“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 route5. 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 mechanisms1,5,9. 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 Micros coils (Micros 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
pressurized flushing apparatus was done. Two Neuroform ste-
nts (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, Epifibatide (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 ul-
trasound GDC and 2mm MPA coils (Micro Therapeutics Inc.,
Irvine, CA, USA) were successfully carried out. The ophthal-
mic artery aneurysm was filled well at its base but slight coil
protrusion into the carotid lumen occurred during the pro-
cEDURE. Protruded coil was removed with EXPLO Retriev-
ner Microsnare (Radius Medical, Maynard, MA, USA) and In-
tegrillin 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 stro-
ke 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 co-
umadin 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 ca-
rotid angiogram disclosed no responsible or newly developed
lesions and she was discharged with some instructions.

**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 se-
vere chronic ischemia. Some biochemical mechanisms, such
as alteration of cyclic adenosine monophosphate (cAMP), heat
shock protein, and regulatory protein in cardiac Ca2+-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.

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 recollusion appears
to be the most common cause of early clinical fluctuation and
worsening after thrombolytic th-

ery for ischemic stroke. Several
potential mechanisms may predis-
pose brain tissue to ischemic stun-
ing. They are edema formation
without hypoattenuation, no-reflow
phenomenon with or without pe-
sistent distal occlusion, proximal
recollusion, and possibly additional
reperfusion injury that may be tar-
ged by different combination the-
rapies with thrombolysis.

Until now, as for the surveil-

ance and imaging of the AIS patients
involved, only TCD and serial neurologic examinations have been utilized for real time monitoring\(^9\). Concerning brain CT, hypoperfusion after AIS is reported to be highly specific for irreversible brain injury only if detection occurs within the first 6 hours. Patients without hypoperfusion 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 hypoperfusion below contrast resolution\(^9\).

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\(^6\). 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.

**References**