

## Case Report

**Successful thrombolysis of a wake-up stroke aided by Computed Tomography Perfusion (CTP) imaging: A case report**

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**Abstract**

An 80-year-old man was admitted with aphasia since wakeup. His Computed Tomography Perfusion (CTP) study of the brain revealed a significant but patchy penumbra with a minimal core. His Magnetic Resonance Imaging (MRI) also confirmed a mismatch between Diffusion-weighted MRI (DWI) and fluid-attenuated inversion recovery (FLAIR) sequences (DWI-FLAIR mismatch) supporting the existence of a significant ischaemic penumbra. He underwent thrombolysis with tenecteplase (TNK) after 5 hours and 40 minutes since waken up and had a good recovery with the improvement of the National Institute of Health Stroke Scale (NIHSS) from 5 to 0. Acute stroke patients could benefit from thrombolysis beyond the window period of 4.5 hours if there is a significant penumbra in the CT perfusion imaging and tenecteplase may have an added advantage over alteplase (t-PA) in such circumstances.

**Keywords:** Computed tomography perfusion imaging, Ischaemic stroke, Wake-up stroke, Tenecteplase

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**Introduction**

Stroke is the second leading cause of mortality and the third leading cause of disability worldwide (1). Acute ischaemic stroke results from obstruction of a cerebral blood vessel. Patients who are fortunate enough to arrive at a well-equipped health care facility within 4.5 hours from the onset of stroke symptoms may undergo thrombolysis with an intravenous recombinant tissue plasminogen activator (r-tPA-alteplase) or tenecteplase (2). However, patients whose onset is unknown or whose presentation is delayed more than 4.5 hours still have a chance of benefiting from thrombolysis if they undergo thrombolysis after careful assessment. To do so, a more

sensitive tool other than non-contrast CT is required to determine the ischaemic penumbra. Computed tomographic perfusion imaging (CTP) and magnetic resonance imaging (MRI) with DWI/FLAIR mismatch are standard techniques useful in these situations, but CT perfusion is more valuable due to its availability and ability to produce quicker results (3). We report the first successful case of CTP and MRI aided thrombolysis of a wake-up stroke in Sri Lanka.

**Case report**

An 80-year-old previously healthy man was admitted to the emergency treatment unit (ETU) of the Teaching Hospital, Anuradhapura at 1020 hours with the inability

to speak since he woke up around 0630 hours. He had been well when he went to bed the previous night, and family members had observed his speech disturbance after waking up. He was accompanied by his son, hence a collateral history was taken. They had not noticed any difficulty in walking, limb weakness or facial asymmetry. The patient was mute and unable to comprehend and respond. The patient was a non-smoker and a teetotaler.

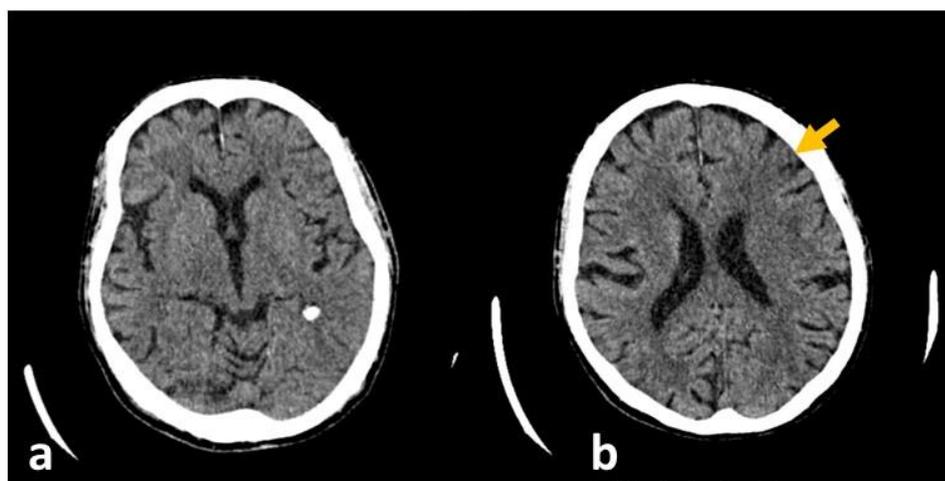
On examination, the patient demonstrated severe expressive aphasia, and he could make only a few incomprehensible sounds with impaired speech reception indicating global aphasia. There was no limb weakness, and his gait was normal. He had no gaze palsy, and bilateral pupils were equally responsive to the light. He exhibited no facial weakness. We could not perform visual field assessment, cerebellar assessment or the test to check extinction or inattention due to his receptive aphasia. The ultimate score of his National Institute of Health Stroke Scale (NIHSS) was 5. At ETU, he had a regular pulse with a rate of 62 beats per minute and blood pressure of 130/90 mmHg. His random blood sugar level was 90 mg/dl.

