

Turning a stroke into a TIA: curative thrombolysis with combined intravenous and intra-arterial tPA

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ABSTRACT

Intravenous tissue plasminogen activator (tPA) is standard treatment for eligible patients with acute ischemic stroke, but may be less effective for very severe strokes caused by proximal intracranial artery occlusions. We report the case of a woman with a devastating stroke who recovered completely following emergency revascularization of an occluded proximal middle cerebral artery using a novel treatment approach that combines both intravenous (IV) and intra-arterial (IA) tPA. This case illustrates the potential value of the combined IV-IA thrombolytic approach, which is an emerging investigational treatment strategy for selected patients with severe acute ischemic stroke.

Key words: acute ischemic stroke; intravenous tPA; intra-arterial tPA; IV-IA thrombolytic approach

RÉSUMÉ

L'administration intraveineuse de l'activateur tissulaire du plasminogène (tPA) représente le traitement standard pour les patients admissibles ayant subi un accident vasculaire cérébral (AVC) ischémique, mais peut se révéler moins efficace pour les AVC très graves causés par l'occlusion d'une artère intracrânienne proximale. Nous présentons le cas d'une femme ayant subi un AVC dévastateur qui s'est rétablie complètement à la suite de la revascularisation d'urgence d'une artère cérébrale moyenne proximale occluse grâce à un nouveau traitement qui combine l'administration de tPA à la fois intraveineuse (IV) et intra-artérielle (IA). Le cas présenté illustre la valeur potentielle de cette nouvelle stratégie de traitement expérimental chez des patients sélectionnés ayant subi un AVC ischémique aigu très grave.

Introduction

In Canada, intravenous tissue plasminogen activator (tPA) has become standard care for eligible ischemic stroke patients who can be treated within 3 hours of symptom onset.¹ However, with intravenous tPA, the chance of suc-

cessful angiographic recanalization is low for proximal large artery occlusions (only 9% for carotid occlusions and 35% for M₁-MCA [M₁ segment middle cerebral artery] occlusions) and best for distal branch occlusions (54% for M₂-MCA occlusions and 66% for M₃-MCA occlusions).² Therefore, for patients with severe stroke, there is growing

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interest in moving beyond IV tPA alone and combining it with IA thrombolysis or techniques for mechanical clot removal or disruption.

Case report

Toronto emergency medical services paramedics transported a 52-year-old previously healthy woman to our regional stroke centre under an acute stroke prehospital redirect protocol 29 minutes after symptom onset. Examination revealed signs of a major right MCA stroke: forced gaze deviation to the right, complete left hemiplegia,

hemisensory loss, and severe hemispatial neglect (anosognosia and extinction to tactile, visual and auditory stimuli). The National Institutes of Health Stroke Scale (NIHSS) score was 17 and the ECG showed rapid atrial fibrillation. Computed tomography (CT) 30 minutes after arrival demonstrated a hyperdense MCA, and CT angiography confirmed a 1.4-cm M₁ segment MCA occlusion (Fig. 1). Early ischemic changes were already present (Fig. 1 [left]) but a larger area of potentially salvageable “tissue at risk” was identified on CT perfusion imaging (Fig. 2).

