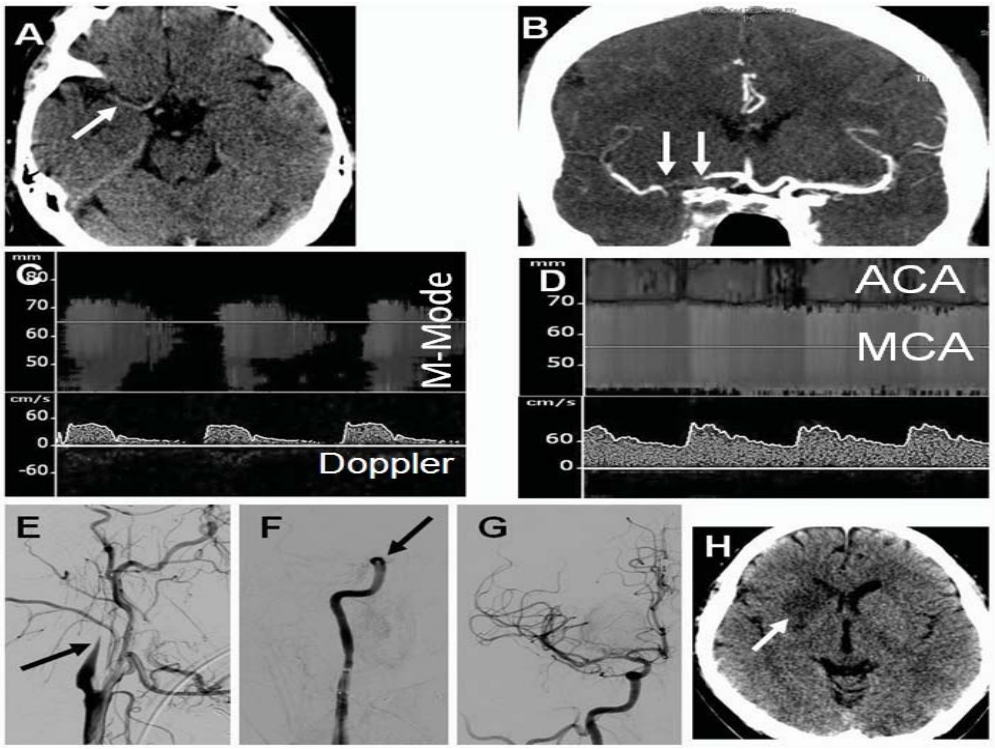
Multimodal Therapeutic Approach in Acute Ischaemic Stroke with Real-time Neurovascular Monitoring

Dear Editor,

Intravenously administered tissue plasminogen activator (IV-TPA) induces thrombolysis and remains the only FDA-approved therapy for acute ischaemic stroke (IS) within the therapeutic time-window according to the current guidelines. However, significantly low recanalisation rates have been demonstrated with intravenous thrombolysis alone. Ultrasound monitoring during IV-TPA infusion[1] and mechanical embolectomy[2] have been reported to enhance the rates of arterial recanalisation. We report a patient with severe acute IS in whom the multimodal therapeutic approach resulted in an excellent recovery. Our patient who underwent continuous neurovascular monitoring and temporal sequence of clinical events in real-time has been described.

Case Report

A 63-year-old Chinese man presented 40 minutes after developing acute left-sided weakness while playing with his granddaughter. He had been taking regular medications for hypertension and did not suffer from any other significant medical illness in the past. On arrival to the hospital, he was conscious but disoriented to time and place. Flaccid weakness (Medical Research Council grade 0) was noted on the left side with right-gaze deviation. National Institute of Health Stroke Scale (NIHSS) score was 19 points. Cardiac rhythm showed atrial fibrillation with a pulse rate of 68 beats per minute and blood pressure 138/68mmHg. Emergently performed non-enhanced computerised tomography (CT) of the brain showed hyperdense right middle cerebral



Figs. 1 A to H. Multimodal neurovascular monitoring in acute ischaemic stroke. Initial unenhanced computerised tomography (CT) of brain shows a 'hyperdense middle cerebral artery (MCA) sign' (1A). CT angiography confirms the presence of an occlusive lesion of the right MCA (1B). Transcranial Doppler ultrasonography before TPA bolus demonstrated occlusion of right MCA as detected by TIBI grade 1 flow (1C). Improved flow (TIBI grade 5) in right MCA at 23 minutes after TPA bolus (1D) demonstrates complete recanalisation. Carotid angiography (1E) shows an occlusion of the right proximal internal carotid artery (ICA). Angiogram repeated after removal of the proximal ICA clot demonstrates a tandem occlusive lesion of right terminal ICA (1F). Mechanical retrieval of the terminal ICA clot results in complete recanalisation of right ICA and MCA with all the distal branches (1G). CT scan repeated after 24 hours shows a right striatocapsular infarction (1H).