From the initial assessment, he had no substantial contraindications to undergo stroke thrombolysis, except the uncertain time of onset. So, the patient underwent an urgent Non-Contrast CT Brain at 1035 hours, and it did not show any well-formed infarction, but some blurring of left frontal grey-white matter demarcation and lentiform nucleus (figure 1). The Alberta stroke program early CT score (ASPECTS) was 7 out of 10. Due to unknown time of onset, an urgent CTP was performed,

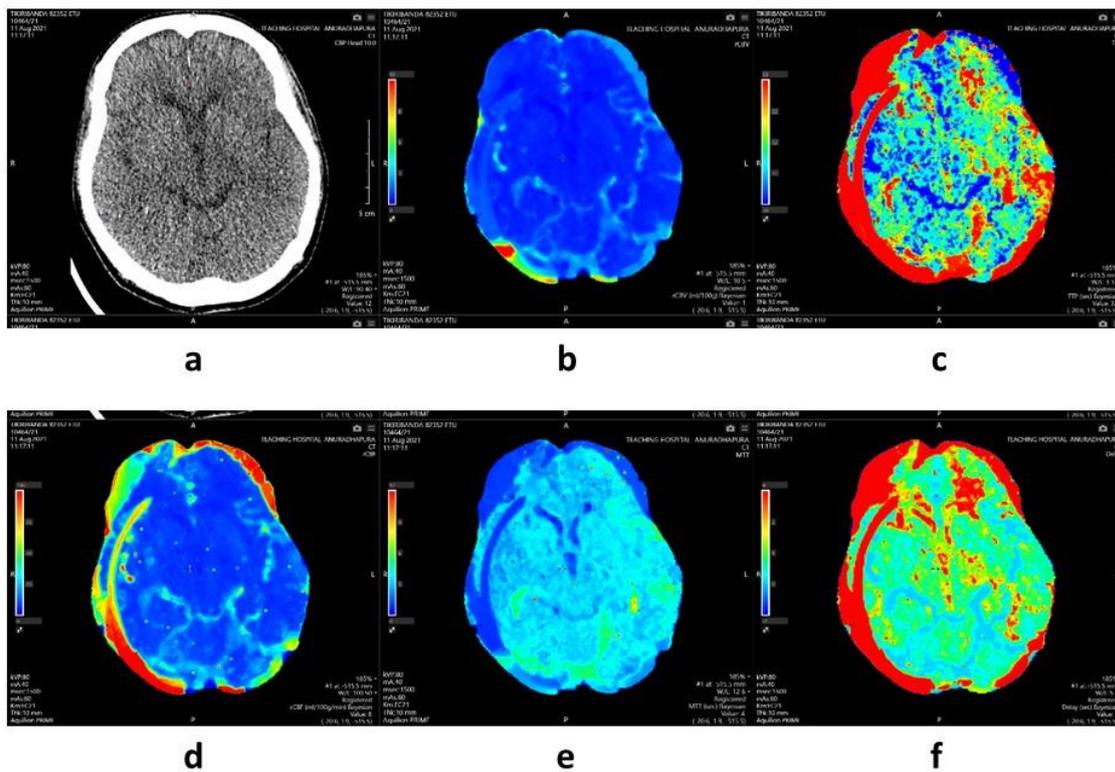
and it showed the prolonged time to peak-TTP (figure 2c) and mean transit time-MTT (figure 2e) in left frontal and temporal regions in a patchy distribution with normal cerebral blood volume-CBV in the same area (figure 2b) suggestive of a large but patchy penumbra with an insignificant core. At the same time, the patient underwent a Magnetic Resonance Imaging (MRI) scan, and it confirmed the presence of patchy acute ischaemic areas over the left MCA territory on the DWI sequence (figure 3a) and the absence of similar lesions in the FLAIR sequence (figure 3b) suggestive of a hyperacute stroke (DWI/FLAIR mismatch). With these findings, it was decided to treat the patient with intravenous thrombolysis. As the patient was not eligible to give valid consent due to his global aphasia, the decision was taken in the best interest of the patient and conveyed to his son. The thrombolysis was performed at 1210 hours with a weight-adjusted standard dose of tenecteplase 13.75 mg (0.25 mg/kg of body weight) instead of alteplase after consideration of the time factor due to prolonged onset to needle time (5 hours and 40 minutes).

