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Journal

The Neurohospitalist, 11(1)

ISSN

1941-8744

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Publication Date

2021

DOI

10.1177/1941874420934333

Peer reviewed

The Neurohospitalist
2021, Vol. 11(1) 54-58

DOI: 10.1177/1941874420934333
journals.sagepub.com/home/NHO
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Mechanical Thrombectomy for Sequential Bilateral Middle Cerebral Artery Occlusions in a Patient With Recurrent Cryptogenic Strokes: A Case Report

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Abstract

Recurrent sequential mechanical thrombectomy for cryptogenic large vessel occlusion (LVO) can lead to excellent clinical outcome. A 68-year-old right-handed male presented with an acute proximal right middle cerebral artery (MCA) ischemic syndrome and underwent successful revascularization by mechanical thrombectomy with normal functional recovery. He was treated with dual antiplatelet therapy for 2 months following discharge, however later discontinued clopidogrel due to side effects. He then developed a recurrent, contralateral MCA occlusion 16 months later and once again received emergent endovascular reperfusion therapy with excellent neurological outcome. He has remained on off-label empiric oral anticoagulation since and has not had recurrent stroke nor evidence of cerebral ischemia. Favorable clinical outcomes can be achieved in patients despite recurrent LVO who underwent emergent mechanical thrombectomy. Optimal antithrombotic secondary stroke prevention strategies following embolic stroke of unknown source remains uncertain as recent evidence does not support rivaroxaban or dabigatran over aspirin. The benefit of apixaban over aspirin for the prevention of recurrent cerebral ischemia is under current investigation.

Keywords

stroke, intracranial arterial diseases, outcomes, neurosurgery, neuroradiology

Introduction

Worldwide, stroke is the second most common cause of mortality and disability, and multiple epidemiologic studies have reported that embolic stroke of unknown source (ESUS) accounts for up to 40% of all ischemic strokes, with a 7% to 21% risk of recurrence.[1-3] Optimal secondary prevention for ESUS remains uncertain.[4] Antiplatelet agents, vitamin K-antagonists, and direct oral anticoagulants (DOACs), such as direct thrombin inhibitors and factor Xa inhibitors, are therapeutic options; however, consensus guidelines have not been established for use in ESUS. The lack of supportive randomized treatment data and high-quality evidence may lead to potential undertreatment and risk of recurrent ischemic events. Herein, we present the clinical course and treatment of a patient with acute recurrent LVO who underwent successful endovascular treatment resulting in excellent neurological outcome.

Case Description

A 68-year-old right-handed male with coronary artery disease, hypertension, and hyperlipidemia presented with acute dysarthria and severe left hemiparesis. On neurologic examination, he had near unintelligible speech, dense left hemiplegia, and significant hemisensory neglect with a National Institute of Health Stroke Scale (NIHSS) score of 17. Computed tomography angiography revealed an occlusion at the right middle cerebral artery (MCA) M1-M2 junction with distal reconstitution of flow without signs of ipsilateral carotid disease (Figure 1A and B). This also demonstrated mild multifocal stenosis of the bilateral cavernous segments of the internal carotid arteries (less than 70% stenosis). Intravenous (IV) thrombolysis was administered within 3 hours of symptom onset followed by emergent endovascular thrombectomy within the following hour with excellent angiographic

