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CASE REPORT

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Two cases of successful recanalization for acute cerebral artery embolism during perioperative period of radiofrequency ablation for atrial fibrillation

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Abstract

To explore the strategy of acute cerebral artery embolism after radiofrequency catheter ablation (RFA) for atrial fibrillation (AF). Reporting two cases with acute cerebral infarction after RFA for AF. Two patients were both with AF, and intracardiac thrombus was excluded through transesophageal echocardiogram (TEE) before procedure. Approach of ablation: circumferential pulmonary vein ablation in left atrium to isolate pulmonary vein plus linear ablation in the top and bottom of left atrium (BOX procedure). They both received Dabigatran Etexilate 110 mg twice daily, starting 6 hr after ablation. Symptoms of major stroke appeared 30 hr after ablation in Case 1. Occlusion was detected in M1 segment of the left middle cerebral artery by MRI 2 hr after symptoms onset. Intravenous thrombolysis was given immediately. In Case 2, the patient presented symptoms of major stroke 34 hr after ablation and occlusion in the basilar artery was confirmed by MRI 4.5 hr after symptoms onset. Although it was beyond the thrombolysis time window, mechanical thrombectomy was taken 7 hr after the symptoms onset. The culprit artery was successfully revascularized in both cases. In Case 1, NIHSS score was reduced from 8 (before thrombolysis) to 0 (24 hr after thrombolysis). In Case 2, NIHSS score decreased from 18 (before embolectomy) to 3 (24 hr after embolectomy). Both of the patients live a normal life without brain function impairment and hemorrhage until the last follow-up. Timely recanalization could attained a good cure effect when acute stoke was happened after RFA for AF.

KEYWORDS
AF and stroke, anticoagulants, recanalization

1 | BACKGROUND

AF is a definite risk factor for cerebral infarction. During the perioperative period of RFA, patient with AF is more susceptible to apoplexy, and the incidence of stroke can reach to 1 ~ 5% (Cappato et al., 2009). The higher incidence is related to the catheter procedure in left atrium, wound healing process in atrium after RFA, atrial stunning and perioperative anticoagulant strategies (Calkins et al., 2017). Considering the existence of the left atrial wound after ablation and the usage of anticoagulant drugs, the bleeding risk was increased during this period. It is

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still not clear whether emergency venous thrombolysis or mechanical thrombectomy should be recommended or not when acute cerebral infarction occurred after RFA. We would discuss the treatment strategy of acute cerebral embolism after RFA in the following paragraph.

