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Successful treatment of VA-ECMO complicated with left ventricular thrombus by intravenous thrombolysis: A case report

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Abstract**BACKGROUND**

Left ventricular thrombus is a rare condition, for which appropriate treatments are not extensively studied. Although it can be treated by thrombectomy, such surgery can be difficult and risky, and not every patient can tolerate the surgery.

CASE SUMMARY

We report a case of a middle-aged man receiving Veno-Arterial Extracorporeal Membrane Oxygenation (VA-ECMO) for acute myocardial infarction who developed left ventricular thrombus despite systemic anticoagulation. After systemic thrombolysis with urokinase, the left ventricular thrombus disappeared, ECMO was successfully withdrawn 9 days later, and the patient recovered and was discharged from hospital.

CONCLUSION

Systemic thrombolysis is a treatment option for left ventricular thrombus in addition to anticoagulation and thrombectomy.

INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) is an important treatment for severe cardiopulmonary insufficiency. In recent years, particularly after COVID-19, ECMO has rapidly developed in China. Recently, ECMO has become more reliable due to improvements in equipment and increased experience, which is reflected in improved results^[1]. However, many complications can occur during ECMO treatment, such as bleeding and thrombosis. Of these complications, intracardiac thrombosis is rare but can be life-threatening. For intracardiac thrombosis, the current guidelines and expert consensus recommend anticoagulation and thrombectomy, but there are no reports on intravenous thrombolysis. We report a case of successful intravenous thrombolysis after left ventricular thrombus which occurred during VA-ECMO therapy.

CASE PRESENTATION

Chief complaints

The patient had undergone cardiopulmonary resuscitation twice in half a day.

History of present illness

A 48-year-old man who suffered from persistent angina pectoris for 2 h was diagnosed with acute extensive anterior wall myocardial infarction in a local hospital on September 19, 2022. Coronary angiography showed total occlusion of the left main ostium. Following implantation of a Medtronic 3.0 × 2.6 mm drug-eluting stent (10 atm, 10 s) in the left anterior descending artery, the blood flow returned to TIMI3. The patient was then admitted to the ICU. Sudden cardiac arrest occurred twice in the ICU, and cardiopulmonary resuscitation was given. The patient required 15 min resuscitation during the first arrest, and 5 min resuscitation during the second arrest. However, his blood pressure was extremely unstable, and the dose of norepinephrine was raised to 120 µg/min. After consultation, VA-ECMO treatment was initiated. The speed of the ECMO centrifugal pump was 3500 rpm, the air flow rate was 2.5 L/min, the oxygen concentration was 100%, and the blood flow rate was approximately 2.4 L/min. His arterial blood pressure increased to 125/114 mmHg, and the dose of

norepinephrine was decreased to 40 µg/min. The patient was then transferred to our department.

History of past illness

The patient had no previous medical ¹history.

Personal and family history

All family members were healthy and denied any history of genetic disease and genetic predisposition.

Physical examination

⁴The patient's temperature was 36°C, heart rate was 86 bpm, blood pressure was 125/114 mmHg with norepinephrine 40 µg/min, and respiratory rate was 15 breaths/min. The patient was in a state of subcoma, moist rales were heard in both lungs, arrhythmia was identified, heart sounds were low and weak, and bowel sounds were not heard.

Laboratory examinations

Laboratory examinations indicated leucocytosis (white blood cell count, $15.96 \times 10^9/L$); glutamic oxaloacetic transaminase 906 U/L; cardiac troponin I 50 ng/mL; N-Terminal pro-brain natriuretic peptide 2000 pg/mL.

Imaging examinations

Echocardiography revealed segmental wall dyskinesia and hypofunction of the left heart.

FINAL DIAGNOSIS

Acute extensive anterior wall myocardial infarction and cardiogenic shock.

TREATMENT

He was given 100 mg/d aspirin, 180 mg/d ticagrelor and 600 U/h heparin. Bedside echocardiography showed that systolic function of the left ventricle was extremely poor, there was no obvious thrombus in the left ventricle, and the patient's blood was in a turbulent state. The mean arterial pressure was 72 mmHg when the dose of norepinephrine was 20 µg/min and the blood flow rate was 3.2 L/min. The active partial thromboplastin time (APTT) was 54.6 s.

