

## Endovascular treatment in acute ischemic stroke patient on factor Xa inhibitor

Siddhart Mehta, MD<sup>\*</sup>, Haitham Dababneh, MD<sup>\*</sup>, Mohammed Hussain, MD,  
Mohammad Moussavi, MD, and Jawad F Kirmani, MD

Stroke & Neurovascular Center at JFK Neuroscience Institute, Edison, NJ 08818, USA

*Author Contributions: Drs. Mehta, Dababneh and Hussain drafted and edited the manuscript. Dr. Moussavi edited the manuscript. Dr. Kirmani has revised the manuscript*

*\*Authors contributed equally*

### Key words

factor Xa inhibitor; intra-arterial tPA (IA tPA); rivaroxaban; stroke

### Background

Warfarin has primarily been used for prevention of ischemic stroke in patients with atrial fibrillation for nearly 30 years [1]. More recent studies and trials have demonstrated the efficacy of new oral anticoagulants (NOACs) such as direct thrombin inhibitors and factor Xa inhibitors as a source of alternative therapy in preventing ischemic strokes in patients with atrial fibrillation. These NOACs also have the added benefit of minimizing labor intense methods such as the routine coagulation parameter monitoring that is often done in the case of warfarin. Therapeutic efficacy was elucidated by the ROCKET-AF trial which demonstrated noninferiority of rivaroxaban, a factor Xa inhibitor, to warfarin in prevention of stroke and systemic embolism [2].

However, treatment of patients who experience an acute ischemic stroke despite being on the aforementioned NOACs such as rivaroxaban has not been documented. The only FDA approved treatment for acute stroke with class I recommendation and holding level A evidence is intravenous recombinant tissue plasminogen activator (IV tPA) [3]. Even patients on warfarin who suffer from an ischemic stroke may be treated with IV tPA provided that the international normalized ratio (INR) and platelet thromboplastin time (PTT) are not elevated [4]. However, owing to the relatively newer profiles of the various NOACs, there are currently no readily available assays in existence to determine their level of anticoagulation in a NOAC user. Inability to determine the state of anticoagulation in turn makes decision to provide treatment with IV tPA difficult in such patients who suffer

from ischemic strokes. Several other articles have been published describing the incidence of complications and recommended discontinuing direct thrombin inhibitors preprocedural [5,6].

To counter such dilemma, intra-arterial tPA (IA tPA) proves to be a viable therapeutic option when the administration of IV tPA is contraindicated [5]. The safety profile of IA tPA for clot dissolution is further strengthened owing to the smaller amount of the total dosage that is ultimately required for clot delivery. In fact, the efficacy of IA tPA application in patients with elevated INR secondary to warfarin use has been reported [7,8]. However, to our knowledge, there are no prior reports of administering IA tPA and mechanical thrombectomy in a patient who is on a factor Xa inhibitor. We report a case of a 79-year-old man on rivaroxaban who presented with acute onset of right gaze deviation and left-sided weakness, and showed clinical improvement with IA tPA

