




Brief Communication

Vertebral to Basilar Thrombus Migration Post Intravenous Thrombolysis

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ABSTRACT: Recombinant tissue plasminogen activator improves outcomes in acute ischemic stroke. Alteplase may result in thrombus migration (TM) distally to a critical arterial supply that can worsen perfusion to eloquent brain tissue. Alteplase-related stroke recanalization and clot migration in vertebral artery (VA) occlusion whereby the clot migrates to the basilar artery (BA) may be harmful. We identified seven subjects with isolated symptomatic vertebral occlusion. Two cases suffered early neurologic deterioration due to TM from VA to BA following alteplase. Precautionary transfer to thrombectomy centers may be warranted in alteplase-treated symptomatic VA occlusions in case of migration to basilar occlusion.

RÉSUMÉ : Migration d'un thrombus de l'artère vertébrale vers l'artère basilaire à la suite d'une thrombolyse intraveineuse. L'activateur tissulaire recombinant du plasminogène peut améliorer l'évolution de l'état de santé de patients victimes d'un AVC aigu. L'altéplase peut par ailleurs entraîner une migration d'un thrombus à distance (*distally*) en direction d'un approvisionnement artériel critique, ce qui peut aggraver la perfusion de zones cérébrales dites « éloquentes ». On le sait, la recanalisation des AVC en lien avec l'administration d'altéplase et la migration d'un caillot de l'artère vertébrale vers l'artère basilaire peuvent être dommageables. Nous avons ainsi identifié sept sujets atteints d'une occlusion symptomatique isolée de l'artère vertébrale. À noter que deux d'entre eux avaient souffert d'une détérioration neurologique précoce en raison de la migration d'un thrombus de l'artère vertébrale vers l'artère basilaire après l'administration d'altéplase. Soulignons que le transfert préventif vers des centres de thrombectomie peut être justifié dans le cas d'occlusions symptomatiques de l'artère vertébrale traitées par altéplase lorsque se produit une migration d'un thrombus vers une artère basilaire.

Keywords: Thrombus migration; Stroke; Posterior circulation; Endovascular therapy

(Received 5 April 2021; final revisions submitted 7 October 2021; date of acceptance 10 October 2021; First Published online 20 October 2021)

Recombinant tissue plasminogen activator (alteplase) achieves recanalization which improves clinical outcomes in patients with acute ischemic stroke but can also cause migration of thrombus which may result in harmful perfusion worsening due to more distal artery occlusion.^{1,2} Patients presenting with an acute ischemic stroke from a large intracranial vessel occlusion are often treated with intravenous thrombolysis prior to endovascular treatment.³ However, in 10% of all cases, intravenous thrombolysis results in recanalization of the occluded proximal artery making endovascular therapy not necessary or not possible due to distal embolization of the clot fragments.⁴

Thrombus migration (TM) has been previously reported in anterior circulation strokes. This pre-interventional clot migration

is more likely with smaller thrombi, thrombi rich in red blood cells, and those with poor collaterals.⁵ Downstream clot fragmentation or migration has been shown to worsen perfusion in 6.6% of patients with internal carotid T occlusions.⁶ Thrombus movement has also been quantified as mild/moderate or marked in degree. Mild/moderate clot movement in proximal occlusion (internal carotid artery or proximal M1 middle cerebral artery (MCA)) was associated with neurological deterioration in 20% of subjects and had less favorable outcomes compared to when marked thrombus movement occurred.⁷ Distal migration/fragmentation of the thrombus has also been found in one-third to more than half of MCA strokes.^{7,8}

TM has not been studied in posterior circulation stroke as yet. In this study, we examine for the frequency of TM in symptomatic

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Cite this article: Banerjee A, Marzoughi S, Ohara T, Horn MK, Zerna C, Menon BK, and Demchuk AM. (2023) Vertebral to Basilar Thrombus Migration Post Intravenous Thrombolysis. *The Canadian Journal of Neurological Sciences* 50: 119–122, <https://doi.org/10.1017/cjn.2021.237>

