Intra-Arterial Thrombectomy for Acute Ischemic Stroke Related to the Procoagulant Effect of Warfarin in A Patient with Atrial Fibrillation and Bioprosthetic Valve Replacement

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Abstract

Purpose: Warfarin is associated with paradoxical procoagulant effect that leads to a transient hypercoagulable state and acute ischemic stroke (AIS). This clinical dilemma is further confounded when the patient has multiple comorbidities and the optimal treatment strategies are unclear.

Case report: We report a 78-year-old male with valvular heart disease, congestive heart failure, and atrial fibrillation, who received bioprosthetic valve replacement and developed AIS related to the paradoxical procoagulant effect of warfarin. Emergent cerebral angiography with mechanical thrombectomy was performed, and recanalization was successfully achieved. After shifting warfarin to nonvitamin K oral anticoagulant (NOAC), the paradoxical procoagulant effect ameliorated.

Conclusion: This report describes the roles of endovascular therapy and NOAC in patients with similar highly complex conditions and has clinical relevance for therapeutic plans in the clinical setting.

Keywords: Anticoagulant, procoagulant, stroke, thrombectomy, valvular heart disease.

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INTRODUCTION

Warfarin is associated with paradoxical procoagulant effect that leads to a transient hypercoagulable state and acute ischemic stroke (AIS)[1,2]. This clinical dilemma is further confounded when the patient has multiple

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comorbidities. This article presents a patient with atrial fibrillation and valvular heart disease who received bioprosthetic valve replacement, experienced severe AIS with total occlusion of the right internal carotid artery successfully achieved recanalization through intra-arterial thrombectomy.

CASE PRESENTATION

A 78-year-old male patient had a medical history of hypertension, valvular heart disease (VHD), congestive heart failure, and atrial fibrillation (Af). The full medical course and its time scale are outlined in Fig. 1. Specifically, in late January 2020, he received mitral and aortic valve replacement with bioprosthetic valves and tricuspid valve repair for partial rupture of the mitral chordae tendineae leading to severe aortic, mitral, and tricuspid regurgitation. After surgery, he was prescribed 1 mg of warfarin daily. Two weeks later, he experienced sudden onset of facial expression asymmetry, slurred speech, and weakness in the limbs on the left side. Brain MRI revealed acute infarcts of the right medial temporal and frontal lobes and the right posterior limb of the internal capsule (Fig. 2a–2b) and occlusion of the right distal internal carotid artery (ICA) (Fig. 2c).

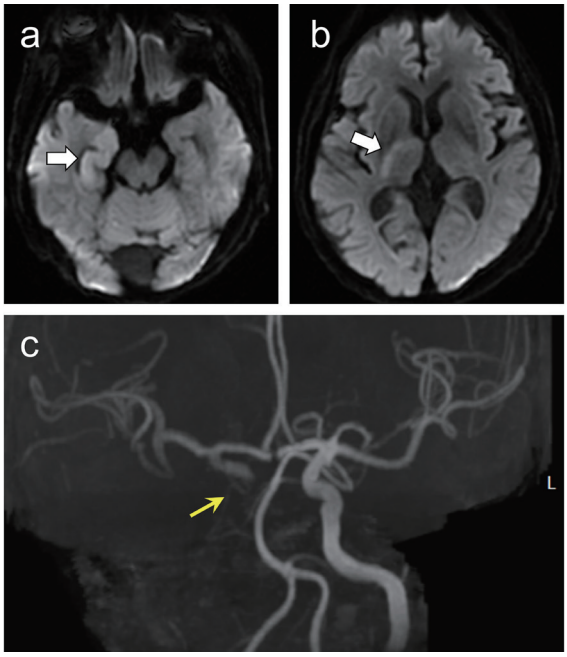

Fig. 2. Multiple mild hyperintense areas at the right medial temporal lobe (a), frontal lobe, and posterior limb of internal capsule (b) on diffusion-weighted imaging, indicative of recent infarct (white arrows). (c) Time-of-flight magnetic resonance imaging (MRI) showed total occlusion at the right distal internal carotid artery (yellow arrow).

