCD and serial neurologic examinations have been utilized for real time monitoring[3]. Concerning brain CT, hypoattenuation after AIS is reported to be highly specific for irreversible brain injury only if detection occurs within the first 6 hours. Patients without hypoattenuation have a more favorable course. And, a normal CT finding in this setting can be explained by focal ischemia above the critical cerebral blood flow level of structural integrity, by ischemia confined to white matter, or by an early stage of ischemic edema causing hypoattenuation below contrast resolution[8].

In the current case, we could not point out the exact mechanisms of postembolization clinical deterioration and delayed recovery after tPA thrombolysis. Because CT scans failed to reveal causes of deterioration, diagnosis of the AIS was given to the patient solely based on the clinical ground. According to Patel et al[7], patients treated with tPA eventually did better whether they had AIS shown on CT scan or not, suggesting that AISs on CT scan are not critical to the decision to treat otherwise eligible patients with tPA within 3 hours of stroke onset. In animal experiment, intravenous tPA thrombolysis seemed to be relatively safe only if embolization preceded no longer than 6~12 hours[5]. Urgent intravenous tPA infusion was justified, but it was followed by delayed clinical improvement of 3 day-duration. Consecutive MRI scans, taken immediately after and 1 day following the tPA thrombolysis, were different in T2 weighted FLAIR images. Within one day, finding of sulcal effacement with high signal on the whole left hemisphere, instead of ischemic or hemorrhagic changes, was newly developed. Normal control angiogram added the evidence of this non-structural, clinical dysfunction. We found no literature written about the occurrence of post-tPA brain stunning following endovascular coiling. These interesting MRI features will be helpful to characterize brain stunning when encountering similar situation. We hypothesize that temporary no-reflow phenomenon with resultant edema formation after tPA infusion is the most suitable explanation for this non-structural presentation.

Conclusion

This is, to our knowledge, the first case report regarding MRI finding of brain stunning. The MRI only showed subarachnoid space that was filled with high signal intensity, instead of hemorrhage or infarction. Brain stunning may occur in the same clinical condition to the present case and therefore, high index of suspicion should be given to such patients, especially when characteristic high signal FLAIR MRI following tPA thrombolysis was shown.

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