2 | CASE 1

Patient, male, 59, due to persistent atrial fibrillation, RFA was operated in November 5, 2015. Before the procedure, oral anticoagulation (dabigatran 110 mg bid po) was administrated for a month and subsequent bridging therapy with low-molecular-weight heparin (Enoxaparin 0.6 ml: 4000 IU q12h ih) was given for 3 days. The left atrial and left atrial appendage thrombus was excluded by pulmonary veins CT angiography and transesophageal echocardiogram (TEE), but the left atrial appendage was large and the blood flow velocity was low (16 cm/s), appearing as dynamic smoke-like echoes. During the procedure, intravenous heparin (80 u/kg)was given after atrial septal aspiration and added by 1,000 u/hr later, which completely covered the whole process of left atrial circumferential pulmonary vein ablation isolating pulmonary vein plus linear ablation in the top and bottom of left atrium (BOX procedure). The endpoint of the procedure was complete pulmonary veins isolation. After ablation, AF turned into regular atrial tachycardia then electrical cardioversion was applied to restore sinus rhythm, which indicated the procedure was successful. Oral anticoagulation (Dabigatran Etexilate 110 mg bid po) was executed 6 hr after procedure. At 18:30 in November 6, 2015, 30 hr after RFA, the patient experienced a sudden syncope with a unconscious fall and recovered consciousness 30 s later. Neurological physical examination showed that the patient got a motor aphasia and could not cooperate to complete instructions. The muscle tension of the patient was low and the muscle strength was level 1+. The bilateral Babinskis' sign was positive. National Institutes of Health Stroke Scale score (NIHSS score) was 8 (Olavarria et al., 2011). Vital signs were stable (blood pressure: 115/74 mmHg, sinus rhythm 60 bpm, SpO_2 99%). Urgent brain MRI + DWI + MRA scan showed no significant sign of acute cerebral infarction in nonenhanced imaging (Figure 1a). The M1 segment in the left cerebral artery was obstructed and the distal branch was undeveloped in MRA images (Figure 1c). The bilateral frontal parietal cortex and the bilateral semioval center have a patchy, slightly low-density shadow and the boundary is blurred, suggesting a relatively fresh infarction in bilateral frontal parietal cortex and semioval center (Figure S1). Since the recommended thrombolytic time window is <4.5 hr (Powers et al., 2018) and thrombolytic contraindication was absent, thrombolysis was indicated then. Coagulation testing is normal, although the patient took oral anticoagulant (Dabigatran Etexilate 110 mg bid). Recombinant tissue plasminogen activator (rt-PA)was given with standard dosage of 54 mg (alteplase 0.9 mg/kg * 60 kg) at 21:20, which is within 3 hr of ischemic stroke symptom onset. The initial 5 mg (about 10% of dose) was given as bolus over 1 min, and the rest was intravenously pumped within 1 hr. The vital signs were stable during the thrombolysis. NIHSS score was 4 when 12 hr after thrombolysis and became 0 when 24 hr after thrombolysis. Meanwhile, the cranial CT showed lacunar infarction in the bilateral semioval center area and no sign of cerebral hemorrhage. Therefore, Aspirin (0.3 g qd po) was given as oral antiplatelet therapy. At the same time, chinese medicine, standard dose of Vinpocetine and Edaravone were given to improve microcirculation and brain function. After 1 week, NIHSS score remained in 0. Aspirin was stopped and Dabigatran Etexilate (110 mg bid po) continued then, the patient was discharged then. At 30 days follow-up, compared to the images a month before (Figure 1a), brain MRI + DWI + MRA (2015–12–6) presented new sign of acute cerebral infarction in frontotemporal lobe and insula in nonenhanced imaging (Figure 1b), the left middle cerebral artery and its distal branches was clearly developed (Figure 1d). The mRs score was 0 in 90 days (Quinn, Dawson, Walters, & Lees, 2009). Up to now, the patient has been followed up for 3 years, he is healthy with maintained sinus rhythm and without obvious sequelae of cerebral infarction.

3 | CASE 2

Patient, male, 52-year-old, was diagnosed with persistent atrial fibrillation. RFA was operated in December 1, 2016. Before the procedure, 7 days of low-molecular-weight heparin (Enoxaparin 0.6 ml: 4000 IU q12h ih) had been administrated as anticoagulant therapy. Pulmonary veins CT angiography and TEE were also undertaken to exclude thrombus from left atrium and left atrial appendage and the result was negative. The left atrial appendage flow rate was above 30 cm/s and there was no cloudy echo in left atrium and the appendage. During the procedure, intravenous heparin (80 u/kg)was given after atrial septal aspiration and added by 1,000 u/hr later, which completely covered the whole process of left atrial circumferential pulmonary vein ablation isolating pulmonary vein plus linear ablation in the top and bottom of left atrial (BOX procedure). The endpoint of the procedure was complete pulmonary veins isolation. After ablation, AF turned into regular atrial tachycardia then electrical cardioversion was applied to restore sinus rhythm, which indicated the procedure was successful. Oral anticoagulation was given 6 hr after the procedure (Dabigatran Etexilate 110 mg bid po). At 22:20 in December 2nd, 2016 (34 hr 20 min after RFA), the patient had an attack of muscle force decrease in left extremities and anesthesia and paroxysmal twitch in right face with apparent sweating. Urgent CT scan showed Cisterna magnano without signs of cerebral infarction and hemorrhage. Therefore, Aspirin 100 mg was given immediately and then the symptoms were gradually relieved but with occasionally mild relapse. At 00:00 in December 3rd, the symptoms suddenly aggravated. The patient suffered dramatically decreased muscle force in right extremities. Meanwhile, numbness and intermittent twitch in left face with apparent sweating was present, which was opposite to the previous symptoms. After the two episodes of strokes, the patient had convulsions over the entire body, with muscle tremor, hypermyotonia, aphasia, negative Babinski's sign, and positive Chadoc sign. Considering the patient had the attack of intersecting neurological symptoms, which indicated a brain stem infarction. Emergent MRI (at 3:00 on December 3rd) indicated possible

