

## Case Series

# Symptomatic Extracranial Carotid Artery Thrombus: An Indian Experience

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### ABSTRACT

**Introduction:** Symptomatic intraluminal carotid artery thrombus (ICT) is an uncommon finding, whose incidence increases with the percentage of stenosis. The optimal treatment modality to address carotid artery thrombus is not well established. We present our data of medical management of carotid artery thrombus with antiplatelet and anticoagulation. **Methods:** We reviewed our data from January 1, 2016 to December 31, 2017. Patients with extracranial carotid artery thrombus underwent a catheter digital subtraction angiogram to confirm the presence of thrombus. Medical management was done with dual antiplatelets along with low-molecular-weight heparin, and a check angiogram was done after 14 days. Factors contributing to the persistence of thrombus were analyzed. **Results:** A total of 21 patients diagnosed with acute ischemic stroke and extracranial carotid artery thrombus. Three patients opted for endarterectomy. Eighteen patients underwent medical management. Nine (50%) had a resolution of thrombus. Those with persistent thrombus were significantly older (average age 64 vs. 43 years,  $P = 0.008$ ). They also had significantly higher proportions of hypertension (100% vs. 44%,  $P = 0.029$ ), diabetes mellitus (89% vs. 11%,  $P = 0.003$ ), and underlying carotid stenosis (100% vs. 33%,  $P = 0.009$ ). **Conclusion:** Our regimen of dual antiplatelets plus short-term anticoagulation is safe and effective in the management of ICT. Large-scale studies are warranted to determine the optimal regimen and duration of medical treatment.

**KEYWORDS:** Carotid artery thrombus, medical management, stenosis, stroke

## INTRODUCTION

In patients presenting with acute ischemic stroke or transient ischemic attack (TIA), symptomatic intraluminal carotid artery thrombus (ICT) is an uncommon finding. The incidence of ICT is directly related to the percentage of stenosis. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) showed that patients with ICT had higher risk of stroke and death.<sup>[1]</sup> Current treatment options suggest carotid endarterectomy (CEA) as an urgent treatment due to risks of recurrent minor strokes and thrombus migration causing large vessel occlusion. Complications with CEA double in the presence of ICT (6% vs. 12%).<sup>[2,3]</sup>

The optimal treatment modality to address ICT in an acute stroke or TIA is not well defined. Published literature shows a variety of treatment options being

used including medical treatment with antiplatelets alone, antiplatelets with anticoagulation, anticoagulation alone, surgery, or stenting.<sup>[4-8]</sup>

We present our data of medical management of ICT with antiplatelets and anticoagulation.

## METHODS AND STATISTICAL ANALYSIS

This study was conducted in a tertiary care hospital with an interventional neurology department and a stroke unit.

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We maintain a prospective stroke registry and details of all patients who are admitted with an acute stroke or TIA are maintained. We reviewed our data from January 1, 2016 to December 31, 2017. Consecutive adult patients, who were admitted with an acute ischemic stroke or TIA and who had a demonstrable thrombus in the ipsilateral common carotid artery (CCA) or extracranial internal carotid artery (ICA), were included in the analysis.

Patients, who had a thrombus that was confined to the intracranial ICA, had associated trauma or arterial dissection, history of carotid stenting ipsilateral to the thrombus, hemorrhagic transformation of the infarct, or contraindications to a digital subtraction angiogram (DSA), were not included.

A predefined performa was used to collect demographic, clinical, and imaging information for each patient. TIA and stroke were defined as per the latest acute stroke guidelines.<sup>[9]</sup> Risk factor assessment was done by clinical history and review of past medical records. Detailed neurological examination and vital charts were recorded. Investigations included a complete blood count, fasting blood glucose levels, glycosylated hemoglobin, troponin I, renal and hepatic function tests, coagulation profile, 2D echocardiogram, electrocardiogram, and 24-hour Holter monitoring. Primary imaging modalities were either magnetic resonance imaging (MRI) with MR angiogram or CT with CT angiogram. Patients presenting within the window for intravenous (IV) thrombolysis received full-dose IV alteplase. All patients received standard stroke care according to the institutional stroke management protocol.

All CT and MRI images were reviewed by a neuroradiologist. As per the institutional protocol, patients who had a thrombus in the CCA or extracranial ICA underwent a catheter DSA to confirm the presence of thrombus (defined as a filling defect visible in at least two planes) and to ascertain the degree of underlying stenosis according to the NASCET criteria. The patients were given options for surgical endarterectomy (CEA) or medical management; those who opted for surgical treatment were excluded from the analysis. Those who opted for medical management were treated with dual antiplatelets (aspirin and clopidogrel) along with low-molecular-weight heparin (dalteparin 100 units/kg q12 h). All patients were monitored for recurrence of stroke or TIA, bleeding events, and adverse drug reactions. Dalteparin was continued for 2 weeks, and then a check DSA was done to look for the resolution of the thrombus. If the thrombus had resolved, dalteparin was stopped and dual antiplatelets were continued for 3 months, following which single antiplatelet was continued. Patients, who had persistent

thrombus, were offered endarterectomy again. All patients were followed up for at least 3 months.