The patient did not develop any post thrombolysis complications and gained marked improvement leading to a reduction of NIHSS from 5 to 0 at 24 hours after thrombolysis, demonstrating complete clinical recovery. Post thrombolysis NCCT performed after 24 hours revealed a small Infarction involving the left frontal lobe.

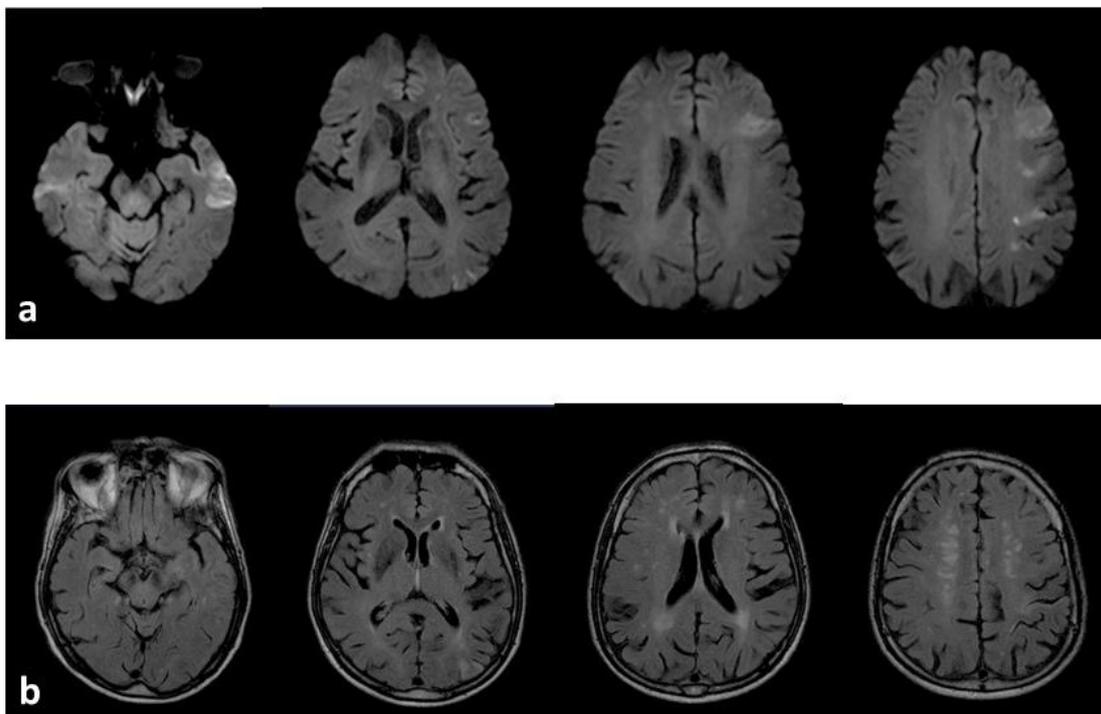
His carotid arterial doppler study revealed a soft plaque at the bifurcation of the left common carotid artery resulting in 53% of luminal narrowing, which could have been the most likely source of embolic clots.