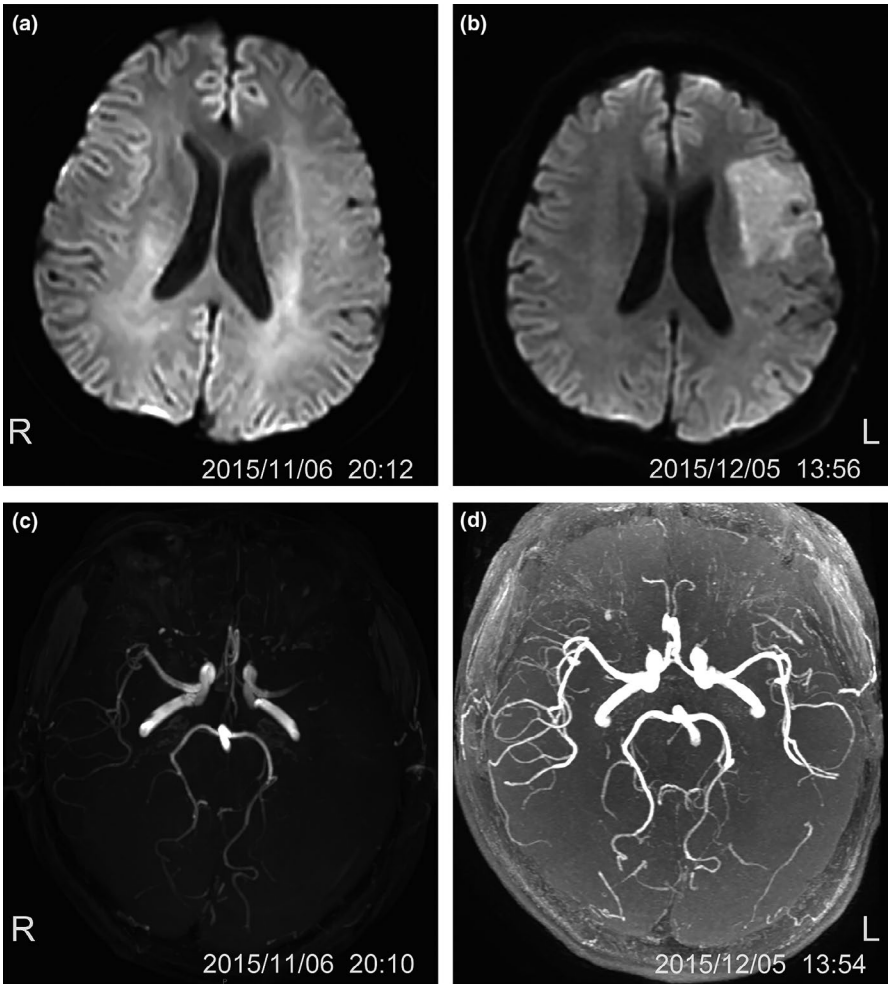

FIGURE 1 Brain MRI + DWI + MRA image. Frontal plane. (a) In DWI mode, brain MRI taken at the onset of acute brain infarction, there is no obvious infarction; (c) In MRA mode, brain image taken at the onset showed the M1 segment in the left cerebral artery was obstructed and the distal branch was undeveloped; (b) In DWI mode, brain MRI underwent 1 month later showed new sign of acute cerebral infarction in frontotemporal lobe and insula; (d) In MRA mode, brain image underwent 1 month later showed the left middle cerebral artery and its distal branch was clearly developed