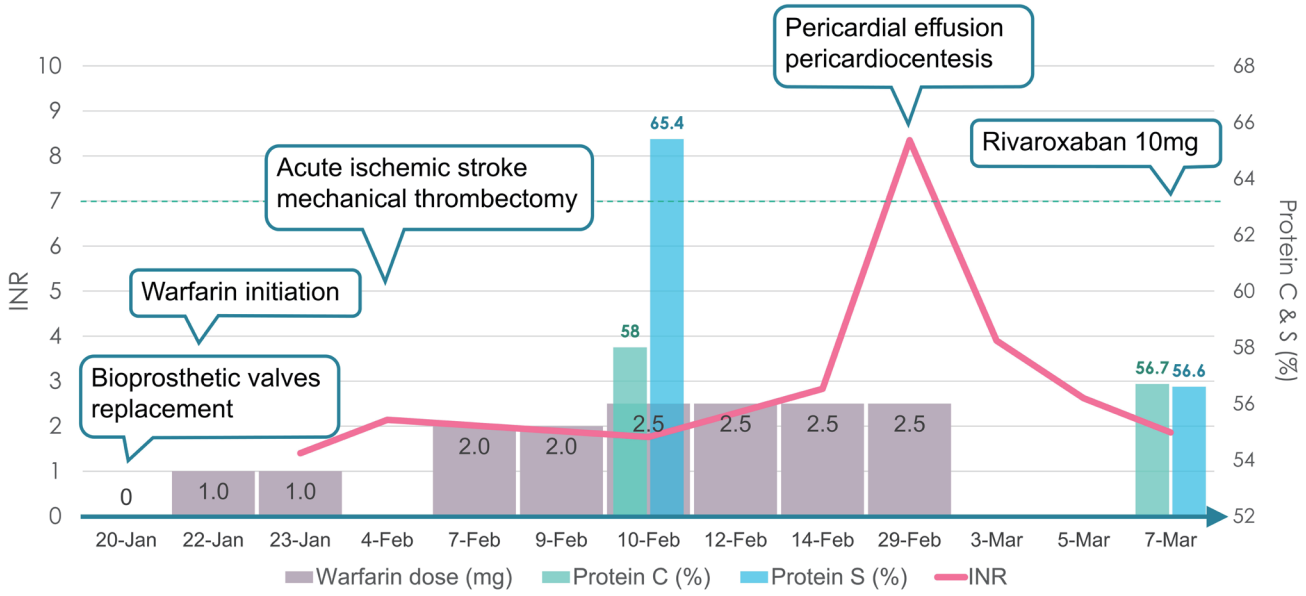

Fig. 1. Brief timeline of the entire clinical course. The dotted line represents the lower limit of normal values of protein C. The left Y-axis represents the INR, and the right Y-axis represents the percentage for protein C and S. INR, international normalized ratio.

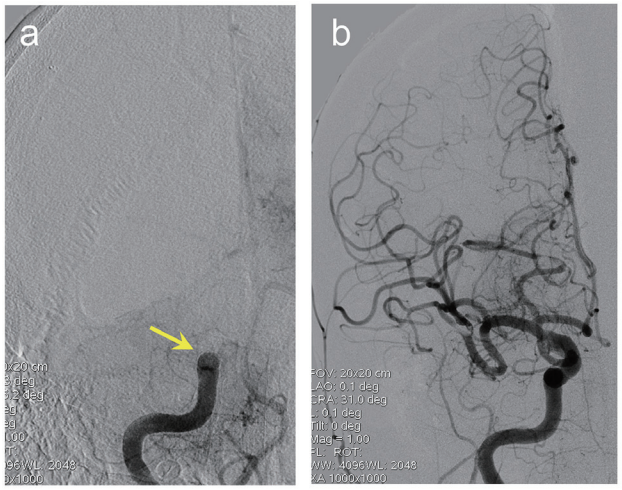

Fig. 3. (a) Emergent cerebral angiography revealed a filling defect at the right supraclinoid internal carotid artery (ICA), indicating total occlusion (yellow arrow). (b) Successful recanalization was achieved through mechanical thrombectomy.