A 0.6-mg/kg intravenous dose of tPA (alteplase) was ad-

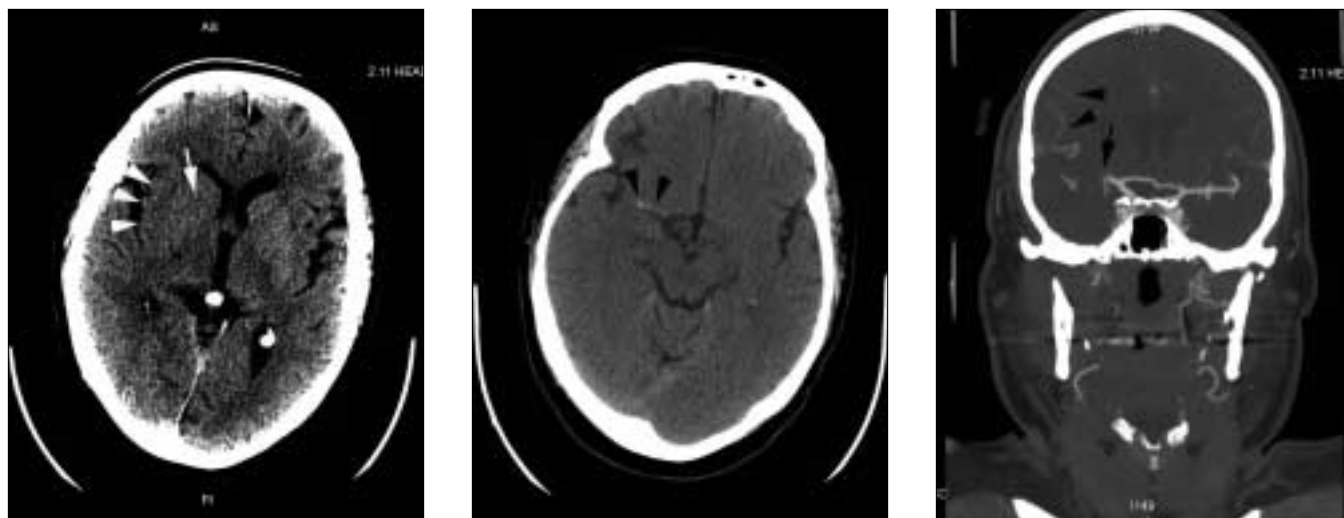


Fig. 1. *Left*: Baseline unenhanced CT head shows hypoattenuation of the corpus striatum (white arrow) and insula (arrowheads) (ASPECTS score 7). *Middle*: A right hyperdense middle cerebral artery (MCA) sign (black arrowheads). *Right*: Contrast-enhanced CT angiogram demonstrates an abrupt cut-off of the first segment (M₁) of the MCA (black arrow) with good collaterals over the perisylvian region (black arrowheads), shown with a coronal reformat slice. Note the correlation with the pre-procedure angiogram in Fig. 3, left).

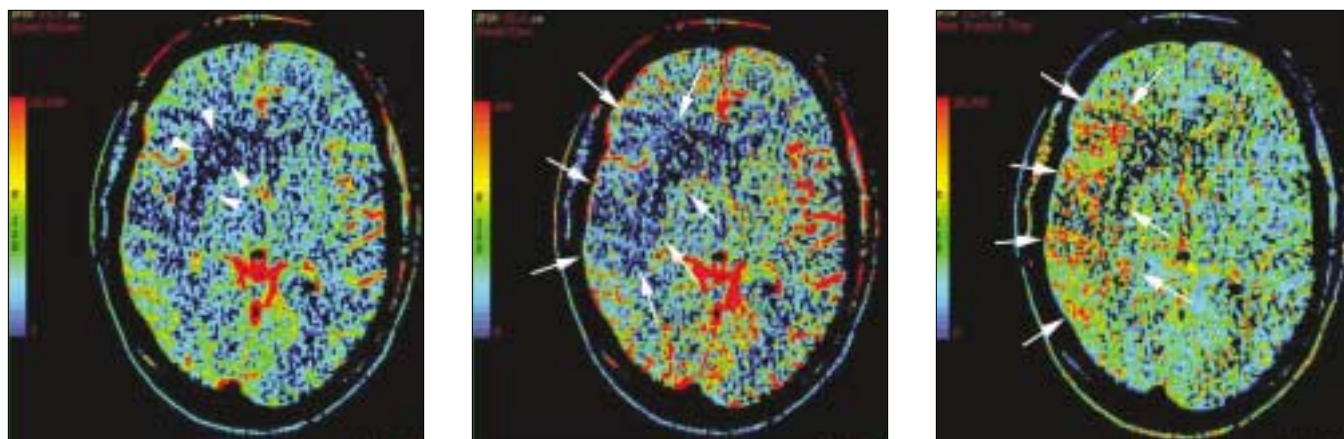


Fig. 2. Baseline CT perfusion imaging confirms (*Left*) preservation of cerebral blood volume except for some reduction within the area of hypoattenuation seen in Fig. 1 Left (white arrowheads), surrounded by reduced cerebral blood flow (*Middle*) and prolonged mean transit time (*Right*) within a larger distribution (white arrows) of the right middle cerebral artery territory (including temporo-occipital and frontal lobes). This mismatch between reduced blood flow and the area of preserved cerebral blood volume is consistent with an ischemic penumbra.

ministered, with 15% given as a bolus, followed by a 30-minute infusion (symptom onset-to-needle time was 89 min). The patient was transported to the angiography suite 105 minutes post-onset, where a diagnostic angiogram confirmed that the M₁ segment occlusion was still present (thrombolysis in myocardial infarction [TIMI] classification 0) (Fig. 3 [left]). An Excelsior 1018 microcatheter (Boston Scientific, Redmond, Wash.) was advanced over a Transend EX platinum (Boston Scientific) 0.36-mm wire through the thrombus into the M₂ segment. After imaging the distal circulation, the catheter was withdrawn while a total of 14 mg of alteplase was administered by intermittent slow injections beyond and directly into the thrombus. The patient experienced a focal epileptic seizure toward the end of the procedure, correlating with reperfusion.

Following the procedure, complete recanalization was achieved (TIMI 3) (Fig. 3 [right]) with immediate dramatic clinical recovery. There were no clinical complications. Post-angiography CT scan showed contrast enhancement of the right basal ganglia, which cleared the following day. A focal area of contrast extravasation was also present in the posterior putamen, compatible with blood–brain barrier breakdown; a susceptibility-weighted magnetic resonance imaging study later confirmed asymptomatic microhemorrhage. The patient was ambulating the next day and discharged home with no detectable neurologic deficit. Re-examination 3 weeks later confirmed a complete neurologic recovery: NIHSS score 0, Folstein Mini Mental State Examination 30/30, Barthel Index 100/100, and normal performance on the Sunnybrook Neglect Assessment Procedure for hemispatial inattention. She was able to resume all her indepen-

dent daily activities. She was prescribed oral anticoagulation for secondary stroke prevention.