cerebral infarction in the left pontine (Figure S2). We urgently reached for cerebral angiography from neurosurgery department to diagnose and revascularize. During this period, the symptoms developed to quadriplegia and coma with snoring breath. Cerebral angiography was conducted at 5:30 in December 3rd). Cerebral angiography showed a complete occlusion in the basilar artery (Figure 2a). Mechanical thrombectomy was strongly indicated and applied. Subsequently, a small amount of thrombus was extracted from the proximal segment by thrombectomy at the first time. The main trunk of basilar artery before the bifurcate was seriously narrowed and the stenosis degree was more than 95%. Accordingly, the distal vessels had no blood flow (Figure 2b), suggesting that the thrombus may move toward to the distal end. Then, second thrombectomy was conducted at the distal and a large thrombus was removed from the main trunk of basilar artery (Figure S3). The blood flow in the distal end recovered soon after. The complete blood flow was recovered at 7:30 in December 3rd. The reperfusion achieved a modified Thrombolysis in Cerebral Infarction (mTICI) 2b to 3 (Marks et al., 2014) (Figure 2c). While the main trunk of basilar artery before the bifurcate was still seriously stenosed with the stenosis degree was more than 95%. Since the symptoms alleviated obviously then and excessive operation time would increase the risk of cerebral bleeding. Revascularization by stent implanting was planned 1 month later. After emergent mechanical thrombectomy, dual antiplatelet drugs should be given. Considering that he had just undergone RFA, ASA (100 mg qd po) and Dabigatran Etexilate (110 mg bid po) were administrated. In the meantime, statin (Atorvastatin 20 mg qn po) was given to stabilize the plaque. At 1 month follow-up, cerebral angiography showed the stenosis in the main trunk of basilar artery had decreased to a 60 ~ 70% (Figure 2d) and the stent implanting was cancelled. Taking the economic status into account, warfarin was administrated for the long-time anticoagulation therapy, keeping the INR within 2–3, with a regular dosage of statin (Atorvastatin 20 mg qn po). In 90 days, the mRs score was 2. The patient had been followed up for almost 2 years and showed no sequelae of cerebral infarction.

4 | DISCUSSION

Here, we reported 2 cases of acute cerebral infarction during perioperative period of RFA for AF. In both cases, thrombus in left atrium and its appendage was excluded. Heparinization was conducted during the procedure and bridged with Dabigatran Etexilate 6 hr after the procedure, which is recommended by guideline of RFA for AF (Calkins et al., 2017). In case 1, acute cerebral infarction occurred 30 hr after procedure. Although TEE showed no sign of thrombus in heart chamber. However, it showed a big left atrial appendage with slow blood

FIGURE 2 Image DSA, Frontal plane. (a) Cerebral angiography before procedure showed a complete occlusion in the basilar artery; (b) Cerebral angiography after the first time mechanical thrombectomy showed the main trunk of basilar artery before the bifurcate was seriously stenosed with a narrowing area more than 95% and the distal vessels still had no blood flow; (c) Cerebral angiography after the second time mechanical thrombectomy showed a complete blood flow was recovered at 7:30 in December 3rd. Distal blood flow in thrombolysis in cerebral infarction scale (TICI) scored II-III grade; (d) After 1 month, cerebral angiography showed the stenosis in the main trunk of basilar artery had decreased to 60 ~ 70%

velocity, which contributed to spontaneous echo contrast (SEC) in left atrium. SEC suggests a hypercoagulable state in left atrium, which is common in patients with AF and related to atrium dysfunction (Black, Hopkins, Lee, & Walsh, 1991). SEC is not a contraindication for RFA, but it suggests a high risk of cardiac thrombus. In such situation, enhanced anticoagulation therapy should be considered. In this case, we used a standard dose of Dabigatran Etexilate (110 mg bid po) during the perioperative period, which is recommended in ESC guideline (Levels of evidence and grades of recommendation: I, A) (Heidbuchel et al., 2013). After comprehensive assessment of thrombosis and bleeding risk factors, earlier (2 hr after RFA) and higher-dose of Dabigatran Etexilate (150 mg bid po) should be considered, which maybe more effective in stroke prevention during perioperative period. In the late ESC guideline for AF, it points out that bridging does not seem to be beneficial, except in patients with mechanical heart valves. Continuing anticoagulation with VKAs or NOAC is recommended during ablation (Kirchhof et al., 2016). Despite this, anticoagulation drug was still suspended in patients undergoing catheter ablation, even in experienced centers of China. Recently, ongoing studies are conducted to compare uninterrupted VKA with NOAC therapy in AF patients undergoing ablation (NCT02227550 and NCT02348723). In the future, more research should be conducted to provide evidence for the optimized anticoagulation strategy for Chinese population during the perioperative period.