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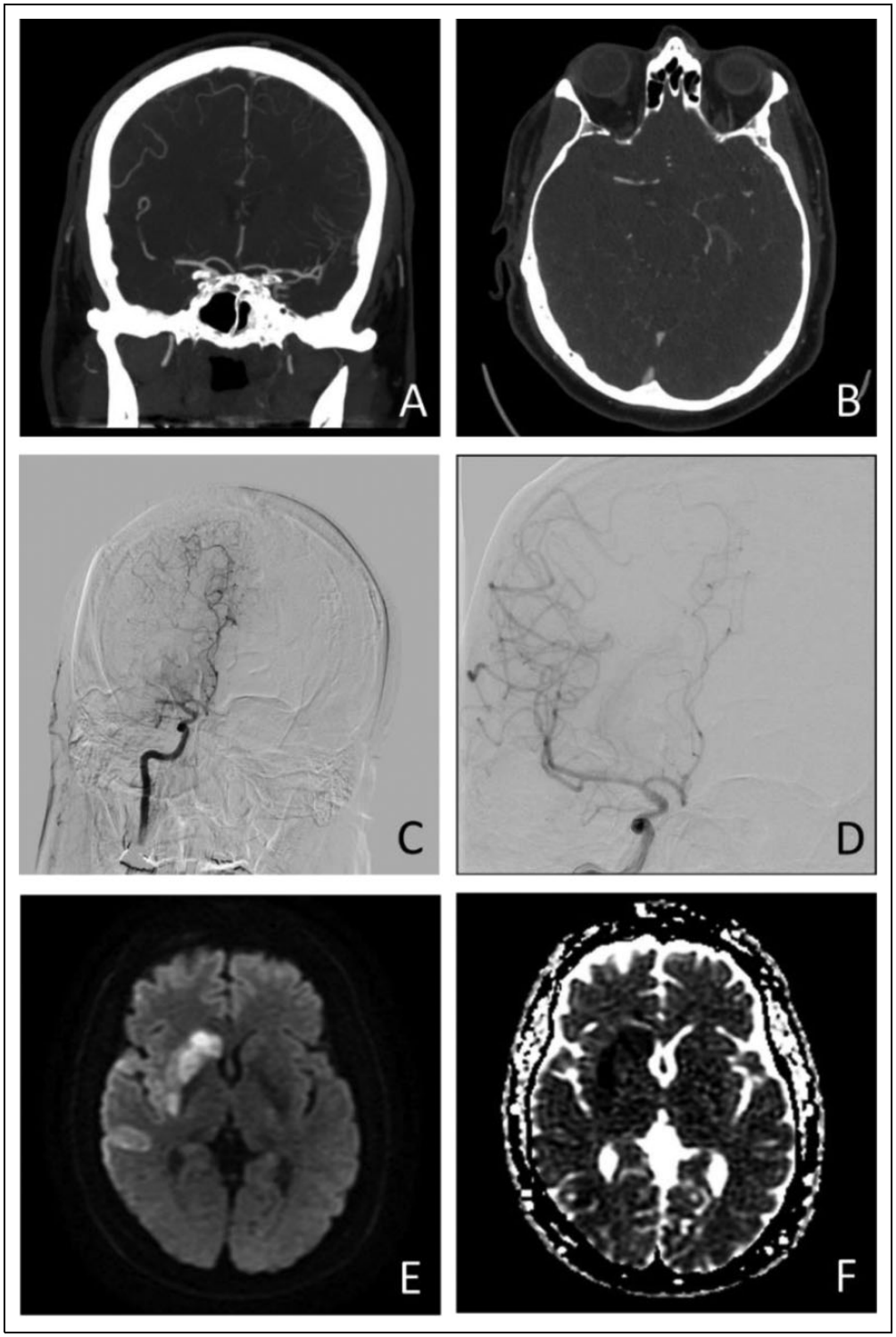

Figure 1. A and B, Computed tomography angiography coronal (A) and axial (B) views demonstrating thrombus in the right middle cerebral artery (MCA) distal M1 branch extending to the proximal M2 junction with loss of flow to the inferior M2 temporal branch and reconstitution of flow to the distal superior M2 temporal branches. C and D, Angiographic anteroposterior views of pre (C) and post (D) thrombectomy showing thrombolysis in cerebral infarction 3 revascularization of the right MCA. E and F, Magnetic resonance imaging diffusion-weighted imaging (E) and apparent diffusion coefficient (F) sequences demonstrating patchy regional infarctions involving the basal ganglia and anterior capsular limb, as well as scattered involvement of the frontal, temporal, and parietal lobes of the right cerebral hemisphere.

