

Case Report

Safety of Repeated Reperfusion Therapy (Thrombolysis and Trombectomy) in Early Recurrent Stroke: A Case Report

Šupe Svjetlana¹, Blažević Nikola^{1*}, Poljaković Zdravka¹, Ozretić David², Ljevak Josip¹, and Perić Ivan¹

¹Department of Neurology, School of Medicine, University Hospital Centre Zagreb, Croatia

²Department of Neuroradiology, School of Medicine, University Hospital Centre Zagreb, Croatia

***Corresponding author**

Nikola Blažević, Department of Neurology, School of Medicine, University of Zagreb, Bednjanska 14, 10 000 Zagreb, Croatia, Tel: 385-99-768-5262; Email: blazevicnikola1@gmail.com

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Abstract

Thrombolytic therapy with Recombinant Tissue Plasminogen Activator (r-tPA) for acute ischemic stroke (AIS) is well established stroke treatment for almost three decades such as mechanical thrombectomy (MT) in the last 10 years. Current guidelines for thrombolytic treatment of AIS cited a history of previous stroke within 3 months as a contraindication to re-thrombolytic treatment, which has not been changed since the beginning of the use of r-tPA for AIS treatment.

These recommendations are based on assumed complications with increased risk of symptomatic intracerebral hemorrhage, hypersensitivity reactions, neurotoxic effect and blood-brain barrier disruption, associated with re-administration of r-tPA in early recurrent stroke with a consequent poor functional outcome. The risk of AIS recurrence within 3 months is about 14-18%, which strictly based on these guidelines, excludes a large number of patients who suffered a stroke recurrence for repeated intravenous thrombolysis (RIVT), regardless of the needs or possibility for MT. In recent years, some large case series and case reports have confirmed the safe and effective use of RIVT in early recurrent AIS (ERAIS), without a significant increase in bleeding risk or poorer clinical outcome. We present the case of patient with ERAIS within 54 hours in whom we conducted RIVT in combination with repeated mechanical thrombectomy with satisfactory functional recovery.

ABBREVIATIONS

ERAIS: Early Recurrent Acute Ischemic Stroke; RIVT: Repeated Intravenous Thrombolysis; IVT: Intravenous Thrombolysis; r-tPA: recombinant tissue Plasminogen Activator

INTRODUCTION

Treatment of acute ischemic stroke (AIS) using recombinant tissue plasminogen activator (r-tPA) has been established for nearly 30 years and intravenous thrombolysis (IVT) within 4.5 h of AIS onset remains standard management worldwide [1].

The pharmacokinetic properties of r-tPA are known, such as rapid elimination from plasma after administration (50% within 5 min.) as well as side-effects with an increased risk of bleeding, especially intracranial haemorrhage, angioedema, reperfusion injury [2,3].

In addition, r-tPA is known to have many, even opposite effects besides thrombolysis. Potentially harmful effects would include excitotoxic neuronal degeneration, damage of blood-brain barrier (BBB) with increased BBB permeability, inflammation, while potentially neuroprotective effects could be attributed to anti-excitotoxic neurotropic and anti-apoptotic effects on neurons [4,5].

Despite its effective and relatively safe therapeutic effect, r-tPA is still insufficiently used in the treatment of AIS for a

number of reasons, including contraindications for intravenous thrombolysis [6]. Current recommendations and guidelines for AIS treatment with IVT highlights recurrent stroke within 3 months as a contraindication to thrombolytic treatment due to the presumed increased risk of symptomatic intracerebral hemorrhage (sICH) and have not changed over the years [7,8].

Early recurrent AIS (ERAIS) represents almost 14.5-18.3% of all ischemic strokes with the greatest risk during the first week and is considered to contribute to an increased risk of sICH, death and a poorer functional outcome [9-11].

Therefore, the possibility of reperfusion treatment with IVT is excluded for a large number of patients with ERAIS (within 3 months), except properly selected patients with proximal occlusions of the large intracranial arteries, suitable for mechanical thrombectomy [12-14].

Published literature with results from some large case series and case reports last year's confirmed the safe and effective repeated application of IVT (RIVT) in ERAIS, without a significant increase of IVT related complications or worse outcomes [15-17].