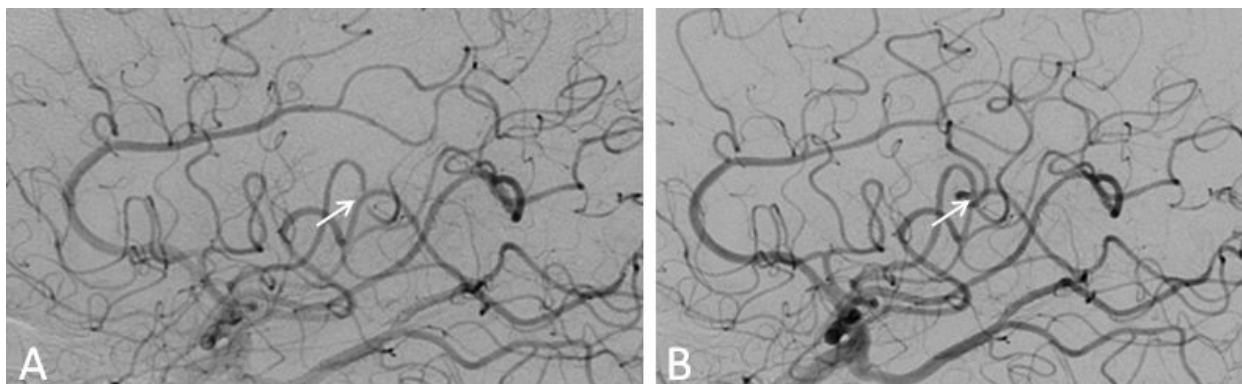
### Case presentation

A 79-year-old man with a history of coronary artery disease, dyslipidemia, and atrial fibrillation, presented to the emergency department within 2.5 h of sudden onset right gaze deviation, left facial droop, left-arm weakness, numbness, dysarthria, and mild left-sided extinction. His initial neurological evaluation objectified by the National Institutes of Health Stroke scale (NIHSS) revealed a total score of 7 [9]. Serum laboratory tests demonstrated normal complete blood counts and metabolic panel with an initial prothrombin time (PTT) of

Published September, 2014.

All Rights Reserved by JVIN. Unauthorized reproduction of this article is prohibited

†Correspondence to: Stroke & Neurovascular Center at JFK Neuroscience Institute, Edison, NJ 08818, USA

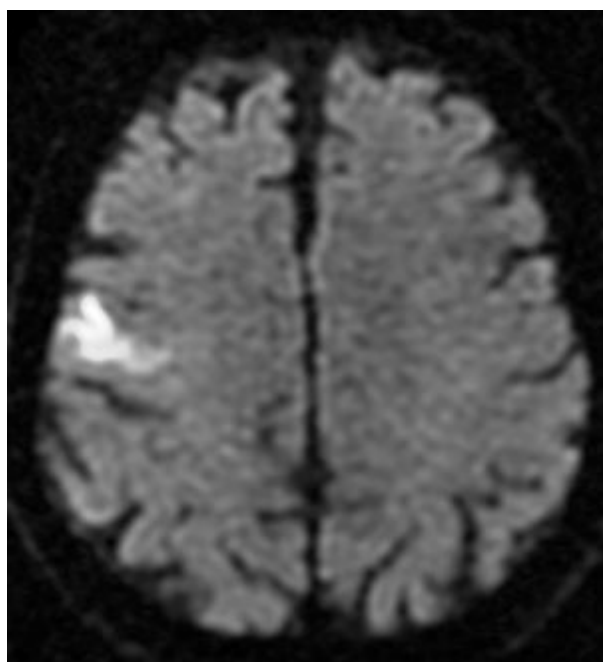


**Figure 1. Cerebral angiogram. (a) Right distal MCA occlusion (arrow). (B) Complete recanalization and reperfusion after intra-arterial therapy.**

14.8 s (normal 12.5–14.8 s), INR of 1.2 and a PTT of 28.5 s (normal 24.4–36.5 s). Emergent brain computed tomogram (CT) without contrast was negative for intracerebral hemorrhage (ICH). Patient's current home medication history included the use of rivaroxaban for atrial fibrillation. The decision was made to take the patient to the endovascular suite for a cerebral angiogram with intention to treat with mechanical thrombectomy and intra-arterial thrombolytic administration, after obtaining an informed consent. The cerebral angiogram obtained subsequently revealed a right distal inferior division of the middle cerebral artery (MCA) occlusion (Figure 1). The clot was manipulated and fragmented with a micro-wire along with a 3 mg infusion of tPA at the M4 segment, within 4.5 h of symptom onset. There was complete recanalization and reperfusion, objectified by a TIC13 score. Post-procedural NIH stroke scale was 1 (right facial droop). The femoral artery puncture site was successfully closed using an Angio-Seal closure device without any complications. The patient was transferred to the Neuro-critical Care Unit (NCCU) for 24 h of close observation. An MRI of brain done during the NCCU revealed an acute right posterior frontal infarct that contributed to the constellation of aforementioned symptoms (Figure 2). The patient was switched from rivaroxaban to warfarin on day number 3 of hospitalization and transferred to acute rehabilitation with a discharge NIHSS of 1 and a modified Rankin Scale (mRS) of 1.

## Discussion

Evidence-based guidelines exist for treatment of acute ischemic strokes in patients with a history of atrial fibrillation on warfarin therapy. These guidelines support treatment with IV tPA during an ischemic stroke, if the INR and PTT are not elevated [10]. Though safety pro-



**Figure 2. MRI diffusion-weighted image depicting right posterior frontal acute infarct.**

file of administering IA tPA in patients treated with warfarin with high INR has been documented anecdotally, there are no guidelines in existence that highlight its dosage and degree of safety.