outcome (Figure 1C and D). The patient had significant neurological recovery in the immediate postoperative period with residual subtle left hemiparesis. A 24-hour posttreatment brain magnetic resonance imaging (MRI) demonstrated patchy regional infarctions (Figure 1E and F). Aspirin and clopidogrel were not initiated until 3 days postictus due to the presence of petechial hemorrhagic transformation within the deep nuclei. Cardiac structural pathology and intrachamber thrombus were excluded by echocardiographic imaging, and both inpatient telemetry and 30 days of outpatient cardiac event recording yielded no evidence of atrial dysrhythmia. He was treated with dual antiplatelet therapy for presumed symptomatic intracranial atherosclerotic disease (ICAD) with planned 90-day course per (Stenting vs. Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial guidelines, but after 2 months discontinued clopidogrel due to side effects (i.e., dysgeusia and significant weight loss) and was maintained on aspirin monotherapy.[5]

Sixteen months following his initial stroke, he re-presented with acute global aphasia and severe right hemiparesis. His NIHSS was 28 and corresponded with a proximal left MCA-M1 segmental occlusion identified on noninvasive angiographic imaging with stable minimal ICAD (Figure 2A and B). He once again received IV thrombolysis within 90 minutes of symptomatic onset followed by successful endovascular thrombectomy 40 minutes later (Figure 2C and D). A subsequent MRI demonstrated patchy regional infarctions (Figure 2E and F). The patient had marked neurologic improvement in language and motor function post thrombectomy but required ongoing rehabilitation after hospital discharge (modified Rankin score of 4 at discharge). Empiric off-label anticoagulation therapy with apixaban was initiated for a suspected cardioembolic mechanism. Repeat echocardiogram demonstrated probable apical septal hypokinesia without evidence of intrachamber thrombus and impaired left ventricular diastolic function without decreased ejection fraction. He underwent oncologic workup involving standard imaging and serologic testing for occult malignancy, which revealed a new diagnosis of monoclonal gammopathy of undetermined significance. Subsequent hypercoagulability testing of antiphospholipid antibody and genetic testing for increased levels of plasminogen activator inhibitor and mutations of factors 2 and 5 were unremarkable.

He had minimal neurological symptoms (modified Ranking Score of 1) 6 months after his second event and by 2 years made complete functional recovery. A prolonged implantable loop recorder showed no evidence of atrial fibrillation to date. He had remained on empiric oral anticoagulation since and has not had recurrent stroke nor evidence of cerebral ischemia.

Discussion

According to the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification of subtypes of acute ischemic strokes, cryptogenic stroke is defined as a stroke not attributable to any other cause (eg, cardioembolism, large artery atherosclerosis, or small artery disease) despite adequate diagnostic workup and can represent 9% to 25% of all ischemic strokes.[4,6] Embolic stroke of unknown source is most frequently seen in those who are young and lack traditional vascular risk factors, and in patients less than 55 years of age, ESUS can comprise up to 42% of all strokes.[7] Proposed mechanisms for cryptogenic stroke include paradoxical emboli related to a patent foramen ovale, unidentified atrial fibrillation, left atrial myopathy, and ulcerative aortic or cervical carotid artery plaques or vessel webs, all of which have variable recurrence risks.[4]

