Case Report

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Successful Mechanical Thrombectomy of Bilateral Middle Cerebral Artery Occlusions Following Apixaban Discontinuation

Bahadar S. Srichawla[1], Ton Fang[1], Abigail Bose[1], Vincent Kipkorir[2], and Annie Ferris[1]

Abstract

Optimal anticoagulation management in patients with atrial fibrillation (AF) during acute ischemic stroke is complex and often poses a significant clinical challenge. An 82-year-old man with AF presented with left-sided hemiparesis and hypoesthesia due to occlusion of the right middle cerebral artery (MCA) after discontinuing apixaban for 5 days. Successful mechanical thrombectomy (MT) achieved thrombolysis in cerebral infarction (TICI) score of 2C. Anticoagulation was postponed due to a small risk of hemorrhagic conversion. However, the patient developed a rare bilateral M1 segment MCA occlusions on the fifth day with a National Institute of Health Stroke Scale (NIHSS) score of 23, leading to an emergent thrombectomy, resulting in TICI 3 and TICI 2C recanalization in left and right MCAs, respectively. The patient required admission to the intensive care unit and was eventually discharged to an inpatient rehabilitation facility with only residual left hemiparesis and moderate dysarthria. This case underscores the delicate balance between the risk of recurrent ischemic stroke and the potential for hemorrhagic conversion when treating anticoagulation in the acute setting. Close monitoring and an individualized approach are necessary for the treatment of patients with AF who have suffered an acute stroke, especially when anticoagulation must be stopped. We encourage future guidelines to incorporate both imaging and clinical data when determining the continuation of anticoagulation in patients with a recent ischemic stroke. This case also depicts the effectiveness of neuroendovascular interventions such as MT to effectively manage rare simultaneous large multi-vessel occlusions with good outcomes.

Keywords

stroke, thrombectomy, middle cerebral artery occlusion, apixaban, anticoagulation

Introduction

Stroke represents a significant public health burden worldwide, with thromboembolic occlusions of the large cerebral arteries being among the most debilitating types.[1] The middle cerebral artery (MCA) is the most affected vessel in ischemic stroke, carrying significant risks of severe disability and mortality.[2] Anticoagulant therapy with drugs such as apixaban is often implemented as a preventive strategy in patients with a high risk of ischemic stroke such as those with nonvalvular atrial fibrillation (AF).[3] Mechanical thrombectomy, a procedure in which a device such as a stent-retriever is used to directly extract the occluding clot from the affected artery, has emerged as a highly effective treatment modality in acute ischemic stroke caused by large vessel occlusion.[4] Despite its demonstrated efficacy, the literature detailing the results of mechanical thrombectomy for bilateral MCA occlusion, particularly in the context of recent anticoagulant discontinuation, is sparse.

This report presents a unique case of successful mechanical thrombectomy performed for bilateral MCA occlusions in a patient who had recently discontinued apixaban after an ischemic cerebrovascular accident (CVA). We aim to contribute to the body of evidence supporting the safety and efficacy of mechanical thrombectomy in complex clinical scenarios and discuss the implications for the timing of resuming anticoagulation after ischemic CVA.

[1]University of Massachusetts Chan Medical School, Worcester, USA
[2]University of Nairobi, Kenya

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Corresponding Author:
Vincent Kipkorir, University of Nairobi, University Way, Nairobi 00100, Kenya.
Email: vincentkipkorir42358@gmail.com