The patient's initial National Institute of Health Stroke Scale (NIHSS) score was 15, indicating severe stroke[3]. The onset-to-hospital time was 3 hours; however, intravenous tissue plasminogen (tPA) activator was not indicated because of the elevated international normalized ratio (INR) of 2.14[4] (reference range: <1.20). Thus, angiography with endovascular thrombectomy was performed. A filling defect was noted at the right supraclinoid ICA, compatible with total occlusion (Fig. 3a). After mechanical thrombectomy and removal of the thromboemboli, recanalization and resolution of the occluded right distal ICA to the M1 segment were achieved (Fig. 3b).

After treatment, the patient's muscle strength gradually recovered and NIHSS score improved from 15 to 4. Laboratory studies on February 12, 2020, showed lower serum protein C levels of 58.0% (reference range, 70%–140%) and protein S levels of 65.4% (reference range, 58.6%–126%)[5].

We discontinued warfarin after thrombectomy and resumed its administration 2 days after AIS. The patient was discharged after hospitalization for 10 days.

Two weeks after discharge, an episode of pericardial effusion with tamponade was noted, and the patient was readmitted for pericardiocentesis. A blood chemistry examination indicated an elevated INR value of 8.35, low protein C level of 56.7%, and protein S level of 56.6%. We discontinued warfarin and shifted to 10 mg of rivaroxaban daily. Four days later, the patient's protein C and protein S were restored to normal levels (87.5% and 81.2%, respectively), and the patient recovered completely from the ischemic stroke without residual neurological sequelae.

DISCUSSION

Warfarin is a highly effective treatment for reducing the risk of cardioembolic stroke in patients with Af[6]. However, patients initiating warfarin have been reported to exhibit a 71% higher risk of AIS in the first 30 days of use[1]. This paradoxical procoagulant effect of warfarin is believed to be induced through blocking of the activation of clotting factors II, VII, IX, and X and the deactivation of protein C and protein S, leading to a transient hypercoagulable state[1,2].

Bridging therapy with heparin or low-molecular-weight heparin can be considered when warfarin therapy is initiated; however, in the acute phase of ischemic stroke, these treatments appear to increase the risk of major bleeding without any net benefit[7,8].

Nonvitamin K oral anticoagulants (NOACs), which block factors Xa and IIa and do not deactivate protein C or protein S, have proved effective and safe for the prevention of embolic events in patients with Af[7,8]. However, VHD frequently coexists with Af[9], and limited data are available on the comparison of NOACs and warfarin after surgical repair for VHD with bioprosthetic valves; thus, the optimal treatment for patients with Af and VHD with bioprosthetic heart valves remains controversial[7-9].

As per contemporary knowledge, our patient developed AIS in the first 14 days of warfarin use, with an INR level within the therapeutic range (therapeutic range: 2.0–3.0[7,8]), which is concordant with the onset time of warfarin-induced thrombotic events[1]. Our patient had low levels of serum protein C and protein S during warfarin treatment, supporting the hypothesis of the paradoxical procoagulant effect during the initial use of warfarin. Protein C has a shorter half-life, and warfarin initially decreases protein C levels[2,5], plausibly contributing to an increased coagulation tendency at the time of the thrombotic event in our patient. Restoration of these two

endogenous anticoagulants to normal levels after warfarin discontinuation also provided evidence of recovery from the paradoxical procoagulant effect induced by warfarin.

Our patient received intra-arterial thrombectomy with successful recanalization and achieved complete recovery from ischemic stroke without residual sequela. Although no direct evidence exists of the benefits of endovascular intervention or tPA therapy in patients with AIS in a hypercoagulable state, Kim and Bang also reported a case with warfarin-related procoagulation and AIS that was successfully treated with thrombectomy[5]. Furthermore, our case report describes a difficult and complicated clinical scenario: Our patient had Af and had recently received bioprosthetic valve replacement for VHD, had experienced severe AIS, and was ineligible for intravenous tPA therapy due to elevated INR.

CONCLUSION

This case highlights the role of the paradoxical procoagulant effect and the value of serial examinations of protein C and S levels to evaluate the risk of thromboembolic events in patients during the initiation of warfarin therapy, and also demonstrated the prominent role of endovascular therapy and NOACs in patients with AIS with the highly complex condition of Af, paradoxical procoagulant effects of warfarin, and VHD recently treated through bioprosthetic valve repair. This report is clinically relevant for patients with similar conditions and provides a reference for decision-making regarding therapeutic plans in emergent clinical settings.

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