

“Calcified Clot March” after Intravenous Thrombolysis

Sir

Thrombus migration in the intracranial circulation is a rare phenomenon and is seen mostly in the cases of middle cerebral artery (MCA) occlusion.^[1] Though this phenomenon has been reported to occur more frequently after intravenous (IV) thrombolysis, some studies disprove the same.^[2,3] Most of the literature available suggests that the thrombus migration is associated with fragility of thrombus resulting in failure to achieve thrombolysis in cerebral infarction (TICI) 3 recanalization. Spontaneous migration of the calcified thrombus is still rarer. We report a case of an elderly male patient who presented with complaints of acute onset of left upper limb weakness due to the occlusion of superior division of the right MCA by a calcified embolus lodged at the origin of superior division. Repeat imaging after IV thrombolysis revealed the distal migration of the calcified embolus. We describe this phenomenon as “calcified clot march” sign.

A 73-year-old male presented to our stroke emergency unit with complaints of acute onset of left upper limb weakness and aphasia for 2.5 hours. His NIHSS at time of admission was 8. There was no history of diabetes mellitus, hypertension, or drug abuse. As per our institutional stroke protocol, non-contrast CT (NCCT) head and CT angiography of head and neck vessels was done. NCCT head revealed an ovoid focus of calcification (mean HU value of 375) in right sylvian

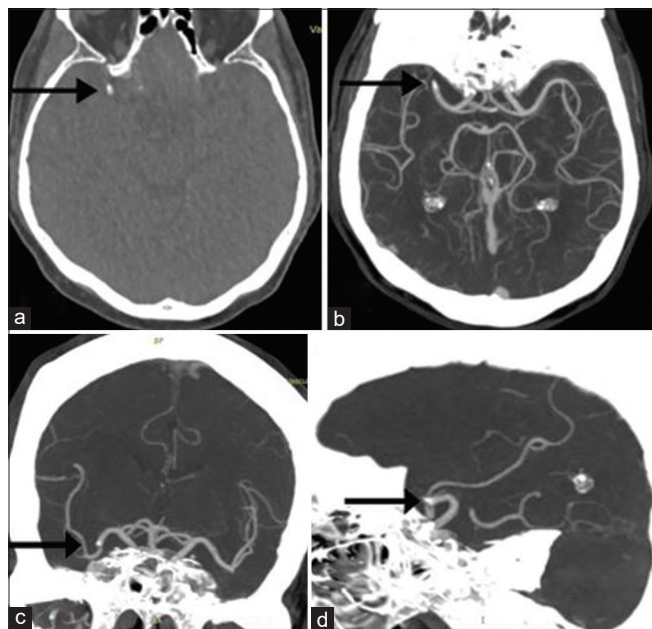


Figure 1: (a) NCCT Head axial section shows calcified focus in right sylvian fissure (black arrow). (b), (c), (d) CT angiogram images in axial, coronal and sagittal planes respectively shows calcified embolus causing complete occlusion of superior division of right middle cerebral artery at its origin (black arrow)

fissure region of 6 mm in length. [Figure 1a]. CT angiography confirmed the presence of calcified focus at the origin of superior division of right MCA [Figure 1b, c and d]. There was no contrast opacification of superior division of right MCA. Inferior division was normally opacified. However, distal leptomeningeal collateral flow was adequate. Neck CT angiogram images showed thick mixed partially calcified plaques in the aortic arch and at the origin of major arch vessels. Calcified plaques were also present at bilateral carotid bulbs resulting in moderate carotid stenosis [Figure 2]. Detailed discussion and counselling about the acute stroke intervention was done with the accompanying patient’s relatives, however, they refused for the endovascular treatment. IV thrombolysis with recombinant tissue plasminogen activator (rtPA) was done as the patient presented well within the stroke window period. However, patient’s Glasgow coma scale (GCS) deteriorated with left upper limb monoplegia. NIHSS score increased to 14. Repeat NCCT showed hemorrhagic transformation of the infarct [Figure 3a]. Follow-up CTA done after 24 hours post-IV thrombolysis revealed the distal migration of the calcified embolus into the superior division of the right MCA. The superior division was opacified for 1.5 mm in length from origin, beyond which it was not opacified [Figure 3b, c and d]. Patient received conservative management and was discharged with residual left upper limb weakness.