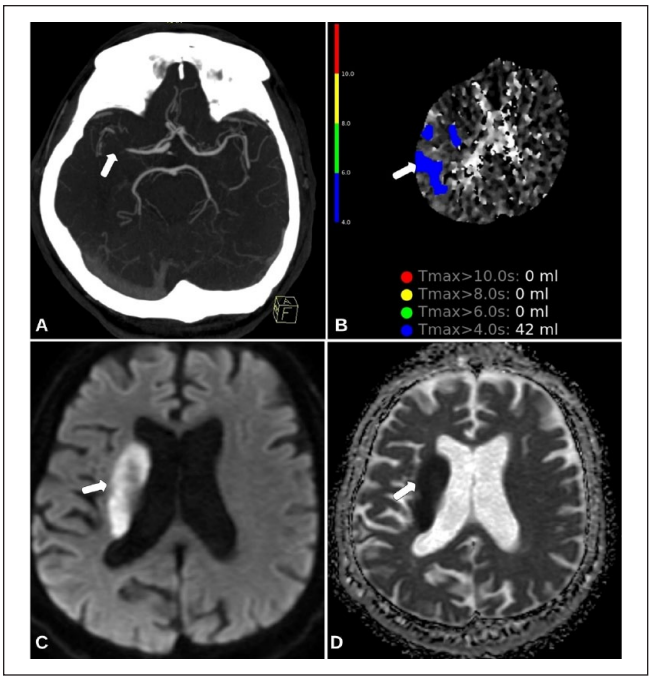

Figure 1. (A) CTA of the head depicting the occlusion (arrow) of the M1 segment of the right MCA. (B) CT perfusion imaging with a 42-mL salvageable penumbra (arrow) within the distribution of the right MCA territory. (C) Diffusion-weighted imaging (DWI) sequence depicting an acute infarction of the right basal ganglia (arrow) (D) correlated with the apparent diffusion coefficient (ADC).

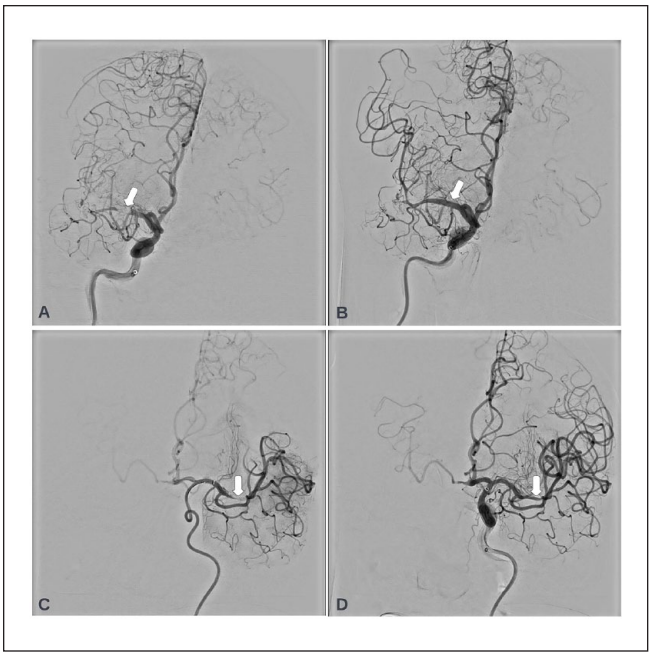

Figure 2. (A) Digital subtraction angiography (DSA) of the anterior view that depicts an occlusion (arrow) of the M1 segment of the right MCA. (B) and successful recanalization of TICI 2C. (C) Occlusion (arrow) of the M1 segment of the left MCA (D) and successful recanalization of TICI 3.

Case Presentation

An 82-year-old man has a medical history of nonvalvular AF, hypertension, and type 2 diabetes mellitus. He had been receiving apixaban as an anticoagulant treatment for his AF. It was determined that the patient had discontinued his apixaban regimen 5 days before presentation for an unknown reason. Relevant home medications include atorvastatin 80 mg daily, metformin extended release 500 mg daily, and metoprolol succinate 50 mg daily. He presented to the emergency department with weakness and numbness on the left side for the past 12 hours, with a National Institutes of Health Stroke Scale (NIHSS) score of 7. The neurological exam was significant for a left-sided facial droop, and 3/5 (Medical Research Council scale [MRCS]) muscle strength in the left upper and lower extremity. The blood pressure on arrival was 148/92 mm Hg. An electrocardiogram showed an elevated heart rate of 105 beats per minute with no p-waves and an irregularly irregular rhythm. Initial serum laboratory values were noncontributory, and the family history was unknown. The blood glucose was 110 mg/dL. The hemoglobin A1C was 6.9% and low-density lipoprotein (LDL) was 69 mg/dL. Computerized tomography (CT) angiogram of the head and neck revealed an occlusion of the right M1 segment of the MCA. CT perfusion imaging showed an increased time-to-peak (TTP) and maximum travel time (MTT) with no associated decrease in cerebral blood volume (CBV) with an approximate 42 mL of salvageable penumbra (Figure 1A-B). Due to the timing of the onset of the symptoms, he was beyond the therapeutic window for intravenous thrombolytic therapy. Mechanical thrombectomy (MT) was performed, achieving a thrombolysis in cerebral infarction (TICI) score of 2C, indicative of partial recanalization of the occluded artery. Subsequent brain magnetic resonance imaging (MRI) confirmed an acute infarction of the right basal ganglia that was seen in both diffusion-weighted imaging (DWI) and apparent diffusion correlation (ADC) with minor hemorrhagic conversion (Figure 1C-D). A transthoracic echocardiogram showed a normal left ventricular ejection fraction of 55% and mild mitral, aortic, and tricuspid regurgitation. Given the risk of further hemorrhagic conversion, the resumption of apixaban was delayed for 5 days.

