

Intraarterial thrombolysis with reteplase in acute ischaemic stroke in a Pakistani center

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Abstract

Acute ischaemic stroke is a major cause of neurological morbidity and mortality across the globe. Recent advances in past two decades have made complete reversal of life threatening stroke a reality. The judicious use of intravenous and intraarterial thrombolysis in acute ischaemic stroke has saved countless lives. The use of thrombolytic therapy in Pakistan in acute stroke is still miniscule. Very limited literature is available from Pakistan on the use of intravenous thrombolysis. Intraarterial thrombolysis has been used only in few patients and there are no published reports of that from Pakistan. We present the case of a young man who came within 1 hour of stroke onset with a large right middle cerebral artery infarct resulting in severe neurological deficit. An urgent cerebral angiography showed complete occlusion of right internal carotid artery at its bifurcation. Successful intraarterial thrombolysis was performed with excellent clinical outcome. To our knowledge this is the first report of use of intraarterial thrombolysis in acute stroke from Pakistan.

Introduction

Intravenous (IV) administration of recombinant tissue plasminogen activator (rtPA) is currently the only FDA-approved therapy for treatment of patients with acute ischaemic stroke presenting within 3 hours of onset. The effectiveness and safety of intravenous rtPA given outside the

3-hour window is still under investigation and yet to be established. rtPA is not routinely available in Pakistan. According to one study carried out at Lahore General Hospital as many as 21% of patients presented within 3 hours of symptom onset.¹ Intraarterial (IA) thrombolysis should be considered in patients considered poor candidates for IV thrombolysis and patients presenting outside the 3 hours window.² The unavailability of rtPA and the larger window of 6 hours have prompted the use of IA thrombolysis in patients who cannot receive IV thrombolysis. We report successful use of IA reteplase (RP) in a young man who presented within one hour of stroke onset.

Case Report

A 43 year old man, smoker, with no other significant co-morbidities developed sudden left hemiplegia and decreased alertness less than one hour prior to presentation. On arrival to emergency room he was found to have BP of 128/68 mm Hg; pulse of 68/minute. He was lethargic, had right gaze preference, complete left hemineglect, mild dysarthria, only minimal extension response in left arm and flexion withdrawal in left leg. His NIHSS score at that time was 17. A CT scan of head without contrast showed no evidence of haemorrhage. An immediate cerebral angiogram was performed that showed occlusion at the bifurcation of intracranial right internal carotid artery (ICA) [Figures 1]. After demonstrating the occlusion of right ICA at bifurcation, intraarterial thrombolysis was initiated. Before the first dose of RP, the right anterior cerebral



Figure 1. Cerebral angiogram showing complete occlusion of right internal carotid artery at its bifurcation.

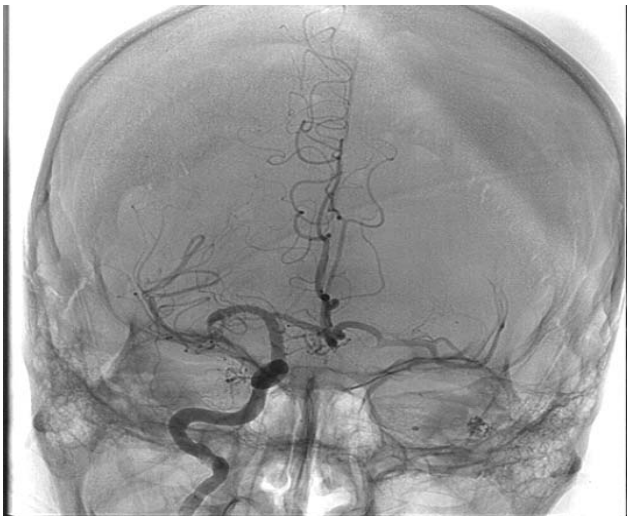


Figure 2a. Cerebral angiogram showing recanalization of right anterior cerebral artery and migration of thrombus resulting in opening of the origin of middle cerebral artery.

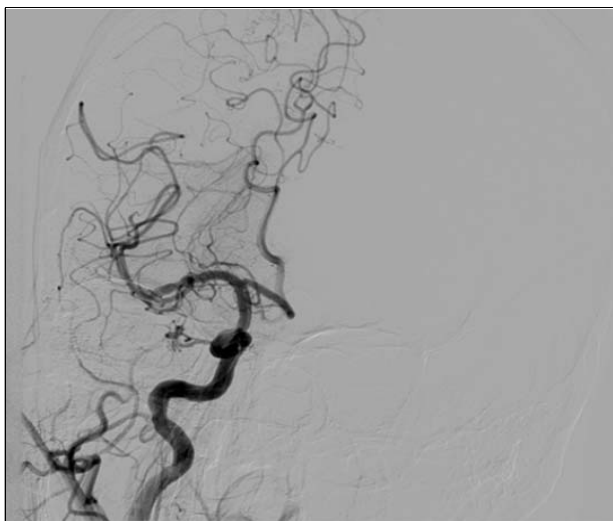


Figure 2b. Cerebral angiogram showing opening of several branches of right middle cerebral artery.

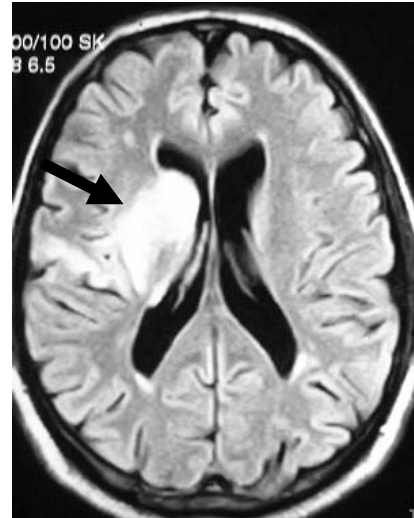


Figure 3a. FLAIR MRI images showing acute infarct in right basal ganglia and adjacent subcortical tissue extending to a small part of cortex.