Calcified cerebral embolus as a cause of stroke was initially reported in 1981 by Yoch DH *et al.*^[4] We could find very limited literature reporting the intracerebral artery-to-artery migration of the calcified emboli.^[5] Walker BS *et al.*^[1] has described the origin of these calcified cerebral emboli from calcific aortic stenosis, mitral valve calcifications or calcified plaques of neck vessels. In their study of 22 cases of cerebral calcified emboli, 86% were spontaneous in origin and the rest

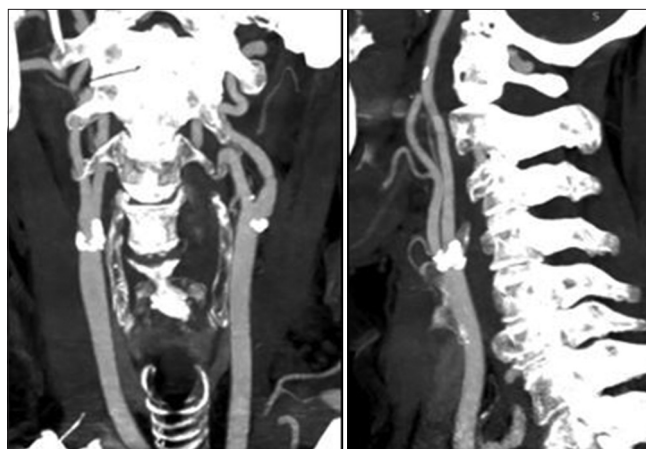


Figure 2: CT angiogram images of neck vessels shows thick calcified plaques at bilateral carotid bulbs causing severe stenosis on right side and moderate stenosis on left side

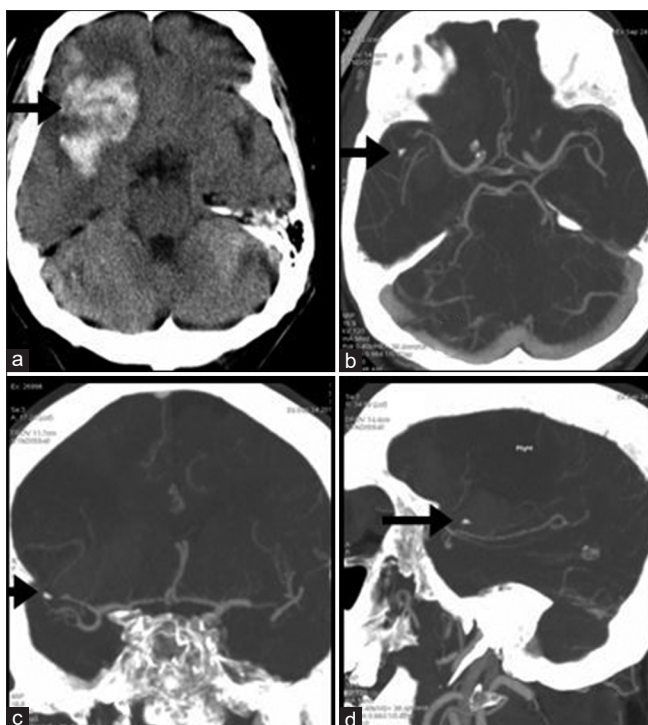


Figure 3: (a) NCCT Head axial section done 24 hours after intravenous thrombolysis, shows intracranial haemorrhage in right frontal lobe (black arrow). (b-d) Axial, Coronal and Sagittal CT angiogram images shows distal migration of calcified embolus in superior division of right MCA (black arrows)

14% were due to some manipulation of the plaques, e.g. left heart catheterization, carotid intervention or cardiopulmonary resuscitation. Our patient did not have any cardiac complaints and his 2D-ECHO was also normal. Thick calcified plaques were, however, seen in both cervical carotids and aortic arch, which we believe were a source of calcified embolus in our patient. It has been postulated that intravenous or intraarterial thrombolytics lead to lysis of the clot with distal migration of its fragments.^[3,6] Middle cerebral artery is considered as the most common site of calcified embolism. Calcified emboli lodged in superficial smaller arteries seen over the surface of brain, as multiple calcifications in pial arteries are termed as “Salted pretzel sign”.^[6] Efficacy of thrombolytics is limited in calcified embolism. In the study by Walker *et al.*, 9 patients received IV thrombolytics, however only 4 of them showed symptomatic improvement. Similar outcome has been reported by other authors.^[7-9] Our patient deteriorated and developed hemorrhagic transformation of infarct one day after thrombolysis, which could be secondary to reperfusion injury after recanalization of proximal superior division. In a case series of 5 patients by O’Cearbhaill *et al.*, one patient underwent mechanical thrombectomy for calcified embolus without significant clinical improvement.^[10]