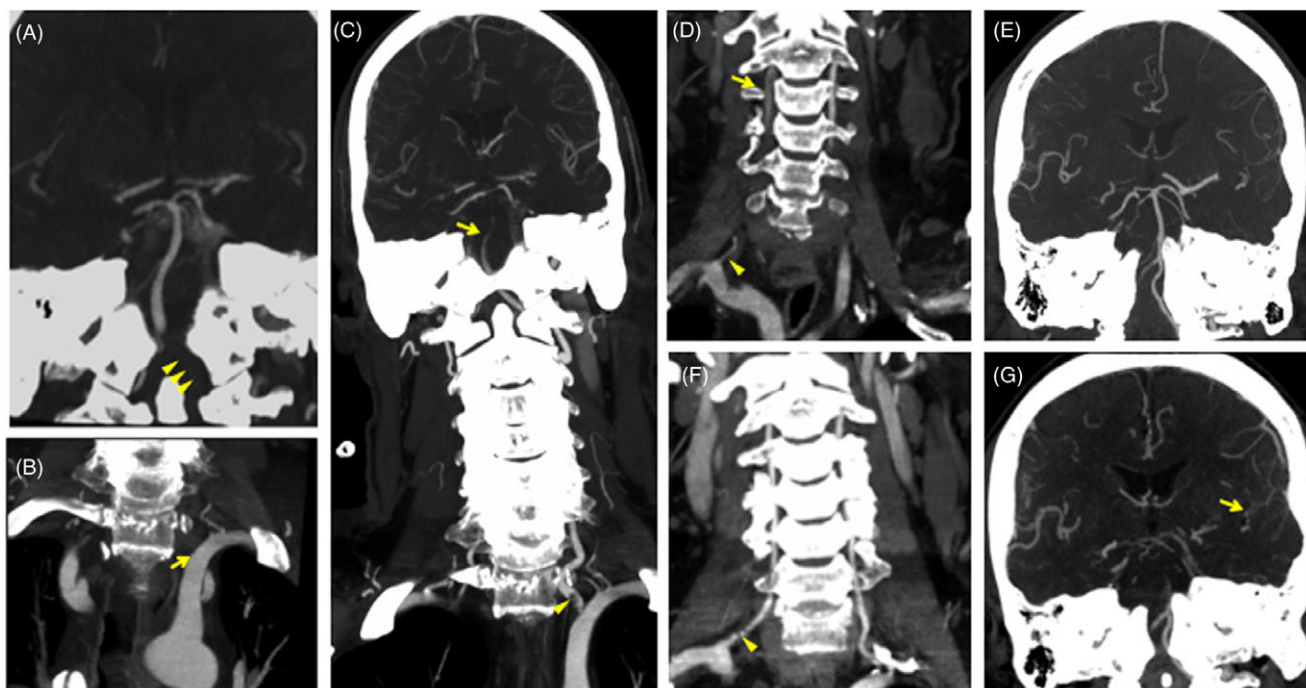


Figure 1: (A–C) are scans from patient 1 and (D–G) are scans from patient 2. *Patient 1:* Baseline CTA (A, B): (A) Lt intracranial VA was not seen (arrowhead). BA was patent. (B) Lt VA was occluded at the origin (arrow). Follow-up CTA (C) Lt VA was recanalized and thrombus at the origin of Lt VA was seen (arrowhead). BA was newly occluded due to thrombus migration from Lt VA (arrow). *Patient 2:* Baseline CTA (D, E): (D) Rt VA was occluded at the origin (arrowhead). The part of Rt extracranial VA was visualized and thrombus was seen in the VA (arrow). (E) The proximal portion of Rt intracranial VA was not seen. BA was patent. Follow-up CTA (F, G): (F) Rt extracranial VA was recanalized with severe stenosis (arrowhead). Thrombus seen on baseline CTA disappeared. (G) BA was newly occluded presumably due to thrombus migration (arrow).

vertebral artery (VA) occlusion subjects treated with intravenous alteplase within a large prospective registry where CTA is performed as standard of care.

The Quality Improvement and Clinical Research (QuICR) registry captures and tracks all treated acute ischemic stroke patients in the province of Alberta, Canada prospectively. The aim of the registry is to provide a province-wide quality improvement and knowledge translation process focusing on access to care and speed of treatment. The QuICR registry is approved by the institutional ethics review board, and individual patient consent is waived. For this study, we searched the QuICR registry from April 2015 to April 2019 for all IV alteplase treatment at a single comprehensive stroke center.