We present the case of patient with ERAIS within 54 hours in whom we have successfully conducted RIVT in combination with repeated mechanical thrombectomy with good clinical recovery. We also wanted to emphasize the importance of telemedicine consultation with the designated CSC "stroke team"

and incorporation of multimodal neuroimaging in assessing the possibilities for repeat IVT and thrombectomy for safe and effective reperfusion treatment in ERAIS.

CASE PRESENTATION

Our patient is a 54-year old man with a history of hypertension and alcoholism presenting to a regional hospital emergency room with a severe right sided hemiparesis, dysarthria, bilateral VI-th nerve palsy and right facial palsy, National Institutes of Health Stroke Scale (NIHSS) of 12, pre-morbidly the patient was without disability (mRS 0). Initial workup, computer tomography (CT) and CT angiography (CTA), showed a basilar artery occlusion (BAO) and right vertebral artery dissection and occlusion (Figure 1). Intravenous thrombolysis was started and after telemedicine consultation with our stroke team the patient was transferred to our comprehensive stroke center (CSC).

Upon arrival to our neurointensive care unit (NICU) the patient had a mild right sided weakness, dysarthria, right facial palsy and bilateral abducens palsy – NIHSS 5, his blood pressure was 170/90 mmHg, heart rate 57. In the angio suite the patient vomited after which he received antiemetics and a nasogastric tube was placed. The first angiography showed recanalisation of the basilar artery with occlusion of the right upper cerebellar artery and partial occlusion of the left upper cerebellar artery (Figure 2A). Full recanalisation was achieved (Figure 2B). Control CT showed a small ischemia of the left mesencephalon and left cerebellar cortex (Figure 3). He was started on a therapeutic dose

of low molecular weight heparin (LMWH) and at discharge from our CSC the patient had dysarthria, right facial palsy and right abducens palsy – NIHSS 3.

53 hours after discharge we received another telemedicine consultation from the regional hospital regarding the same patient. This time the patient presented with impairment of consciousness with a Glasgow Coma Score (GCS) of 5, involuntary movements of the right extremities and with a surge of systolic blood pressure above 200 mmHg, he was treated with diazepam, urapidil and was intubated for airway protection. Workup showed reocclusion of the basilar artery with formerly described ischemia (Figure 4). Considering the severity of the clinical presentation of the new infarct, favorable outcome with only minimal ischemic changes on the control CT done at our institution we advised a repeated intravenous thrombolysis (RIVT) which was administered 54 hours from the first application and subsequently the patient was transferred to our CSC for another thrombectomy. Upon arrival the patient was sedated, intubated with small reactive pupils. In the angio suite angiography showed residual thrombus in the lumen of the middle third of the basilar artery, occlusion of the left superior cerebellar artery and left posterior inferior cerebellar artery (Figure 5A) which were aspirated with complete recanalisation. Right dissected artery was identified as the source of the new emboli, as a preventive measure we occluded the artery using 5 endovascular coils (Figure 5B). Control MRI showed acute

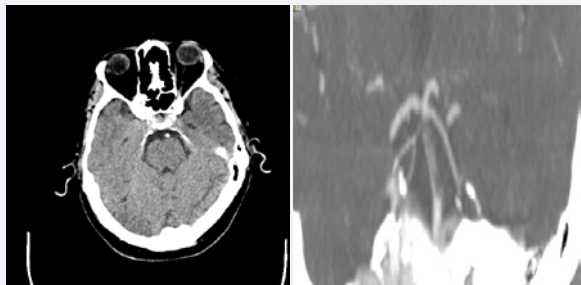


Figure 1 Native CT (A) of the brain and CT angiography (B) during initial workup in the regional hospital showing basilar artery occlusion.



Figure 3 Control CT showed a small ischemia of the left mesencephalon and left cerebellar cortex.



Figure 2 (A) – The first angiography showed recanalisation of the basilar artery with occlusion of the right upper cerebellar artery and partial occlusion of the left upper cerebellar artery (B) - Complete recanalisation with manual aspiration and using a stent retriever.