Our patient had significant vascular risk factors and presented with recurrent cryptogenic LVO. He was initially treated with standard dual antiplatelet therapy followed by monotherapy for presumed symptomatic ICAD. However, given the minimal stenosis, recurrence while on therapy, and bilateral acute nature with multiple associated cardiac risk factors, ESUS remained our leading diagnosis. Following the subsequent infarction, off-label empiric anticoagulant therapy with apixaban 5 mg twice daily was initiated for a suspected cardioembolic mechanism of which he has continued to remain event-free at 2 years. The use of DOACs for stroke prevention following ESUS is under active investigation, an anticoagulant class with a favorable side effect profile when compared to warfarin.[8-10] In contrast, warfarin is neither advantageous nor recommended for preventive therapy following cryptogenic stroke owing to an increase in hemorrhagic complications.[11,12] Of note, empiric anticoagulation for ESUS is off-label outside of clinical trials and is not supported by guidelines. However, given recurrent LVO despite adherence to antiplatelet therapy, an unrevealing standard diagnostic workup, and optimal control of other stroke risk factors, we felt it was reasonable to begin treatment in our patient.

Optimal stroke prevention following ESUS remains unknown. NAVIGATE ESUS (Rivaroxaban Versus Aspirin in Secondary Prevention of Stroke and Prevention of Systemic Embolism in Patients With Recent Embolic Stroke of Undetermined Source) was a randomized trial comparing secondary stroke prevention effectiveness between once-daily rivaroxaban 15 mg and aspirin 100 mg. The study was terminated early due to the lack of benefit in the anticoagulant arm (recurrent stroke risk 4.7% in both groups) and was also associated with greater risk of bleeding (1.8% vs 0.7%).[13] In a similar secondary prevention trial following cryptogenic stroke, RE-SPECT ESUS (Dabigatran Etexilate for Secondary Stroke Prevention in Patients With Embolic Stroke of Undetermined Source) randomized patients to receive dabigatran at a dose of 150 mg or 110 mg twice daily as compared with aspirin at a dose of 100 mg once daily.[14] Recurrent stroke occurred in 6.6% of dabigatran patients (4.1% per year) and 7.7% of aspirin patients (4.8% per year) for a hazard ratio of 0.85 (95% CI: 0.69-1.03).[14] This showed a strong but admittedly nonsignificant trend toward reduction in recurrent stroke