Among such subjects, we identified all cases of symptomatic isolated VA occlusion(s). Medical records and diagnostic imaging reports were reviewed in each of these VA occlusion subjects.

Among the 615 patients who received IV alteplase from April 2015 to April 2019, we identified seven cases of intra- or extracranial VA occlusion treated with alteplase, a 1.1% incidence of symptomatic VA occlusion without basilar involvement. Of these seven cases, two subsequently received endovascular therapy following alteplase administration due to worsening clinical status of the patient. Modified TICI scores have been used in a trial of posterior circulation stroke,⁹ therefore the TICI scores have been mentioned in our study when available. In both cases, migration of the thrombus from the vertebral to the basilar artery occurred. These two TM cases are reported below in detail. Of the five cases that did not result in TM, four had favorable outcomes with 24-hour National Institutes of Health Stroke Scale (NIHSS) follow-up of 1–3 and 90-day follow-up NIHSS of 2. Their infarcts were consistent with presenting symptoms and no compelling evidence of TM

or distal embolization was found on imaging. One patient died due to brainstem infarction caused by bilateral intracranial VA occlusion after a goals of care discussion with the family resulted in the decision to withdraw active therapy. This subject had evidence of an embolic shower with several multi-territory infarcts (left medullary, central pontine, bithalamic, and bilateral superior cerebellar). However, the patient did not have a baseline MRI and there was no clear neurologic deterioration after IV alteplase, therefore it cannot be confirmed if these infarcts represent distal clot migration/embolization following the administration of alteplase.

Thrombus Migration Case 1

A patient with a medical history of atrial fibrillation and current smoking was initially admitted with an acute onset of vertebrobasilar symptoms. Upon presentation, the patient had a left-sided weakness and ataxia and a NIHSS score of 9. Initial computed tomography angiogram (CTA) showed an occlusion of the origin of left VA. The basilar artery (BA) was patent (Figure 1A, B). The patient was promptly treated with alteplase but did not experience any improvement in symptoms. The patient was admitted to the stroke ward where, approximately 90 minutes after presentation to the emergency department, experienced a saliva aspiration event with pulseless electrical activity arrest and received two minutes of cardiopulmonary resuscitation (CPR), after which the patient was intubated and taken to the intensive care unit (ICU).

Subsequent CTA revealed recanalization of left VA and a thrombus in the proximal BA (Figure 1C). The patient underwent endovascular therapy with thrombectomy that resulted in residual clot migration to the posterior cerebral arteries (PCAs) resulting in a successful mechanical thrombectomy of BA occlusion and non-

target emboli of the right PCA. The next day, the patient developed posterior fossa swelling requiring decompression by neurosurgery, thus remained in ICU. The patient's neurological status improved slightly post-decompression with some improvement in power of all four limbs. The patient was then kept intubated in ICU for another 11 days, was given antibiotics for ventilator-associated pneumonia, and experienced mild improvement in breathing. A trial of extubation was undertaken on the 12th day after posterior fossa decompression, following which the patient developed respiratory failure, requiring reintubation. At this point goals of care were reviewed with family, and the patient was transitioned to comfort care and passed away the following day.

Thrombus Migration Case 2

A patient with prior medical history of coronary artery disease, diabetes, dyslipidemia, and hypertension but no known history of atrial fibrillation, presented with a 3-day history of nausea and vomiting and was brought to the hospital 1 hour after being found by their partner with a left hemiplegia with facial droop (NIHSS of 9). The patient's initial computed tomography (CT) scan revealed no acute infarct but CTA revealed a right VA occlusion from the origin to the mid cervical segment with large thrombus burden (Figure 1D, E). The patient was given alteplase after which became bradycardic and hypoxic and was admitted to ICU in the hours following alteplase administration. Follow-up CT/CTA scan revealed recanalization of right VA and migration of the clot into the BA with involvement of the entirety of the vessel (Figure 1F, G). There was also evidence of bilateral cerebellar infarcts as well as a left PCA infarct. The patient underwent interventional endovascular therapy upon deterioration for retrieval of the clot which resulted in a successful mechanical thrombectomy of a BA occlusion, demonstrating Thrombolysis In Cerebral Infarction scale 2b (TICI 2b) flow within the vascular territory. Unfortunately, the patient rapidly deteriorated with significant impairment of brainstem reflexes, and after a goals of care discussion with the family the patient was transitioned to comfort care and passed away the day after the presentation.