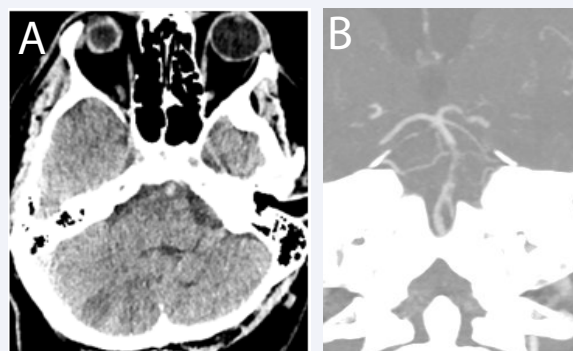


Figure 4 Control native CT (A) angiography (B) showing reocclusion of the basilar artery and with ischemia of the cerebellum and mesencephalon.

ischemia of the left and right cerebellar hemisphere and thalamus with minimal zone of hemorrhage, in the right pons showed on SWI images (Figure 6). In the postoperative course the patient was sedated for three days after which we weaned him off the respirator, on day 5 he was extubated. Of note is that he had a pseudoaneurysm (PSAN) of the right communal femoral artery which was treated with compression. On day 10 the patient was transferred back to the regional hospital with a recommendation of clopidogrel 75 mg/d and other supportive therapy. On follow up the patient was discharged home after 10 more days with dysarthria, mild di hemiparesis and ataxia, his NIHSS score was 4 and his mRS score was 2.

DISCUSSION

Stroke, especially ischemic stroke represents an epidemic of

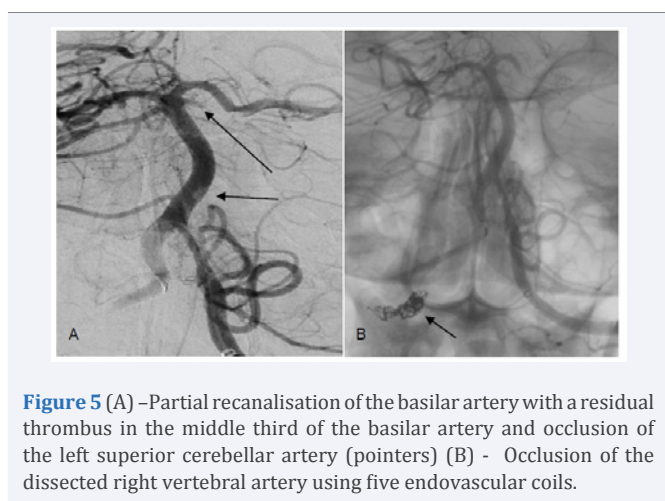


Figure 5 (A) -Partial recanalisation of the basilar artery with a residual thrombus in the middle third of the basilar artery and occlusion of the left superior cerebellar artery (pointers) (B) - Occlusion of the dissected right vertebral artery using five endovascular coils.

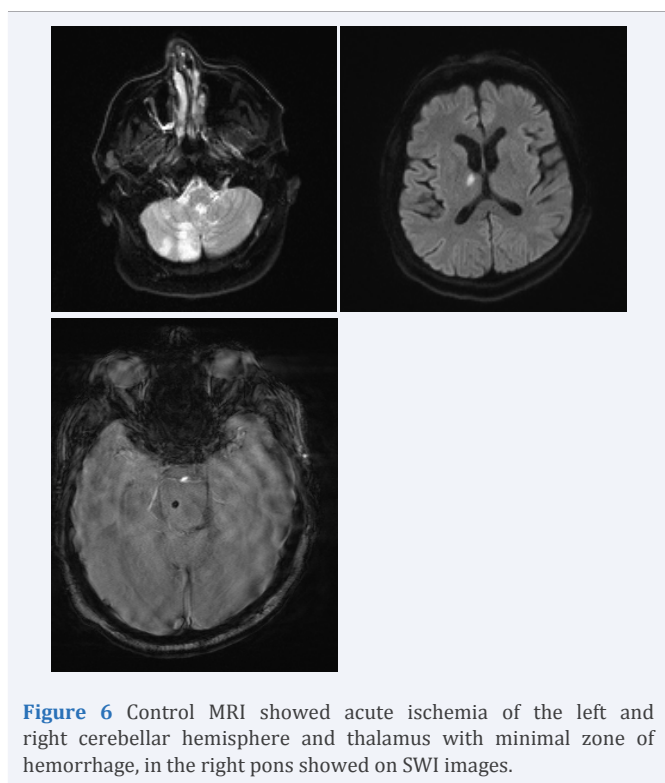


Figure 6 Control MRI showed acute ischemia of the left and right cerebellar hemisphere and thalamus with minimal zone of hemorrhage, in the right pons showed on SWI images.

the contemporary world population with a high rate of mortality and disability [18]. Therefore, the goal of AIS treatment is aimed at achieving an early reperfusion in order to prevent and reduce these consequences.

