Hemorrhagic Transformation And A New Ischemic Accident During Thrombolysis Treatment With rtPA

A Hernandez, M Rochera, R Angles, M Farre, J Caballero

Citation

Abstract
Administration of intravenous recombinant tissue plasminogen activation (rtPA) administered within 3 hours of symptom onset is an effective therapy for acute ischemic stroke (1,2). The efficacy of thrombolysis has been demonstrated despite an increased risk of severe hemorrhagic transformation (HT) in patient treated with rtPA. (3) We report a case of acute ischemic stroke in a woman who during thrombolysis treatment with rtPA suffered an intracerebral haemorrhage and a new ischemic stroke on the opposite side.

CASE HISTORY
A 68 year old woman non-smoker was transferred from another hospital to our A&E department 80 minutes after an abrupt onset of left side weakness and difficulty in speaking. Past medical history included hypertension and paroxysmal atrial fibrillation without on aspirin or any other anticoagulant therapy.

On arrival in the emergency room, patient underwent standard cardiological and neurological examination. Patient was haemodynamically stable, blood pressure (BP) was 140/60 mm Hg. The ECG revealed atrial fibrillation (AF) with rapid ventricular response while the routine laboratory tests and chest X-Ray were within normal limits. The neurological examination revealed left flaccid hemiplegia, facial weakness and dysarthria 100 min from onset of symptoms. GCS was 14/15 and the corresponding National Institutes of Health Stroke Scale (NIHSS) score was 18 on admission. The AF was reverted back to sinus rhythm by giving 300 mg Amiodarone intravenously.

Urgent non-contrast CT scanning was performed which showed normal findings. (Fig 1) Carotid ultrasonography study did not show any occlusion and the cerebral arteries were insonated through the temporal window with a standard Transcranial Doppler ultrasonography (TCD). Spectral wave forms from the proximal middle cerebral artery (MCA) were obtained at a depth of 45 to 65 mm from the left and right transtemporal window. On the right side a minimal, grade 1 signal as measured on the TIBI scale with absent diastolic flow is seen on power-motion Doppler images and spectral-transcranial Doppler images.

She was eligible for thrombolytic treatment (Table 1), the usual monitoring of BP, temperature, and glucose levels were done according to the European Stroke Initiative recommendations (4). BP was 140/68, heart rate-96 bpm, temperature-36.4°, oxygen saturation-97%, BM-166 mg/dl. Thrombolysis was initiated according to European Cooperative Acute Stroke Study (ECASS) II criteria within the 6-hour time window (5) and she was given rtPA in a standard 0.9-mg/kg dose (10% bolus, 90% continuous...
infusion during 1 hour) 160 minutes after of symptoms onset.

During infusion of rtPA, the patient showed a brief neurological improvement (NIHSS 12) and TIBI grade 3 dampened signals (i.e. cycles with positive end-diastolic flow) indicating the beginning of the recanalization of the proximal middle cerebral artery.

However immediately after this improvement, a rapid neurological deterioration and deterioration of consciousness was evidenced (NIHSS 23). The vital parameters at this point were BP-220/160, HR- SR122 bpm, temperature-38.4°C, and BM-115 mg/dl. GCS had dropped down to 6, pupils were equal, miotic although reactive.

Hence a repeat CT scan was performed which showed ischemic cerebral infarction in the deep of right middle cerebral artery, corresponding to malignant middle cerebral artery syndrome. 12 hours after stroke onset, CT scan was repeated and MRI performed, which revealed HT in the existing right cerebral infarct and a development of a new ischemic cerebral infarction on the left side. (Fig 2). Patient was transferred to intensive care unit and unfortunately died 10 days later.

**DISCUSSION**

The National Institute of Neurological Disorders and Stroke (NINDS) recombinant tPA (rtPA) Stroke Study showed a clear benefit for intravenous rtPA in selected patients with acute stroke. The rationale for thrombolysis for acute ischemic stroke is recanalization of occluded arteries to reestablish brain function by saving tissue at risk. Although the time windows from onset of symptoms to treatment can be up to 180 minutes, the evaluation will require at least 30 minutes in most cases (CT scan, laboratory test performed and results returned, IV access obtained, and neurological exam and history). Indications for administration of intravenous recombinant tissue plasminogen activator (rtPA) for acute ischemic stroke are shown on Table 1.

**Table 1: Indication for rtPA treatment**

<table>
<thead>
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<th>Indication</th>
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<td>Clinical diagnosis stroke</td>
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<td>Onset of symptoms to time of drug administration &lt;= 3 h</td>
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<td>CT scan showing no hemorrhage or edema of &gt; 1/3 of the MCA territory</td>
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<tr>
<td>Age over 18 years</td>
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<td>Consent by patient or surrogate</td>
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The beneficial effect obtained by thrombolysis-induced recanalization may be counteracted by an increased risk of HT. The relationship between reperfusion and HT and the contribution of early and delayed recanalization after thrombolysis to the risk of HT remains uncertain. The risk of intracranial hemorrhage appears to rise with larger strokes, longer times from onset of symptoms, and higher doses of rtPA administered.

**Table 2: Increased intracranial hemorrhage risk with rtPA treatment**

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<tr>
<th>Risk Factor</th>
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<td>Older age</td>
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<tr>
<td>Female sex</td>
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<tr>
<td>Black ethnicity</td>
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<td>Systolic blood pressure &gt;= 140 mmHg</td>
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<tr>
<td>Diastolic blood pressure &gt;= 100 mmHg</td>
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<tr>
<td>History of stroke</td>
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<tr>
<td>rtPA dose &gt; 1.5 mg/kg</td>
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<tr>
<td>Lower body weight</td>
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Although HT is a complication of thrombolysis treatment, a new ischemic accident occurring during thrombolysis treatment is a very rare complication. The patient had an acute cardio-embolic stroke in the MCA territory because she had atrial fibrillation on admission, and suffered a massive infarction of the territory of the right middle cerebral artery with HT episode. The cause of the infarction on the opposite side was unknown although we think that probably she may have had a thrombus in the atrium which during thrombolytic therapy led to a new thromboembolic accident.

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References

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