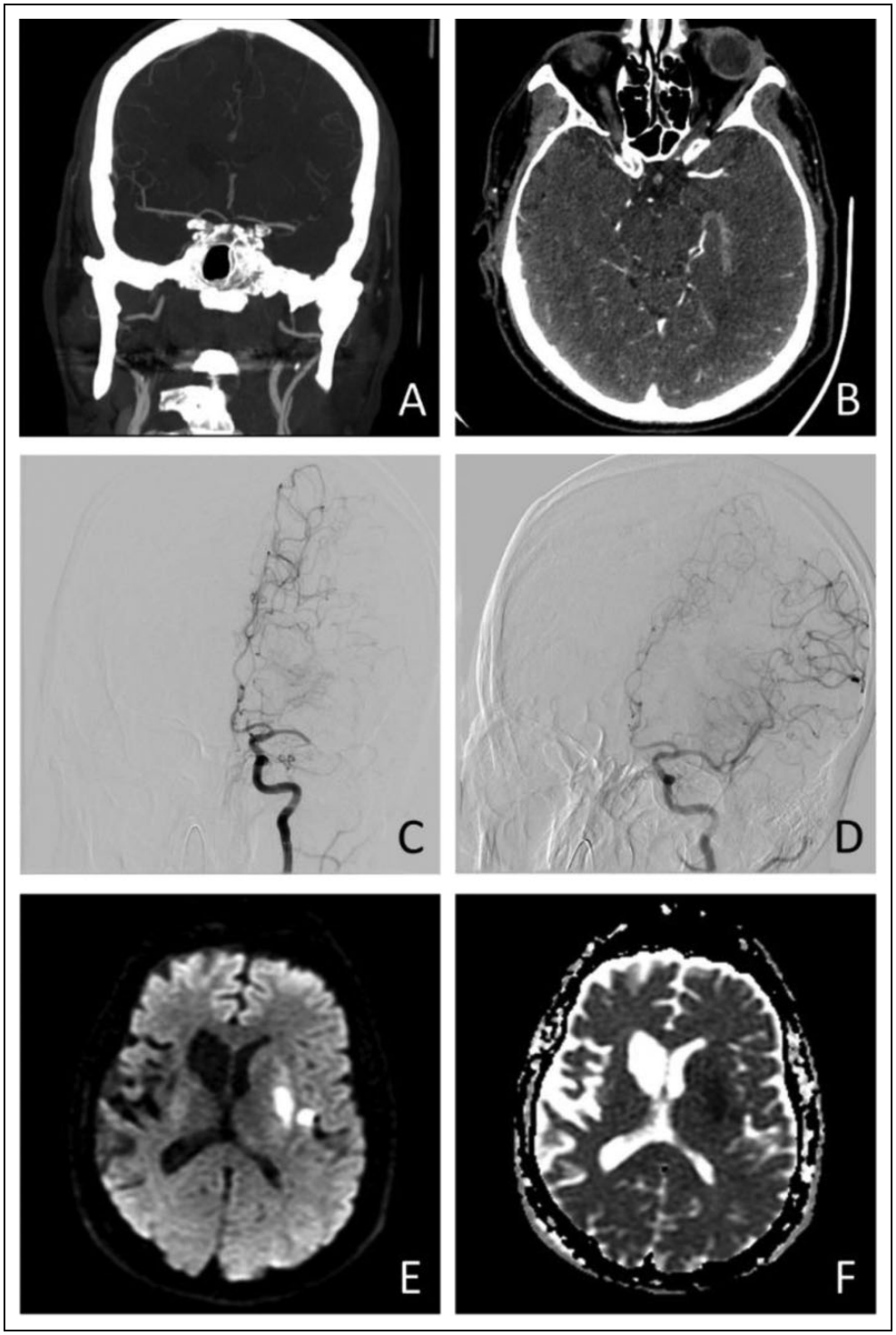

Figure 2. A and B, Computed tomography angiography coronal (A) and axial (B) views demonstrating left mid M1 occlusion. C and D, Angiographic anteroposterior views of pre (C) and post (D) thrombectomy showing thrombolysis in cerebral infarction 2a revascularization of the left M1 segment with delayed perfusion to a small caliber M3 insular branch. E and F, Magnetic resonance imaging diffusion-weighted imaging (E) and apparent diffusion coefficient (F) sequences demonstrating patchy regional infarctions involving the left lentiform and caudate nuclei with smaller foci involving the left frontal and temporal opercula. Right cerebral hemisphere encephalomalacia from the previous stroke is also demonstrated.

with dabigatran, with a post hoc analysis suggesting that there may be an effect on stroke recurrence after 1 year. Dabigatran was also found to have no significant difference in major bleeding (defined as intracranial, gastrointestinal, life-threatening, or fatal) but a significant increase in clinically relevant nonmajor bleeding (1.6% per year vs 0.9% per year).[14] These data along with others also demonstrated that the risk of recurrence is 7% to 11% within 3 months of a minor ischemic event in those receiving aspirin monotherapy.[15,16] Ongoing trials in Europe (ATTICUS, Apixaban for Treatment of Embolic Stroke of Undetermined Source) and the United States (ARCADIA, AtRial Cardiopathy and Antithrombotic Drugs In Prevention After Cryptogenic Stroke) are now testing the effectiveness of apixaban in the prevention of stroke following ESUS.[8,17]

This case report demonstrates that favorable clinical outcomes can be achieved in patients despite recurrent LVO who underwent emergent mechanical thrombectomy. Optimal antithrombotic secondary stroke prevention strategies following ESUS remain uncertain as recent evidence does not support rivaroxaban or dabigatran over aspirin. The benefit of apixaban over aspirin for the prevention of recurrent cerebral ischemia is under current investigation.

Authors' Note

Informed consent was obtained from the patient and he consented to the publication of this case report.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

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