An early successful surgical treatment of fibrinolysis-related symptomatic intracerebral hemorrhage without procoagulant therapy

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ABSTRACT

تخثر الدم مع الأنسجة المأشوبة لمنشط مولد البلازمين يعد علاج فعال لعلاج الجلطة الدماغية الحادة. ولكن استعمال علاج تخثر الدم ملازم ويرفع من خطورة نزف داخل المخ. ومازال سبب نزف داخل القحف الذي يحدث بعد قطع القحف خلال الساعات الأولى بعد العملية غير معروف. نستعرض هنا تقرير لامرأة صينية تبلغ من العمر 69 عام ومصابة بانحلال الفبرين المصاحب لنزف داخل المخ وسنناقش في هذا السياق فعالية وأمان قطع القحف. تم إزالة ضغط القحف بشكل عاجل من خلال طريقة تريون بدون استخدام أي علاج محفز للتخثر قبل العملية. ولم يظهر أي نزف جراحي غير مقبول خلال الساعات الأولى بعد ظهور نزف داخل المخ ونتائج هذه المريضة مقبولة نوعاً ما. يعد إزالة ضغط القحف لعلاج انحلال الفبرين المصاحب لنزف داخل المخ علاج فعال وقد يطور من النتائج الإكلينيكية.

Thrombolysis with recombinant tissue plasminogen activator (rt-PA) is clinically effective at treating acute ischemic stroke. However, the use of thrombolytic therapy is associated with an increased risk of symptomatic intracerebral hemorrhage (sICH). Whether unacceptable surgical hemorrhage occurs after emergent decompressive craniotomy during the first hours for sICH remains unknown. We report a 69-year-old Chinese woman with a fibrinolysis-related sICH, and discuss the efficacy and the safety of craniotomy in this setting. An urgent decompressive craniotomy was performed through a standard pterional approach without any procoagulant therapy before operation. No unacceptable surgical hemorrhage occurred during the first hours after onset of sICH, and the outcome of this patient is fairly good. Early urgent decompressive craniectomy in the treatment of fibrinolysis-related sICH may be a safe therapy, which may improve clinical outcomes.

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Thrombolysis with recombinant tissue plasminogen activator (rt-PA) is clinically effective at treating acute ischemic stroke.[1] However, the use of thrombolytic therapy is associated with an increased risk of symptomatic intracerebral hemorrhage (sICH) in 3-9% of patients treated intravenously with tPA. Whether unacceptable surgical hemorrhage occurs after emergent decompressive craniotomy during the first hours for sICH remains unknown.[2] We report a 69-year-old Chinese woman with a fibrinolysis-related sICH, to discuss the efficacy and safety of emergent craniotomy in this setting.

Case Report. A 69-year-old woman was admitted to our emergency department, one hour after the onset of left-sided weakness, slurred speech, and left-sided facial droop. Her medical history, obtained from the patient's family included hypertension, cardiopathy, and diabetes mellitus for at least 10 years. Home medications included metformin (Novo Nordisk, Tianjin, China), insulin (Sine, Shanghai, China), nifedipine (Disha, Weihai, Shandong, China), and enalapril (Pidi, Kaiping, Guangdong, China). She did not smoke, use illegal drugs, or drink alcohol. She was found to have a blood pressure of 120/55 mm Hg, and a regular heart rate of 72/min. The CT scan of the head

was normal (**Figure 1**), and she was diagnosed with an acute ischemic stroke. After consulting a neurologist, rt-PA (Actilyse, Boehringer Ingelheim, German, 0.9 mg/kg) was administered intravenously at 2 hours and 30 minutes after the onset of hemiparesis, but her weakness and speech did not improve initially. Approximately 8 hours later, the patient was found sleepy, with a Glasgow Coma Scale score of 11, and a reactive right dilated pupil. A repeated cerebral CT scan demonstrated a right malignant middle cerebral artery (MCA) infarction, and massive cerebral intraparenchymal hemorrhage with a temporal and subfalcine herniation (**Figure 2**). An urgent decompressive craniotomy was performed through a standard pterional approach, and the hematoma was macroscopically removed. Red blood cell (2 U) and cryoprecipitate (2 U) were transfused during the operation. There was no extensive capillary hemorrhage, or obvious difficulties with hemostasis in this operation. Due to the high risk of cerebral herniation and urgent need of craniotomy, the patient did not receive any procoagulant therapy before the operation as her coagulation parameters were almost normal (prothrombin time/activated partial thromboplastin time - 11.1/23.6 s [normal value: 10-14/22.7-32.7 s]; and fibrinogen - 1.56 g/l [normal value: 1.8-3.7g/l. A follow-up CT scan performed at 24 hours from operation showed almost no secondary intracerebral hemorrhage (**Figure 3**). At 6 months follow-up, the patient was ambulating with left hemiparesis, had excellent comprehension with mild expressive aphasia, and was living dependently at home.