Distal intracerebral arterial-to-arterial embolus migration is very rare with only limited available literature. Migration of noncalcified soft fragile emboli is a well-known phenomenon, but migration of calcified emboli is uncommon. In our patient,

distally migrated embolus had similar size as was seen on initial scan confirming the migration of complete embolus rather than its fragmentation. Walker BS *et al.*^[1] have reported distal intracerebral artery-to-artery migration of calcified emboli on repeat imaging in 14% of patients. This “clot march” confirms the presence of calcified embolus rather than intracranial arterial calcification or small hemorrhage. On follow-up scans, distally migrated intracerebral calcified emboli may result in infarcts at unexpected locations, or onset of new focal neurological deficits.^[2] Increased incidence of repeated strokes has been reported in such cases. Patients with calcified embolus should undergo further evaluation to find out the source of embolus as they are prone to recurrent strokes as well.

To conclude, intracerebral artery-to-artery migration of embolus, though rare, could lead to infarcts in unexpected territories with new neurological deficits. Both intravenous thrombolysis and mechanical thrombectomy have lower success rates in cases of ischemic stroke due to calcified embolism. Looking at the size of the embolus on follow-up imaging could confirm the distal migration of complete embolus rather than its fragmentation. Patients with calcified embolus should undergo further evaluation to find out the source of embolus as they are prone to recurrent strokes as well.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Vivek Agarwal, Neha Choudhary, Sameer Vyas, Ajay Kumar, Manoj Goyal¹

Departments of Radiodiagnosis and ¹Department of Neurology, PGIMER, Chandigarh, India

Address for correspondence: Dr. Sameer Vyas,

Department of Radiodiagnosis, PGIMER, Chandigarh, India.

E-mail: sameer574@yahoo.co.in

REFERENCES

- Walker BS, Shah LM, Osborn AG. Calcified cerebral emboli, a “do not miss” imaging diagnosis: 22 new cases and review of the literature. *Am J Neuroradiol* 2014;35:1515-9.
- Fischer U, Kaesmacher J, Mendes PV, Chapot R, Siddiqui A, Froehler MT, *et al.* Direct mechanical thrombectomy vs combined intravenous and mechanical thrombectomy in large artery anterior circulation stroke. *Stroke* 2017;48:2912-8.
- Yoon JH, Shin YS, Lim YC, Kim HS, Nam HS, Heo JH. Distal migration of thrombus during intraarterial thrombolysis. *Eur Neurol* 2010;63:62-6.
- Yock DH Jr. CT demonstration of cerebral emboli. *J Comput Assist Tomogr* 1981;5:190-6.
- Yong SW, Lim TS, Hong JM, Joo IS. Migrating calcification on

- CT angiography: Another sign of an embolic stroke. *Eur Neurol* 2010;63:126.
6. Christian BA, Kirzeder DJ, Boyd J, Laing J, Gash J. Showered calcific emboli to the brain, the 'salted pretzel' sign, originating from the ipsilateral internal carotid artery causing acute cerebral infarction. *Stroke* 2009;40:319-21.
 7. Gokhale S, Lahoti S, Rojas R, Caplan LR. Tissue plasminogen activator and calcific emboli. *JAMA Neurol* 2013;70:642-3.
 8. Halloran JJ, Bekavac I. Unsuccessful tissue plasminogen activator treatment of acute stroke caused by a calcific embolus. *J Neuroimaging* 2004;14:385-7.
 9. Kissela BM, Kothari RU, Tomsick TA, Woo D, Broderick J. Embolization of calcific thrombi after tissue plasminogen activator treatment. *J Stroke Cerebrovasc Dis* 2001;10:135-8.
 10. O'Cearbhaill RM, Moriarty HK, Crosbie I, Gd K, Bolster F, Ao H, *et al.* Calcified cerebral emboli: A case series and review of literature. *J Syst Integr Neurosci* 2016;2:180-3.

Submitted: 21-Oct-2019 **Revised:** 08-Nov-2019 **Accepted:** 18-Jan-2020

Published: 29-Jun-2020

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

DOI: 10.4103/aian.AIAN_532_19