In Case 2, acute cerebral infarction occurred 34 hr after RFA. Despite no sign of thrombus or SEC in heart chambers, the basilar artery supplying the posterior circulation was completely obstructed, which was extremely dangerous. Since various stress may induce acute thrombosis in previous stenosed arteries during the perioperative period of RFA. Not only cardiac thrombus, but also acute in situ thrombosis based on atherosclerotic lesions should be accounted. The distal blood flow of basilar artery recovered well after mechanical thrombectomy, but severe stenosis remained in the trunk, suggesting local atherosclerosis. Normally, Aspirin and Atorvastatin should be recommended as primary prevention for stroke in patients with atherosclerosis. For patient with high risk of atherosclerosis, such as hypertension, diabetes, kidney disease, et al., further research should be conducted to evaluate whether antiplatelet and anticoagulant drugs should be used together during the perioperative period or in the long run. In addition, for these patients, whether more comprehensive assessment should be applied to assess the risk of stroke, including brain MRI + MRA. These are very critical issues in our clinical work.

In general, the treatment principle for acute ischemic stroke, whether it is caused by cardiogenic factors (thrombus embolus from heart) or brain-derived factors (acute thrombosis based on atherosclerotic lesions), is emergent recanalization. Thrombolytic therapy has become the first choice for patients in therapy time window. In 1995, the National Institute of Neurological Disorders and Stroke (NINDS) trial has fully confirmed the safety and efficacy of rt-PA for stroke within 3 hr of symptom onset (NINDS, 1995). In 2018, the American Stroke Association had extended

the time window to 4.5 hr (Powers et al., 2018). Studies have shown that the prognosis of patients with acute ischemic stroke after thrombolytic therapy is worse in patients with atrial fibrillation, compared to patients without atrial fibrillation (Frankel et al., 2000).The possible reason is patients with AF predisposes to have larger and obsolete emboli, which results in poor response to thrombolytic drugs and increasing risk of intracranial hemorrhage transformation (Kimura et al., 2008). However, recently, it has been demonstrated that intravenous thrombolysis with rt-PA could benefit cerebral infarction patients with AF after adjusting the NIHHS score and age, and the benefits were the same as the patients without AF (Frank, Fulton, Weimar, Shuaib, & Lees, 2012). The use of IV alteplase in patients taking direct thrombin inhibitors or direct factor Xa inhibitors has not been firmly established but may be harmful. The American Stroke Association advised that IV alteplase should not be administered to patients taking direct thrombin inhibitors or direct factor Xa inhibitors unless laboratory tests such as APTT, INR, platelet count, ecarin clotting time, thrombin time, or appropriate direct factor Xa activity assays are normal or the patient has not received a dose of these agents for >48 hr. In case 1, the patient suffered acute infarction stroke only 30 hr after ablation. Thrombolytic therapy would cause atrial perforation or pericardial tamponade, for the fresh wounds in the atrium is vulnerable. After weighing the pros and cons, rt-PA was given as emergent thrombolysis. On one hand, rt-PA was used 9 hr after the last administration Dabigatran Etexilate. Coagulation testing was normal at then. On the other hand, the patient suffered from acute cerebral infraction during the perioperative period of ablation, inferring freshly-formed thrombus (obsolete atrial emboli was excluded preoperatively), which is more sensitive to fibrinolytics and benefits more from the early recanalization. It turns out the intravenous thrombolysis was successful in this patient with the NIHHS score dropped to 0 point 24 hr after the treatment. It was safe and effective without any bleeding sign and cardiac complications.