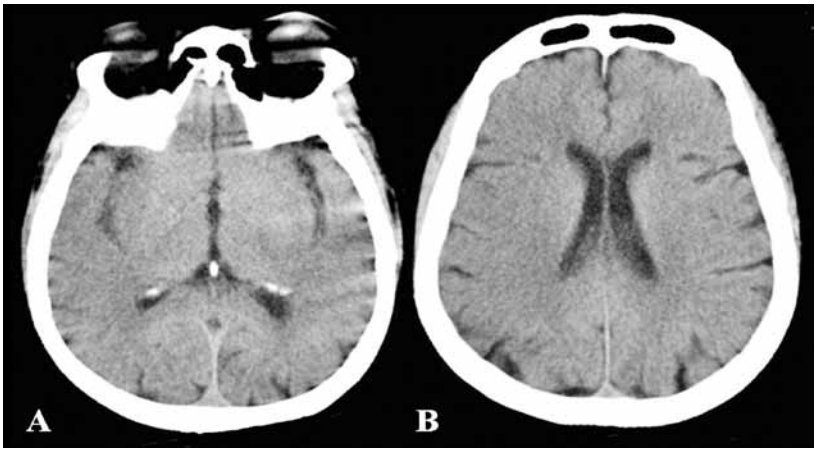

Figure 1 - Computed tomography scans performed less than 2 hours after symptom onset. Baseline CT scans showed no obvious hypo-attenuation with swelling or effacement in any regions (**A** & **B**).

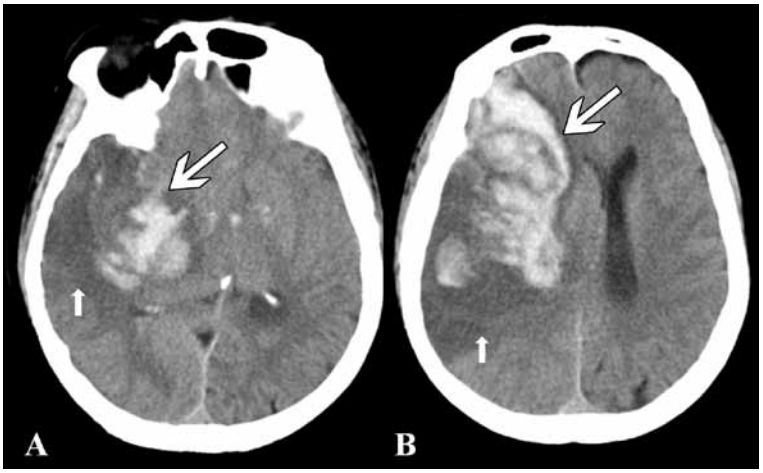

Figure 2 - A preoperative CT scans showed: **A**) right malignant middle cerebral artery infarction (short arrow); and **B**) massive intracerebral hemorrhage (long arrow).

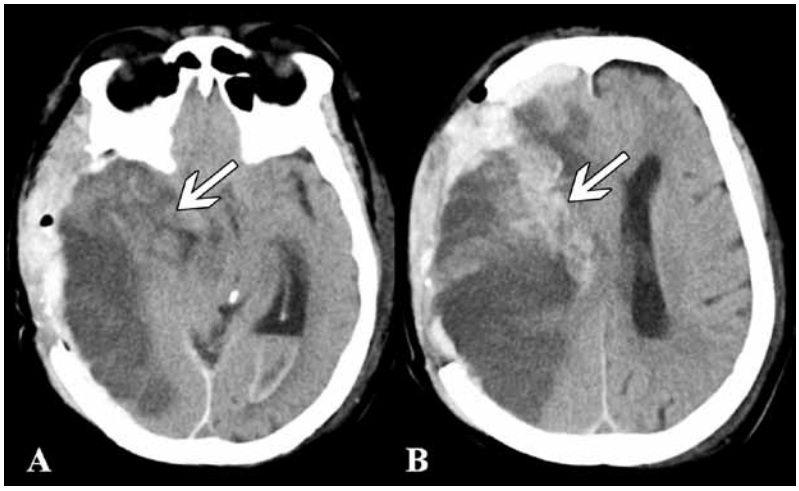

Figure 3 - Postoperative CT scans (**A & B**) showed a decompressive craniectomy with almost no secondary intracerebral hemorrhage (arrows).

Discussion. Intravenous administration of rt-PA is currently the only FDA-approved therapy for treatment of patients with acute ischemic stroke, and sICH is the most feared complication of this therapy.[3] The onset of sICH after fibrinolysis carries a poor prognosis, because these hemorrhages tend to be massive, multifocal, and associated with a 30-day death rate of 60% or more.[4,5]

In this patient, early urgent decompressive craniectomy after sICH has improved clinical outcome possibly. However, the risks of fibrinolysis-associated hemostasis in this urgent operation have not been established. The American Heart Association suggests empirical therapies to replace clotting factors and platelets to control this sICH.[2] At the same time, they acknowledge the lack of evidence to support any specific therapy.[2] Otherwise, a more recent study[1,6] mentioned that currently used rt-PA dosing regimens (alteplase, 0.9 mg/kg) may unlikely induce hypofibrinogenemia and sICH following rt-PA may not be the result of the systemic fibrinolytic state, but reperfusion of cerebral vessels, whose integrity has been disrupted by severe ischemia.[7] Consistently, no extensive capillary hemorrhage and obvious difficulties with hemostasis was observed in our case.

In summary, there are no evidence-based guidelines that address management of fibrinolysis-associated sICH. The experience and result of surgical treatment for such patient has not been mentioned before. The major contribution of this paper is to raise awareness of the safety of early urgent decompressive craniectomy in the treatment of fibrinolysis-related sICH, which may improve clinical outcomes. More randomized clinical trials are needed to demonstrate the safety, or any recommendation for emergent neurosurgical operation with this deadly type of fibrinolysis- associated sICH.

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