TM in intracranial vessels in ischemic stroke involving the anterior cerebral circulation has been reported in multiple case reports.^{1,2} TM has been reported to occur in approximately one-third to over one half of MCA stroke and of approximately 54% of cases after alteplase administration with most cases demonstrating clinical improvement with 7% demonstrating clinical deterioration.⁷ Some patients who receive alteplase have TM distally that can make thrombus inaccessible to endovascular therapy.¹⁰ The incidence, pathophysiology of TM, and dependence on alteplase administration or endovascular therapy (EVT) are not well studied in posterior circulation stroke however.¹¹

TM has been well described in the anterior circulation with emboli to distal intracranial vessels associated with poor outcome.¹² Data from one prospective cohort of ischemic stroke patients with TM in the anterior circulation suggested that erythrocyte-rich thrombi that are smaller in size tend to migrate more often with better collateral circulation resulting in limiting migration.⁵ Several studies have investigated the safety and efficacy of endovascular intervention for clots in the vertebrobasilar circulation with two randomized trials revealing no significant benefit with endovascular therapy compared with medical therapy^{9,13} although a trend toward benefit was seen. Both trials concluded that further larger studies are required to reach a definite

conclusion given a wide confidence interval for the primary outcome. This may also indicate that a case-specific approach may have to be taken to determine suitability for endovascular or medical therapy for patients with posterior circulation strokes. In addition, a recent retrospective study on posterior circulation thrombectomy revealed frequent evidence of distal migration even pre-procedurally similar to what we report.¹⁴

This study identified seven cases that presented as an isolated VA occlusion and received alteplase. Detrimental TM was seen in two out of seven patients. Both patients subsequently deteriorated neurologically resulting in the need for immediate endovascular therapy. These cases illustrate the importance of having awareness of the possibility of TM in the posterior circulation post-alteplase administration. Although magnetic resonance imaging (MRI) may be a useful tool in determining the extent of ischemic changes in the posterior circulation, particularly if there is evidence of diffusion restriction, the challenge will be the amount of time lost in obtaining the scan, risking further ischemic damage to a critical area. At our institution, we believe that the potential additional data that may be provided by MRI scan in the acute setting does not justify delaying endovascular therapy. This is supported by a recent study on diffusion weighted imaging (DWI) - posterior circulation- ASPECTS score revealing that even with a score of less than 6, favorable outcomes can be achieved with endovascular reperfusion therapy.¹⁵ Two other reports of EVT in patients with "hazy" or extensive DWI changes in the pons still resulted in good outcome further cast doubt in DWI MRI to prognosticate futility if reperfusion is achieved quickly.^{16,17} We recommend such patients receiving IV alteplase should be transferred to a thrombectomy facility for close observation to reduce delay and ensure access to endovascular therapy in the event of clinical deterioration due to basilar occlusion from distal TM. Given that in our tertiary center this only applied to a total of seven patients over a span of 4 years, there should not be a significant logistical barrier to arranging for such potential transfer given the infrequent nature of such. This small cohort of VA occlusion patients receiving IV TPA sheds light on the risk of clot migration to BA that may necessitate rescue mechanical thrombectomy. Given the rarity of occlusion in the intracranial segment of the VA, future randomized trials are likely not feasible leaving us to personalize decision making on a case by case basis which should include consideration of transfer to a thrombectomy facility for close observation.

Acknowledgements. We gratefully acknowledge access to the QUICR registry led by Dr. Michael Hill. We also thank team members of the Calgary Stroke Program for all their efforts maintaining this registry.

Funding. No targeted funding was reported.

Disclosures. Andrew Demchuk reports honoraria received from Medtronic and Boehringer Ingelheim remaining authors reports no disclosures.

Statement of Authorship. Dr. Banerjee: Concept, acquisition of data, and writing and revising of the manuscript.

Dr. Marzoughi: Concept, acquisition of data, and writing and revising of the manuscript.

Dr. Ohara: Acquisition of data and revision of manuscript for intellectual content.

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Dr. Zerna: Acquisition of data and revision of manuscript for intellectual content.

Dr. Menon: Critical revision of manuscript for intellectual content.

Dr. Demchuk: Concept and critical revision of manuscript for intellectual content.

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