Data analysis was done using the Statistical Package for Social Sciences version 22.0 (International Business Machines Corporation, New York, NY, USA). Continuous variables were expressed in the form of mean and standard deviation and categorical variables as percentages. The analysis was done by dividing the patients into two groups based on the persistence of thrombus. The *t*-test and Fisher's exact test were used to compare variables between the groups.

Clearance from the Institutional Ethics Committee was obtained. A written, informed consent was obtained from all patients or their legally authorized representative if the patient was unable to give consent.

## RESULTS

In the study period, we found a total of 21 patients who had an acute ischemic stroke with a CCA or cervical ICA thrombus. Out of these, three patients opted for CEA directly. The remaining 18 patients were included in the analysis. In this group, 14 (78%) were male. The average age was 54 years. 13 (72%) patients had hypertension, 9 (50%) had diabetes mellitus, while dyslipidemia, cardiac dysfunction, or hypothyroidism was present in 3 (17%) patients each.

All the patients received dual antiplatelets plus 14 days of dalteparin except for two patients who received aspirin plus dalteparin. Of these two patients, one had an unsecured intracranial aneurysm, while the other developed an allergic reaction to clopidogrel. Check DSA done after 14 days showed the resolution of thrombus in 9 (50%) patients.

We compared patient and DSA characteristics between patients who had a resolution of thrombus and those who had persistent thrombus. Those with persistent thrombus were significantly older (average age 64 vs. 43 years,  $P = 0.008$ ). They also had significantly higher proportions of hypertension (100% vs. 44%,  $P = 0.029$ ), diabetes mellitus (89% vs. 11%,  $P = 0.003$ ), and underlying carotid stenosis (100% vs. 33%,  $P = 0.009$ ). There was no gender difference between the two groups.

A total of six patients underwent carotid endarterectomy, three directly and three, after 2 weeks of medical management.

There were no incidences of recurrence of stroke or TIA, bleeding events, or adverse drug reactions in any patient in the medical management group. Out of the three patients who underwent CEA directly, one developed a postoperative ischemic stroke.

## DISCUSSION

Symptomatic ICT increases the risk of recurrent stroke. This makes a definitive treatment imperative. Unfortunately, the optimal treatment paradigm for ICT is not yet established. Several case series have reported varied treatment modalities including medical, surgical, and endovascular treatments.<sup>[4-8]</sup>

Medical treatment that has been tried has consisted of antiplatelets, anticoagulation, or a combination of both. Medical treatment has been used alone and in combination with delayed revascularization. Studies with antiplatelets alone have reported an 11% risk of stroke and death at 1 month.<sup>[2]</sup> In another study of six patients treated with anticoagulation alone, there were no recurrent ischemic events. The authors treated an additional three patients with anticoagulation and delayed revascularization with no recurrence between starting anticoagulation and surgery. One patient in that study had a fatal post-CEA stroke.<sup>[5]</sup>

Earlier, emergent surgical intervention was considered in the setting of ICT. However, results from multiple studies have demonstrated a high risk of perioperative stroke (12%–29%).<sup>[2,4,5,10,11]</sup> In one study, there was a 17% risk of perioperative stroke or death after early carotid stenting.<sup>[12]</sup> A small case series by Caplan *et al.* reported no stroke recurrence after early CEA.<sup>[13]</sup> As can be seen from the above studies, neither the optimal mode of treatment (medical versus surgical) nor the optimal regimen of treatment is well established.

A few studies have reported the use of short-term parenteral anticoagulation with good results. Another study by Vellimana *et al.* reported the use of antiplatelets plus anticoagulation in patients with ICT. They reported a low rate of recurrent ischemic events with that regimen.<sup>[3]</sup>

In this study, we report the use of a dual antiplatelet plus parenteral anticoagulation regimen. Half (50%) of our patients had resolution of the ICT on follow-up DSA. There were neither any recurrent ischemic events nor bleeding episodes. Factors contributing to the persistence of thrombus included underlying stenosis, older age, hypertension, and diabetes mellitus.

Despite the results, our study is not without limitations. It is a retrospective case series. We have not analyzed stroke recurrences in patients who underwent CEA as a first-line treatment nor have we followed up patients after delayed revascularization. There were two patients who were treated with single antiplatelet and anticoagulation but still had a resolution of the ICT. We also did not evaluate all patients for hypercoagulable states.

Finally, our sample size is small, and the occurrence of recurrent ischemic events or adverse reactions might be underestimated.

## CONCLUSION

Our regimen of dual antiplatelets plus short-term anticoagulation is safe and effective in the management of ICT. It offers a noninvasive modality of treatment. Patients who do not respond to the regimen can then be offered the option of revascularization. Further large studies are warranted to establish the optimum regimen of medical treatment and to delineate the factors contributing to nonresolution of the thrombus.

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## Conflicts of interest

There are no conflicts of interest.

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