In Case 2, the stroke was latent and intermittent. When acute cerebral infarction was realized, the time for emergency thrombolysis (<4.5 hr) had exceeded. The basilar artery supplying brain stem, the vital center, was occluded. It is a low-incidence event with high mortality in acute ischemic stroke, which often leads to serious consequence with a mortality rate as high as 40%–80% in the acute period. Previous studies showed that the ischemic tolerance time was longer in posterior circulation than that in the anterior circulation (Pagola et al., 2011).As a result, the time window for recanalization in posterior circulation can be extended accordingly. Other studies reported that the recanalization rate of intravenous thrombolysis in posterior circulation was low, but mechanical thrombectomy could improve the recanalization rate. For patients who have causative occlusion of basilar artery beyond 6 hr of symptom onset, there is no specific recommendation in the 2018 AHA guideline. While the DAWN study extended the time window of mechanical thrombectomy in some patients with acute ischemic stroke from 6 to 24 hr. The study included patients with acute ischemic stroke who had a postawake stroke or 6 ~ 24 hr of onset, requiring large vessel occlusion (intracranial segment of the internal carotid artery or M1 segment of the middle cerebral artery) and unmatched infarct size and clinical score (infarct size is small, but clinical manifestations are more severe, suggesting that many brain tissues are in an ischemic but noninfarct state, although they are dysfunctional, they can still be reversed). (Nogueira et al., 2018) Therefore, emergent mechanical thrombectomy was operated 7 hr after the stroke symptom onset in this case, and complete recovery of blood flow was attained within 9 hr with TICI score II to III. The critical patients eventually recovered.

For patients with acute cerebral infarction accompanied by atrial fibrillation, mechanical thrombectomy had the following advantages compared to conventional intravenous thrombolysis: (a) It increases the recanalization rate significantly and shortens the recanalization time, saving more time for the reversible ischemic brain tissue (Liebig, Reinartz, Hannes, Miloslavski, & Henkes, 2008); (b) The time window for recanalization can be extended to 8 hr. Many scholars believe that no matter the specific time of the stroke onset, as long as a larger ischemic penumbra was detected in MRI, mechanical thrombectomy should be performed. Therefore, the time window for mechanical thrombectomy needs further study (Layton, White, Cloft, Kallmes, & Manno, 2006); (c) The incidence of hemorrhagic transformation was reduced. It was reported that about 95% of cardiogenic stroke would be secondary to hemorrhagic transformation. (Tong, Adami, Moseley, & Marks, 2000) As intravascular recanalization requires no thrombolytic drugs, which reduces the risk of hemorrhagic transformation and improves safety (Saver, 2006); (d) Extended indication. Patients with thrombolytic contraindications could be included after strict screening in the following circumstance (Powers et al., 2015): for example, surgery history in the last 3 months, hemorrhagic propensity or tumor with bleeding tendency, recent history of gastrointestinal ulcer or upper gastrointestinal bleeding, overdue thrombolytic time window. In addition, abnormal coagulation testing is present in patients underwent RFA, for heparin applying in the procedure and bridging treatment with anticoagulant drugs in the postoperative, which is a contraindication for thrombolysis. At this point, we can carefully weigh the choice of mechanical thrombectomy.

In brief, two patients suffered from acute ischemic stroke during postoperative period of RFA were successfully treated by intravenous thrombolysis or mechanical thrombectomy. The treatment strategy should be based on a comprehensive evaluation, including time window (Powers et al., 2018) (intravenous thrombolysis <4.5 hr, mechanical thrombectomy <6 hr, ischemia in posterior circulation <24 hr), culprit blood vessel (endovascular intervention for posterior circulation lesions could improve the recanalization rate of occlusive vessels) clinical feasibility (green channel allocation for emergent DSA). After excluding the contraindications, the basic principle, time is the brain, is the key to clinical decision-making.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

Conception and design: Jin Xu and Jun Bu; Case collection and manuscript writing: Yana Li; Manuscript revising: Jin Xu and Jun Bu.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the institute's committee on human research.

CONSENT FOR PUBLICATION

Our patients and their family have given their written informed consent to publish their case (including publication of images).

DATA AVAILABILITY STATEMENT

The datasets used during the current study are available from the corresponding author on reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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