Thrombolytic therapy with Recombinant Tissue Plasminogen Activator (r-tPA) for acute ischemic stroke (AIS) is well established AIS treatment for almost three decades such as mechanical thrombectomy (MT) in the last 10 years [1,19]

Current guidelines for thrombolytic treatment of AIS pointed a history of previous stroke within 3 months as a contraindication to re-thrombolytic treatment, which has not be changed since the beginning of the use of r-tPA for AIS treatment [7,8,20]. These recommendations are based on an assumed increased risk of sICH due to neurotoxicity, BBB disruption, dysfunction of the vascular basal lamina associated with re-administration of r-tPA in ERAIS, especially in the area of the former infarct which is presumed that is not yet recovered, as well as potentially higher risk of severe immune reactions [2-5,21,22]. However, the results of a series of studies have shown that sICH occurs very rarely in the area of previous ischemic infarction. In addition, the pharmacokinetic properties of r-tPA exclude the possibility of a negative cumulative effect of readministration in ERAIS [2,4,5,17].

The risk of early AIS recurrence within 3 months is about 14.5-18.3% according to data from the Oxfordshire Community Stroke Project (OCSP) [23,24]. ERAIS is thought to be associated with higher mortality and poorer outcome which strictly related on current guidelines for thrombolytic treatment, excludes a large number of patients who suffered a ERAIS for repeated intravenous thrombolysis (RIVT), regardless of the needs or possibility for MT [25].

In assessing the risk and potential efficacy of RIVT, studies emphasized the importance of the residual neurological deficits, severity of the new ERAIS and the findings of multimodal neuroimaging [15-17,26,27].

Recent clinical trials and recommendations for ERAIS treatment considered that mechanical thrombectomy is superior to systemic thrombolysis alone in patients with large vessel occlusion (LVO) [19,20,28].

But in situations when the primary stroke center is far away from the comprehensive stroke centre (CSC), it is necessary to repeat neuroimaging and seek telemedicine consultation with the designated "stroke team" to assess the potential need to re-apply thrombolysis before transport to CSC for possible MT [19,29]. We demonstrated the efficacy of RIVT, in combination with the, "drip-and-ship" model for mechanical thrombectomy in addition to telemedicine consultation, in our patient, in whom the RAIS was due to early reocclusion of the same artery from the dissected right vertebral artery, despite the best medical treatment [30]. Our case with successful re-reperfusion therapy and good functional outcome as well as the results of previous studies support effective reperfusion treatment (repeated IVT and repeated MT) in patients with ERAIS, including prior multimodal neuroimaging and a "stroke team" consultation for effective assessment and selection of patients. We also consider that depending on adequate assessment for RIVT, taking into account the previous neurologi-

cal deficit and the severity of ERAIS estimated by National Institute of Health Stroke Scale (NIHSS), there may be a greater pool of patients who can still benefit from RIVT treatment [17].

These results of the effectiveness of RIVT in RAIS require an answer to the question posed by Wu in his article, after revising the relevant publications “Is it time to reconsider the inclusion criteria and exclusion criteria of intravenous thrombolysis?” [26]. In accordance to our clinical experience, we also believe that the current guidelines on contraindications for RIVT in ERAIS should be modified and changed, incorporating neuroimaging findings for safe and effective retrombolytic treatment. Additional research and larger studies should be directed to the revision of exclusion and inclusion criteria and recommendations for the repeated IVT in ERAIS.

CONCLUSION

Our case report suggests that repeated IV thrombolysis, followed by repeated mechanical thrombectomy may be safe and efficacious in patients with early recurrent ischemic stroke, including prior adequate neuroimaging and “stroke team” consultation.

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