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Small but Severe Residual Hypoperfusion Relates to Symptomatic Hemorrhage Even after Early Perfusion Improvement in Tissue Plasminogen Activator Therapy

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Background

Symptomatic intracerebral hemorrhage (sICH) is the most unfavorable complication arising after intravenous tissue plasminogen activator (tPA) therapy. In multivariate analyses of sICH after tPA therapy, a high serum glucose level [1], a large diffusion-weighted imaging (DWI) lesion volume [2] and late reperfusion after persistent arterial occlusion [3] are regarded as independent predictors; however, we encountered a tPA-treated patient with sICH, which was not applicable to the above predictions. We present this case and discuss a relationship between the development of sICH and findings of early posttreatment single-photon emission computed tomography (SPECT).

Case Report

A 70-year-old man who did not take any regular medication presented at the emergency room 73 min after the sudden onset of an impaired level of consciousness, dysarthria, left-sided hemiparesis and left-sided neglect. His NIHSS (National Institutes of Health Stroke Scale) score was 16. His blood pressure was 121/87 and his laboratory data showed glucose 126 mg/dl, a platelet count of 192,000/mm³ and normal liver and kidney function. DWI showed small ischemic changes in the head of the right caudate nucleus, the periventricular area and the frontal cortical area (fig. 1a). MR angiography revealed occlusion of the M1 segment of the right-middle cerebral artery (MCA) (fig. 1b). Since the head of the caudate nucleus is usually supplied by the recurrent artery of Heubner, in addition to MCA, branches of the right anterior cerebral artery were thought to be occluded. After confirming that the patient met all eligibility criteria for tPA therapy, administration of a total dose of 0.6 mg/kg tPA with 10% of the dose given as a bolus was started at 140 min after onset according to the directions for the use of tPA in Japan. His symptoms improved from 30 min after the start of the tPA infusion and his NIHSS score was 7 by the end of it. ^{99m}Tc-ethyl cysteinate dimer SPECT imaging 1 h after the end of the tPA infusion revealed a mild hypoperfusion in the cortex of the right MCA territory and a small but severe hypoperfusion in the head of the right caudate nucleus (fig. 1c, d). The early clinical improvement and the SPECT findings suggest that early perfusion improvement due to an increase in collateral flow or partial recanalization occurred in the MCA territory except for in the right caudate nucleus. Although post-treatment vital signs and the neurological status were uneventful,

Fig. 1. MRI, SPECT and CT of the case in our study. **a** DWI on admission showed small high signals in the head of the right caudate nucleus, the periventricular area and the frontal cortical area. **b** MR angiography on admission showed an absent flow signal in the M1 segment of the right MCA. **c** ^{99m}Tc-ECD SPECT imaging 1 h after tPA infusion showed a mild hypoperfusion in the cortex of the right MCA territory and a small but severe hypoperfusion

in the head of the right caudate nucleus. **d** Cerebral blood flow in the area enclosed by the circle in the ipsilateral side was 12.3 ml/100 g/min and the ipsilateral/contralateral cerebral blood flow ratio was 0.39. **e** CT scan 13 h after tPA infusion showed a huge high density mass in the head of the right caudate nucleus, which extended into the lateral ventricle.

he had a convulsion 13 h after tPA therapy and then lapsed into a near coma. CT scan showed massive sICH in the head of the right caudate nucleus, which had ruptured into the lateral ventricle (fig. 1e). The next day, he underwent external ventricular drainage, but his modified Rankin scale score remained 5 with dementia and severe left-sided hemiparesis 3 months after onset.

Discussion

In this case, although the patient did not have a large DWI lesion and indeed showed marked clinical improvement in his symptoms after tPA therapy, he developed sICH which resulted in severe brain damage. In this situation, we have to predict the development of sICH by a method other than the DWI lesion volume. Perfusion imaging may be helpful for this purpose. Recently, it has been demonstrated that regional, very low cerebral blood volume in bolus contrast MRI predicts hemorrhage better than DWI lesion volume or threshold apparent diffusion coefficient lesion volume [4, 5]. In this case, ^{99m}Tc -ECD SPECT imaging demonstrated that a small but severe hypoperfusion area was colocalized in the center of sICH (fig. 1c, e). These results suggest that a severe perfusion deficit may promote the development of sICH in tPA therapy, but further clinical studies are needed to confirm this.

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