Discussion

This case demonstrates that acute stroke thrombolysis can be very effective in the appropriate candidate. Without treatment, spontaneous recovery would not have been expected given the extent of the proximal MCA thrombus and the early neuroimaging signs of evolving infarction.

A hyperdense MCA sign on baseline CT³ correlates with severe stroke and predicts a poor outcome, even after treatment with IV tPA.⁴ We used an acute stroke imaging protocol consisting of plain head CT, CT angiography, CT perfusion, and post-contrast head CT (total scan time approximately 2 min), which can facilitate patient selection for thrombolysis by providing rapid information about the vascular lesion, extent of infarction and presence of potentially salvageable brain tissue.

The PROACT II Trial demonstrated that IA thrombolysis with prourokinase within 6 hours is an efficacious treatment for MCA occlusions, with improved outcomes in treated patients compared with placebo in terms of recanalization rate (66% v. 18%) and favourable clinical outcome on the Rankin Scale (40% v. 25%), but a higher rate of symptomatic intracranial hemorrhage (10% v. 2%).⁵ However, IA thrombolysis is available only at selected stroke centres as an “off-label” intervention. Our preferred term for this treatment is “intra-clot lysis” to distinguish it from infusion of an intra-arterial thrombolytic proximal to the target occlusion, for example, from the carotid artery in the neck.

Because favourable outcomes from tPA are highly depen-

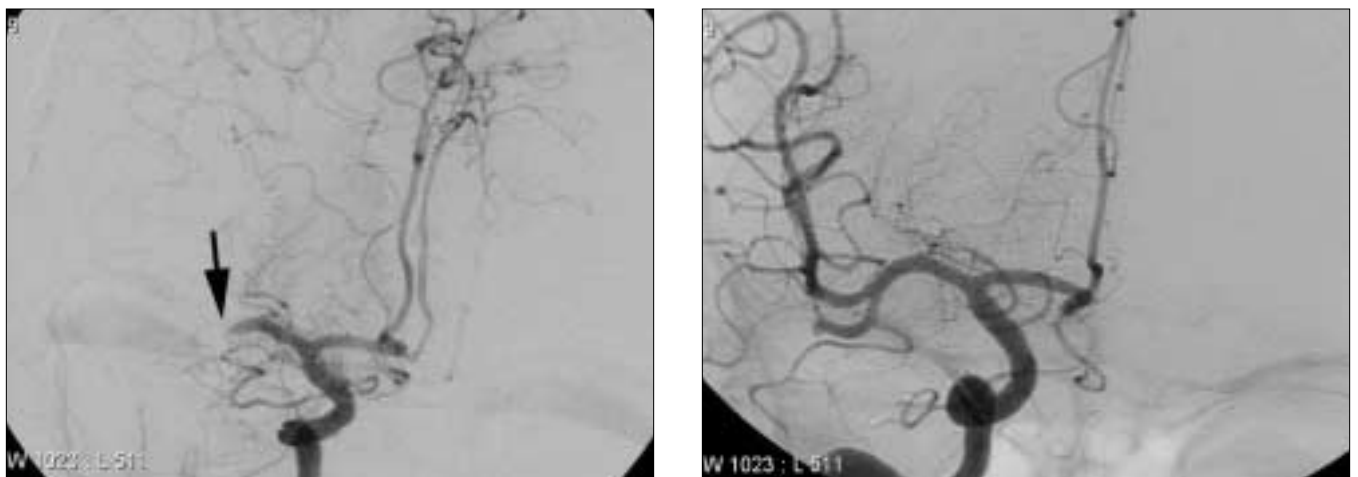


Fig. 3. Procedural catheter digital subtracted angiogram. *Left:* Pre-treatment angiogram shows occlusion of proximal right middle cerebral artery (thrombolysis in myocardial infarction [TIMI] classification 0; black arrow). *Right:* Post-treatment angiogram shows complete recanalization (TIMI 3), which correlated with immediate neurological recovery.

dent on shorter stroke onset-to-needle times,⁶ immediate administration of a partial dose of IV tPA first (two-thirds of the standard dose) has the advantage of initiating treatment quickly while the patient is being transferred for angiography for direct intra-clot lysis. The EMS Bridging Trial, which randomized 35 patients, showed that the IV–IA combination approach improved recanalization rates compared with IA treatment alone.⁷ Safety and feasibility of this combined IV–IA approach was further demonstrated in an IMS study of 80 patients with a 6.6% symptomatic intracranial hemorrhage rate,⁸ and in 2 smaller prospective studies.^{9,10}

The IMS-III Trial (www.uc.edu/news/NR.asp?id=3136) aims to provide more definitive investigation about the efficacy and safety of the combined IV–IA thrombolytic approach.

Conclusions

Many centres are gaining experience using the combined IV–IA thrombolytic approach as a treatment option for carefully selected individuals with severe acute ischemic stroke, although it remains an investigational procedure that awaits further study in randomized trials.

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