

Letter to the Editor

## Successful outcome after endovascular thrombolysis for acute ischemic stroke even after 24 h of symptoms onset?

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Sir,

I read with great interest the article by Mattei *et al.* reporting a patient with acute ischemic stroke (AIS) who was treated with mechanical thrombectomy and additional intra-arterial thrombolysis more than 24 h after the onset of the initial symptoms.<sup>[6]</sup> As a result, complete vessel recanalization was experienced and a significant improvement in the neurological sequela was achieved. I agree with the strictly valuable aspect of this rare case; however, I would like to comment on some points hoping to provide a better understanding of the issue.

First, a crucial discussion may be about the evaluation processes of the patient up to the time of clinical worsening. The patient had admitted 10 h after symptom onset and the initial MRI had showed diffusion restriction on the right globus pallidus and head of the caudate nucleus. However, the patient had presented with progressive worsening of neurological status 12 h after admission to Emergency Department; second magnetic resonance imaging (MRI) had showed significant compromise of the perfusion in the whole right middle cerebral artery (MCA) territory and magnetic resonance angiography (MRA) had showed occlusion of the right MCA at the M1 segment. However, no data of any antiplatelet or anticoagulant therapy administered in the interval period from arrival to the clinical worsening (stated as 12 h) was mentioned in the report. Oral administration of aspirin within 24–48 h after stroke onset is recommended for treatment of most patients outside the therapeutic window and unsuitable for thrombolysis (Class I, Level of Evidence A).<sup>[5]</sup> On the other hand, this is also evidence recommending anticoagulation in some specific stroke subtypes, including cardioembolic stroke and stroke with documented intraluminal thrombus or arterial

dissection.<sup>[7]</sup> Taken together, although the prognosis of the patient was good, I think that clinical evaluation of this patient should be enlightened in detailed. I wonder if the authors might indicate that if any anticoagulant or antiplatelet agent was administered before thrombectomy procedure to avoid misleading conclusions for clinical approaches.

Second, another topic of discussion may be about the rationale of administrating thrombolytic treatment in this case. The analyses of the crucial studies of ECASS I, ECASS II, ATLANTIS A, and ATLANTIS B focusing on the efficiency of use of intravenous recombinant tissue plasminogen activator (rtPA) up to 6 h after stroke onset revealed that administration of rtPA in the specifically 4.5-h to 6-h window resulted in higher parenchymal hematoma (6.9% to 1.0%) and mortality rates (15% to 10%).<sup>[1-4]</sup> Considering the limitation of major side effect of parenchymal hematoma in AIS, intravenous

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thrombolysis is recommended in the time period of 3–4.5 h after stroke (Class I, Evidence B), whereas it is estimated as <6 h for endovascular interventions (Class I, Evidence B).<sup>[5]</sup> Hence, interpreting the course of this patient in whom thrombolytic therapy was administered more than 24 h after the initial symptoms may give misleading results and should be discussed very deliberately.

Although, some very crucial limitations mentioned above, I agree that this report constitutes an extremely substantial illustration of a devastating experience for the area of acute stroke community. The authors emphasize the need for future studies to determine the utility of distinct factors (other than the time from initial symptoms) such as MRI perfusion/diffusion-weighted imaging (PWI/DWI) mismatch for basing the decision making in these patients. I agree with the importance of this consideration of that multimodal evaluation of patients with stroke is essential. On the other hand, I also think that this case may draw attention to the need for future studies to determine differing therapeutic windows for thrombolysis in distinct subtypes of ischemic stroke scenarios. For instance, secondary worsening in minor strokes in the setting of progression of partial major artery occlusions to total occlusions as hypothesized in this case may constitute an interesting topic for future, prospective studies. A crucial question at this point may be that if the secondary worsening time of symptoms in these patient subtypes can be assumed as the starting point during evaluation of the therapeutic window for thrombolytic therapy? In conclusion, the interesting course of this patient may add crucial perspectives remarking that understanding the mechanisms in acute stroke as well as determination of the accurate treatment method is an extremely hard and complicated matter. In addition, there seems to be still many discussions to be elucidated

in future reports in this area. Addressing these points in the future studies may add substantial perspectives to the fields of AIS approach as well as understanding of the underlying pathophysiological processes.

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### Conflicts of interest

There are no conflicts of interest.

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