At the other spectrum, patients with atrial fibrillation who are on NOACs suffering from ischemic strokes also create a unique dilemma in terms of clinical management. At present there is not enough data to suggest clear-cut guidelines highlighting safety for administering IV or IA tPA in such patients, though isolated case

reports have been published depicting the safety profile of giving IV tPA in patients on NOACs [11].

To our knowledge, this is the first documented case of a patient with atrial fibrillation on NOAC developing acute ischemic stroke that received IA tPA. IA tPA therapy when compared with IV tPA presents several advantages in terms of an overall lower rate of complications. In particular, the delivery of thrombolytic agent directly into the site of occlusion increases its intraclot concentration, thus reducing the total dose needed to achieve reperfusion. A lower total amount of thrombolytic agent in turn has shown to minimize the risk of systemic side effects, with bleeding being the most prominent [12, 13]. Our case reinforced the safety profile since complication of ICH or gastrointestinal blood loss was not seen. In addition, it should be noted that despite the use of IA tPA, the good outcome in our case may have also been owing to the application of direct guide wire induced mechanical thrombolysis. The risk of bleeding complications in patient with femoral artery access approach may increase under antiplatelet and anticoagulation therapies as reported in cardiac literature, and therefore, caution should be exercised in these patients [14].

Randomized clinical trials in multicenter settings are needed to further evaluate and reinforce the safety and efficacy of IA tPA in patients on any anticoagulation suffering from ischemic stroke.

## References

1. Besson G, Bogousslavsky J. 1991;[European atrial fibrillation trial (EAFT). Secondary prevention with anticoagulants and aspirin in patients with non-valvular atrial fibrillation having suffered a transient ischemic attack or a regressive vascular accident]. *Rev Med Suisse Romande* 111(1):49–55.
2. Patel MR, et al. 2011;Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med* 365(10):883–91.
3. Adams HP Jr, et al. 2007;Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: the American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. *Circulation* 115(20):e478–534.
4. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. 1995;Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med* 333(24):1581–7.The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group
5. Watanabe M, Siddiqui FM, Qureshi AI. 2012;Incidence and management of ischemic stroke and intracerebral hemorrhage in patients on dabigatran etexilate treatment. *Neurocrit Care* 16(1):203–9.
6. Watanabe M, Qureshi AI, Siddiqui FM. 2011;Periprocedural management of patients on dabigatran etexilate treatment. *AJNR Am J Neuroradiol* 32(8) E166
7. Linfante I, et al. 2005;Intra-arterial thrombolysis in patients treated with warfarin. *Cerebrovasc Dis* 19(2):133–5.
8. Janjua N, et al. 2007;Feasibility of IA thrombolysis for acute ischemic stroke among anticoagulated patients. *Neurocrit Care* 7(2):152–5.
9. Brott T, et al. 1989;Measurements of acute cerebral infarction: a clinical examination scale. *Stroke* 20(7):864–70.
10. Adams HP Jr, et al. 1996;Guidelines for thrombolytic therapy for acute stroke: a supplement to the guidelines for the management of patients with acute ischemic stroke. a statement for healthcare professionals from a Special Writing Group of the Stroke Council, American Heart Association. *Stroke* 27(9):1711–8.
11. Lee VH, Connors JJ, Prabhakaran S. 2012;Intravenous thrombolysis in a stroke patient taking dabigatran. *J Stroke Cerebrovasc Dis* 21(8):916 e11–2.
12. Furlan A, et al. 1999;Intra-arterial prourokinase for acute ischemic stroke. the PROACT II study: a randomized controlled trial. Prolyse in Acute Cerebral Thromboembolism. *JAMA* 282(21):2003–11.
13. Chalela JA, et al. 2001;Safety of intra-arterial thrombolysis in the postoperative period. *Stroke* 32(6):1365–9.
14. Wang YB, et al. 2012;Randomized comparison of radial versus femoral approach for patients with STEMI undergoing early PCI following intravenous thrombolysis. *J Invasive Cardiol* 24(8):412–6.