However, on the fifth day before the planned reinstatement of apixaban, the patient was found to be minimally responsive with quadriparesis and global aphasia, with an elevated NIHSS score of 23. The neurological exam was consistent with global aphasia, bilateral facial droop, and quadriparesis (2/5 muscle strength). His well-known time was approximately 5 hours before the last neurological assessment was completed. An urgent CT angiogram of the head and neck showed bilateral occlusions of the M1 segment of the MCA. A single endovascular neurosurgeon

performed a digital subtraction angiography (DSA) and an emergent bilateral mechanical thrombectomy with a stent retriever and aspiration catheter. TICI 3 (complete) recanalization of the left MCA and TICI 2C (partial) recanalization for the right MCA were obtained (Figure 2). Recanalization was completed in 3 passes bilaterally, and stenting was not indicated. MT was completed within 6 hours from the last known well time. After the procedure, the patient was admitted to the intensive care unit for further management. Neurological assessments were completed every hour for the first 12 hours and then were assessed every 4 hours thereafter. The groin puncture site was monitored daily for the first week. Apixaban was cautiously reintroduced 7 days after the second ischemic event. A repeat MRI of the brain was not completed due to patient agitation in the intensive care unit. The patient's post-discharge plan included inpatient rehabilitation to address residual left-sided weakness and dysarthria, yielding a discharge Modified Rankin Score (mRS) of 3. His atrial fibrillation was managed with metoprolol succinate 50 mg daily, and apixaban 5 mg twice daily, and continued on statin therapy. At his 6-month follow-up appointment at the vascular neurology clinic, the patient demonstrated neurological stability with a slight improvement in his residual symptoms.

Discussion

Anticoagulation management in patients with atrial fibrillation is a delicate balance between preventing thromboembolism and minimizing the risk of hemorrhagic complications. Our case highlights this clinical challenge, particularly in the context of acute ischemic stroke. The self-discontinuation of apixaban in our patient precipitated an initial ischemic stroke, which was effectively managed by MT. However, he later suffered from a bilateral MCA occlusion after withholding apixaban due to a minor hemorrhagic conversion. The early start of anticoagulation after an ischemic CVA can increase the risk of hemorrhagic transformation.[5] This risk is especially high in patients with large infarcts, elevated blood pressure, cardioembolic etiologies, and those who received thrombolytic therapy. The resultant intracerebral hemorrhage can lead to significantly worse neurological outcomes, including increased disability and mortality.[6,7] Individuals with a CHA_2DS_2-VASC score of 9 have a 12.2% annual risk of ischemic CVA, and oral anticoagulation provides a 75% relative risk reduction. Furthermore, the risk of recurrent stroke is elevated in the initial 4-week period.[5] Factors such as blood-brain barrier breakdown, impaired cerebral autoregulation, and increased local inflammation may contribute to an increased risk of hemorrhagic transformation after an ischemic event.[8] Therefore, the resumption of anticoagulation must be based on a careful determination of risks and benefits. Few cases of bilateral MCA occlusions requiring MT have been reported in the literature. Story et al reported the case of a 64-year-old woman who had AF and held apixaban for 5 days before a cerebral angiogram who developed bilateral MCA occlusions. The patient underwent successful bilateral MT with TICI 3 revascularization.[9]