**Figure 1:** Non-contrast computer tomography brain taken at 1035 hours: (a), blurring of the left lentiform nucleus; (b), blurring of an area of left frontal grey-white demarcation (arrow)



**Figure 2:** CTP images;(a) Plain CT, (b) Normal CBV, (c) Prolonged Tmax in left hemisphere, (d) Normal CBF,(e) Prolonged MTT in left hemisphere, (f) Prolonged delay in left hemisphere.



**Figure 3:** (a), MRI-DWI images showing patchy hyperintense lesions in left cerebral hemisphere; (b), MRI – FLAIR images showing no equivalent hyperintense lesions to DWI lesions.

## Discussion

This case report demonstrates the successful use of CTP imaging and MRI imaging in thrombolysis of a wake-up stroke with unknown onset time.

Studies such as European Cooperative Acute Stroke Study (ECASS), Alteplase Thrombolysis for Acute Noninterventional Therapy in Ischemic Stroke (ATLANTIS), National Institute of Neurological Disorders and Stroke (NINDS), and Echoplanar Imaging Thrombolysis Evaluation Trial (EPITHET) helped to demonstrate the effectiveness of the thrombolysis therapy in acute ischaemic stroke (3-6). Updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials proved that the patients with acute ischaemic strokes who present within 4.5 hours would benefit from intravenous thrombolysis with alteplase (r-tPA), and the benefit can be maximized by reducing the time interval between onset and thrombolysis (7).

Because a delay of more than 4.5 hours increases the risks of haemorrhage, a delay of more than that became an exclusion criterion among numerous other criteria for thrombolysis. However, when thrombolysis was established, the exclusion criteria were far stricter, and those were subsequently eased to allow more patients to undergo thrombolysis. One such trial was the "Third European Cooperative Acute Stroke Study" (ECASS - 3), which demonstrated benefit in individuals presenting more than three hours after stroke onset. The trial concluded that thrombolysis with alteplase is advantageous up to 4.5 hours after the onset of the stroke (3).

EXTEND, ECASS 4-EXTEND, and EPITHET studies evaluated the efficacy of intravenous thrombolysis in patients with ischaemic strokes 4-5–9 hours after onset or wake-up strokes based on perfusion-diffusion MRI or CT perfusion imaging and demonstrated better functional outcomes (8).

Interestingly, our case suggests that thrombolysis yields promising results in patients even after 4.5 hours if patients are chosen with precision. After 5

hours and 40 minutes from wake-up with stroke symptoms, our patient benefited from thrombolysis because the CT perfusion study and MRI with DWI and FLAIR revealed a reasonably large penumbra with a minimally infarcted core.

A study by Szithra *et al.* revealed that the CT perfusion mismatch model might help the decision of thrombolysis up to 6 hours after the onset time, which demonstrated comparable results to the group thrombolysed within 3 hours of symptom onset using NCCT (9).

Instead of alteplase, our patient received thrombolysis with tenecteplase. While alteplase is the most often used medication for acute ischaemic stroke thrombolysis, tenecteplase demonstrated non-inferior safety and probably better recanalization rates compared to alteplase (10,11). Tenecteplase offers an advantage over alteplase in terms of preparation and administration time. Tenecteplase is administered as a single 5-second intravenous bolus, whereas alteplase is administered as a bolus followed by a 60-minute infusion. This is useful in delivering an effective dose of the thrombolytic agent in a short period of time, especially for patients with a significant penumbra who present late.

## Conclusion

Thrombolysis is a well-established therapeutic intervention for acute ischaemic stroke. Nonetheless, many patients lose the opportunity to undergo thrombolysis due to delayed presentation and the strict exclusion criteria in place. As observed in this case, patients who present beyond 4.5-hour window can undergo thrombolysis aided by CTP and /or MRI and benefit from it. Additionally, it is time to consider using tenecteplase for thrombolysis, which is more feasible, cheaper and may provide an added benefit over alteplase in cases who present late. However, this must be validated and integrated into regular practice through appropriate large-scale trials.

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