artery (MCA) sign (Fig. 1A). CT angiogram of the brain demonstrated occlusion of right proximal MCA (Fig. 1B). Intravenous thrombolysis with TPA in the standard dose (0.9mg/Kg body weight) was commenced at 85 minutes from symptom-onset. Continuous transcranial Doppler (TCD) monitoring (SONARA-Nicolet Viasys) was performed during TPA infusion to assess the blood flow in right MCA. The temporal sequence of clinical events was:

1100 H	Onset of symptoms
1140 H	Arrived at emergency department and evaluated by neurologist (attending neurologist received the patient as he was informed during patient's transfer to the hospital). NIHSS-20 points.
1150 H	Brain CT and CT angiogram performed.
1220 H	TPA bolus given. TPA infusion and TCD monitoring started. TCD showed TIBI (Thrombolysis in brain ischaemia) grade-1 flow signals in right MCA (Fig. 1C).
1242 H	Complete recanalisation (TIBI grade-5) of right-MCA (Fig. 1D).
1245 H	Clinical improvement noted. Power- MRC grade 4 in left extremities. NIHSS-9 points. Normal flow signals persisted in right MCA. Frequent micro-embolic signals (MES) noted in right MCA during next 35 minutes.
1320 H	TPA infusion completed. NIHSS-7 points.
1325 H	Carotid duplex ultrasonography (GE Logiq-5) performed due to frequent MES in right MCA. A large'fresh'mobile thrombus seen in proximal right internal carotid artery (ICA).
1340 H	Power in the left upper limb deteriorated (MRC grade 2). NIHSS 11 points. Frequent MES noted but right MCA flow remains normal. Neuro-interventionalist activated. No further neurological worsening or fluctuations.
1450 H	Carotid angiography revealed the thrombus occluding the right proximal ICA (Fig. 1E). Clot removed from right ICA (MERCI® retrieval system) but another occlusion noted at right terminal ICA (carotid-T) (Fig. 1F).
1455 H	Clot removed from right terminal-ICA by MERCI® retrieval system. Angiography demonstrated complete recanalisation of right-ICA as well as MCA and its distal branches (Fig. 1G).

Mechanical embolectomy by MERCI® retrieval system was performed under general anaesthesia, according to the interventionalist's preference. The patient was kept on mechanical ventilation for about 15 hours. After extubation, the only abnormality noted on neurological examination was mild left facial asymmetry (NIHSS-1point). Assessment of his functional status revealed modified Rankin scale of 1. CT scan of the brain performed on day 2 showed a right striato-capsular infarction (Fig. 1H). Although difficult to substantiate, we believe that a large area of the right cerebral hemisphere was salvaged with this therapeutic approach. He was commenced on anticoagulation for secondary stroke prevention and discharged within 72 hours of symptom-onset. He returned to normal activities within a week.

Our case demonstrates that early arterial recanalisation in acute IS results in a good clinical recovery, especially in the presence of some residual flow at the site of intracranial occlusion on TCD.[3] Fast-track neurovascular assessment by cerebrovascular ultrasononography[4] and neuroimaging contributed towards optimal therapeutic decision-making.

Ultrasound exposure of the clot with 2-MHz TCD during TPA infusion may enhance the rates of arterial recanalisation as well as clinical recovery.[1] We often perform continuous TCD-monitoring in our patients during thrombolytic therapy, as per the CLOTBUST-trial protocol.[1,5] In addition to potentially enhancing clot-lysis by TPA, TCD monitoring provides valuable information about cerebral haemodynamics, arterial patency and recanalisation in real-time as well as detects spontaneous MES.[4]

We performed an urgent cervical duplex sonography in search of the source of frequent MES in right MCA even after achieving recanalisation. A 'fresh' hypoechoic and mobile thrombus was noted in the right proximal ICA. Initiating any antithrombotic therapy (anticoagulants or even antiplatelet agents) is not recommended within 24 hours of TPA therapy. Furthermore, some clinical deterioration prompted us to seek the help of an experienced neuro-interventionalist. Our approach might be interpreted as too-aggressive and potentially 'risky', especially after treatment with full dose of IV-TPA and achieving a significant neurological recovery (improvement of NIHSS score by 9 points). However, our decision for an urgent neurointervention proved appropriate since the ICA clot had fragmented and embolised into the terminal ICA (revealed by angiography performed just prior to the clot removal).

Early arrival to the hospital, rapid clinical assessment and fast-track neurovascular evaluation contributed towards timely institution of thrombolytic therapy. In addition to possible augmentation of the thrombolytic activity of TPA, continuous 2-MHZ TCD guided us to diagnose the carotid thrombus and subsequent intervention. The multimodal therapeutic approach resulted in an excellent clinical outcome and our patient returned to normal activity within few days of a potentially devastating stroke. Our case highlights the importance of a comprehensive acute stroke centre where coordinated 'team-effort' by various members could result in better clinical outcomes.

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