Figure 3b. FLAIR MRI image at 6 months showing small residual encephalomalacia in right basal ganglia and external capsule region.

artery (ACA) had recanalized, likely due to migration of thrombus [Figure 2a]. Thrombolysis was done initially with 1 unit, and subsequently with 0.5 unit increments of RP. Selective angiography done 5 to 10 minutes after administration of every dose of RP showed gradual recanalization of several branches of right middle cerebral artery (MCA) [Figure 2b]. A total of 7 units of reteplase were administered and the procedure was completed within approximately 4 ½ hours of symptom onset. MRI brain done on second day showed small acute infarction in right basal ganglia and adjacent subcortical region [Figure 3a]. The patient made gradual neurological recovery evident by improvement in his NIHSS score to 11 at 24 hours; 7 at 48 hours; 2 at 3 months and 1 at 6 months follow up. MRI scan done at 6 months showed small residual area of encephalomalacia in right basal ganglia and external capsule region [Figure 3b].

Discussion

Ischaemic stroke represents a huge global burden, being the leading cause of physical disability and the third leading cause of death worldwide. Although rigorous epidemiological data from Pakistan is lacking, stroke is certainly the commonest reason for admission to a neurology ward in our part of the world, as elsewhere.³

The treatment options for acute ischaemic stroke in first few hours of onset include IV thrombolysis, intraarterial thrombolysis (IAT), mechanical reperfusion strategies⁴ and combination of these.⁵ Successful use of intra-arterial fibrinolytic therapy for acute stroke in vertebrobasilar circulation was first described in 1983 by Zeumer et al.⁶ IA thrombolysis has a broader time window of 6 hours as compared to 3 hours for IV thrombolysis.² In an analysis of 27 studies including 852 patients receiving IAT and 100 control subjects, it was observed that IAT was associated with a reduction in mortality and an improvement in favorable outcomes but it was also associated with an increased risk of haemorrhagic complications compared with the control group.⁷ Among the patients treated with IAT, those who had supratentorial strokes were more likely to have favorable outcomes than those with infratentorial strokes.⁷ Intraarterial thrombolysis requires the patient to be at an experienced stroke center with immediate access to cerebral angiography and interventional neuroradiology.² In patients who have vertebrobasilar thrombosis, intraarterial thrombolysis is the only therapy to date that has reduced mortality and improved outcomes. Moreover, the window for thrombolysis in the posterior circulation- while not currently established- may be 12 hours or more after stroke onset. However, these findings are not from a randomized trial.⁸

The combination of administering IV therapy and then IA therapy has been reported. This strategy could allow for early treatment of stroke with IV medication while the resources to deliver IA therapy are organized.⁹ Zaidat et al. studied the response to IA and combined IV and IA thrombolytic therapy in patients with acute distal ICA occlusion and found that there was no difference in recanalization rate, symptomatic haemorrhage and NIHSS for IV/IA versus IA alone. Shorter intervals between onset and treatment were found to be correlated with higher rate of recanalization and improved outcome.¹⁰ IAT may also be an option for patients not showing early response to full dose IV thrombolytic therapy.¹¹

Recombinant tissue plasminogen activator used in a few studies of IAT. In one study, Qureshi et al. found out that IA reteplase in doses upto 8 U with or without angioplasty resulted in higher rate of recanalization.¹² In our patient we used 7 U of reteplase, initially one unit followed by 0.5 U increments. We also found

progressive recanalization with increasing dose of reteplase.

In Pakistan, no randomized trials or large series have been published on this subject. A recent abstract at the meeting of Pakistan Society of Neurology reported 24% haemorrhagic conversion, and 19% mortality in 21 patients who received IV rtPA.¹³ The high mortality rate was thought to be lack of adherence to strict guidelines for IV rtPA use.¹³ In our patient, the timings and CT findings were consistent with the approved use of IV rtPA; however, we could not administer IV thrombolysis because of unavailability of rtPA. After informed consent of the family, we decided to pursue intra-arterial thrombolysis, and had successful outcome with almost complete resolution of neurological deficit at 6 months from a baseline of devastating large right MCA infarct.

Our case suggests that intraarterial thrombolysis is effective in selected candidates. This case also argues for the need of availability of rtPA in tertiary care centers, as most centers do not have facilities for interventional neurological procedures, but receive patients within a time window where rtPA can be administered. In our own center, we are currently conducting a study on time of stroke arrival in emergency room (ER). Among the 120 patients enrolled so far, 80 (67%) sought some form of medical attention within 3 hours of stroke onset, and 90 (75%) within six hours. Among these, 35 (29%) presented to our emergency department within 3 hours and 45 (38%) presented within 6 hours of symptom onset [unpublished data]. The data from Basharat et al¹, our own unpublished data, and the present case all prove that the belief that patients with stroke do not seek medical attention in timely fashion is not true. There needs to be efforts from medical community as well as socio-political circles to make rtPA available in Pakistan, which is a potentially life saving medication.

Conclusion

We believe this is the first report of IA thrombolysis with reteplase in Pakistan. Our patient is an example of successful recanalization with significant clinical outcome. This case underscores the need for availability of thrombolysis therapy and trained personnel in major centers of Pakistan to save many lives and reverse or limit the devastation of large ischemic strokes.

Disclaimer

This case report was presented as a poster at the 15th Annual Meeting of Pakistan Society of Neurology, held in Peshawar, April 5th and 6th, 2008.

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