Current strategies to determine the resumption of anticoagulation after an ischemic CVA include both an imaging-based and clinical approach. The rule "1-2-3-4 days" adopts a clinical approach based on the NIHSS to determine when to start direct oral anticoagulation (DOAC). This study involved a cohort of 1797 patients derived from a Japanese stroke registry that determined that early initiation of DOAC within 1, 2, 3, or 4 days was reasonable to decrease the risk of recurrent CVA, but also a major bleeding event. The "1-2-3-4 day" rule recommends the following: (a) Mild stroke (NIHSS $<$ 8) DOAC initiation 2 days after the event. (2) Moderate stroke (NIHSS 8–15) DOAC initiation 3 days after the ischemic event and after evaluating for hemorrhagic transformation on CT or MRI on the same day of initiation. (3) Severe stroke (NIHSS $>$ 16) DOAC initiation 4 days after the ischemic event and after evaluating for hemorrhagic transformation on CT or MRI on the same day of initiation.[10] Taking this study into account, the ideal time to restart apixaban in our case was appropriately delayed given the hemorrhagic conversion. In clinical practice, caution is exhibited due to limitations and complicating factors when only using a clinical-based marker such as the NIHSS when making decisions. For example, many patients are admitted to the intensive care unit (ICU) after a CVA and develop superimposed delirium that can artificially inflate the NIHSS. The TIMING trial is a Swedish registry-based cohort study of 888 patients that determined that early initiation of DOAC was not inferior to delayed start after acute ischemic stroke in patients with atrial fibrillation.[11] In 2020, a survey with 238 responses from stroke specialists in the United States (ACT-SAFe) was completed on the best practices of reinstatement of anticoagulation after an ischemic stroke. For a mild ischemic stroke occupying $<$1/3 of the MCA territory without hemorrhagic conversion or thrombolysis, 51% of the respondents chose to anticoagulate within the first 4 days. In patients with a large MCA territory stroke ($>$1/2 MCA territory), evidence of hemorrhagic conversion or cerebellar infarct $>$ 60 ccs, 65% of the respondents chose to wait at least 7 days before starting anticoagulation.[12] In addition, a prior study determined that individuals with an ischemic stroke with AF would benefit from DOAC initiation without bridging therapy.[13] Prior clinical trials have also established that DOACs are just as effective as vitamin-K antagonists (e.g. Coumadin) at preventing recurrent AF-related ischemic stroke.[14] Close monitoring, including frequent neurological checks, is a cornerstone of effective management in patients who have had an acute ischemic stroke, especially when anticoagulation has been paused. Regular assessments allow healthcare providers to quickly identify any neurological changes that may indicate the onset of recurrent stroke or hemorrhagic conversion. These checks often involve repeated measures of consciousness, motor strength, language, vision, and other neurological functions

using standardized tools such as the NIHSS. In addition, close monitoring can guide the timing of when to safely reintroduce anticoagulation, as any sign of clinical stabilization or improvement may indicate a lower risk for hemorrhagic conversion.[15] This case encourages further research on optimal strategies and standardized international guidelines for anticoagulation management in the context of recent cerebral infarction to minimize both ischemic and hemorrhagic risks. These guidelines should incorporate both clinical and imaging data to provide an individualized approach, tailoring decisions based on factors such as the patient's age, overall health status, stroke severity, and specific imaging findings like the size of the infarct or the presence of hemorrhagic conversion.[16] The guidelines would also benefit from including clear protocols on when and how to safely discontinue and resume anticoagulation. The development of such guidelines would contribute significantly to standardizing care, reducing variability in treatment approaches, and potentially improving patient outcomes. Future randomized controlled studies that incorporate both clinical and imaging-based strategies to determine the optimal timing of anticoagulation in ischemic CVA with AF are needed.

Despite the complexity of his clinical course, the outcomes of our patient were favorable, in part, due to the prompt recognition of his condition and the immediate intervention with thrombectomy. However, his residual symptoms underscore the potential severity of the neurological sequelae of such events. In addition, this case emphasizes the vital importance of patient education and compliance with anticoagulant medication. The temporary cessation of apixaban may have contributed to the development of the first and subsequent ischemic strokes of the patient. Hence, ensuring that patients understand the critical importance of consistent anticoagulant use is essential to prevent similar instances. This case serves as a valuable lesson for clinicians in managing similar future cases.

Conclusions

In the management of patients with atrial fibrillation, it is critical to balance the prevention of thromboembolism and mitigation of hemorrhagic risk, particularly in the setting of acute ischemic stroke. The impact of discontinuing anticoagulation, as illustrated in this case, can be severe and life-threatening. Prompt intervention with mechanical thrombectomy proved vital in managing acute stroke events in this patient, with a relatively favorable outcome despite multiple cerebral infarctions. This case underscores the need for patient education on the importance of medication compliance and highlights the need for further research into optimal anticoagulation management strategies in the context of a recent cerebral infarction. This includes timely initiation and discontinuation of therapy, individualization of care based on patient characteristics, and considering the extent of brain infarction and hemorrhagic conversion. Furthermore, this case highlights the effectiveness of mechanical thrombectomy in minimizing this rare bilateral occlusive event of the large cerebral vessels. The unique complexities and challenges posed by this case can provide a valuable learning experience for clinicians in the management of similar future scenarios.

Author Contributions

B.S.S. completed the literature review, drafted the initial manuscript, generated illustrations/figures, provided intellectual verification of the topic, and edited the final manuscript. A.B. and V.K. drafted the initial manuscript. T.F. provided guidance on revisions. A.F. provided intellectual verification on this topic. All authors reviewed the final draft of the manuscript.

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Ethical Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

Consent for Publication

Written informed consent was obtained for the patient in the publication of this case report.

ORCID iDs

Ton Fang https://orcid.org/0000-0003-2119-9015

Vincent Kipkorir https://orcid.org/0000-0001-6946-8857

Availability of Data and Materials

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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