Eight hours later, bedside echocardiography showed a large left ventricular thrombus (Figure 1). However, the Antithrombin-III was only 46.6%, which did not improve after plasma infusion. We administered argatroban 1 mg/h for anticoagulation instead of heparin. After one day of treatment, bedside echocardiography showed that the thrombus had not decreased (Figure 2). We added urokinase 50 000 U/h for thrombolysis. Six hours later, there was no obvious bleeding sign, and the dosage of urokinase was increased to 100 000 U/h. Twenty-four hours after thrombolysis, the thromboelastogram showed that the patient's R time was 10.3 min, K time was 6.2 min, alpha angle was 50.9°, max amplitude was 35.2 mm, and LY30 was 0.0%. Thirty-four hours after thrombolysis, blood leakage increased at the ECMO catheter in the femoral artery. The dose of argatroban was reduced to 0.6 mg/h, the dose of urokinase was reduced to 50,000 U/h, and local compression was added to stop the bleeding. However, the bleeding was not controlled. Therefore, urokinase was stopped 46 h after initiation, and the total dose of urokinase was 4.6 million U (changes in the patient's coagulation function during thrombolysis are shown in Table 1). During thrombolysis, the left ventricular thrombus gradually decreased (Figure 3) and then disappeared on the second day after urokinase was stopped (Figure 4, 5). No signs of thromboembolism were found on head, chest and abdominal computed tomography (CT). We successfully removed ECMO on the ninth day.

OUTCOME AND FOLLOW-UP

One month later, the left anterior descending branch stent was found to be blocked, the stent was re-inserted, and the patient was successfully discharged from hospital with New York Heart Association class II-III.

DISCUSSION

VA-ECMO provides good hemodynamic support for adults with cardiogenic shock. However, thrombosis is an important complication during VA-ECMO support and can occur in lines, oxygenators, pumps, and ventricles. The reported incidence of these complications is as high as 17%^[2]. Among them, left ventricular thrombus is a serious complication. According to the registration report of Extracorporeal Life Support Organization (ELSO) in 2017, left ventricular thrombus accounts for 5-6% of all complications of VA-ECMO. Left ventricular thrombus leads to increased mortality.

The formation of left ventricular thrombus in ECMO is mainly related to the primary disease (such as myocardial infarction)^[3], decreased myocardial contractility^[4], critical illness, sedation, frequent blood transfusion^[5], ECMO tubing and the membrane oxygenator in contact with blood leading to fibrinogen and thrombin activation^[6], *etc.* The patient in this report had the abovementioned high-risk factors for thrombosis. At the same time, the patient's antithrombin-III (AT-III) was only 40-60%, and the anticoagulant efficiency of heparin decreased^[7], which eventually led to the formation of a left ventricular thrombus.

The fundamental way to prevent left ventricular thrombus formation is anticoagulant therapy and the prevention of left ventricular dilatation^[8]. However, there are few guidelines for the treatment of left ventricular thrombus. At present, the guidelines of the American Heart Association (AHA)^[9], American Stroke Association (ASA) and American College of Cardiology (ACC)^[10] mainly recommend anticoagulation. In this case, heparin was initially administered for anticoagulation. However, the patient's AT-III was low, and did not increase significantly after plasma transfusion. At the same time, plasma transfusion may bring the risk of coagulation. According to the literature reports, 27% of patients developed intracardiac thrombus

after plasma transfusion^[11]. Therefore, in this case, argatroban anticoagulation was administered when left ventricular thrombus occurred, but anticoagulation alone failed to decrease the thrombus.

There are also many reports on surgical thrombectomy or thrombus removal^[12, 13]. However, this approach exposes patients to additional surgical risks and further complications^[14]. Ventriculotomy negatively affects the contractility of an already failing heart^[15], and anticoagulation after surgery is a huge challenge. Installing a left ventricular decompression device such as the Impella reduces thrombosis by decreasing blood stasis in the left ventricle^[16]. Use of the AngioVac system (AngioVac®) to remove ECMO-associated ventricular thrombi has also been reported^[17]. Local thrombolysis in the left ventricle has been performed using a left ventricular decompression tube^[18], and the thrombus was even removed from the cut aorta through a bronchoscope^[15].

At present, there is no convincing evidence in the guidelines that a thrombolytic drug is superior to other drugs^[19]. The best thrombolytic agent is still under debate^[20]. At present, in most infants and young children, systemic thrombolysis is used to treat ECMO-related left ventricular thrombus^[18, 21]. The thrombolytic drug used is alteplase. There are few reports on the application of urokinase in left ventricular thrombus. Although the advantages of alteplase have become increasingly prominent in recent years, clinicians have a better understanding of the dose, time, safety and efficacy of urokinase^[19]. It has been reported that compared with alteplase, urokinase has a higher thrombus lysis rate^[22], lower bleeding risk and better safety^[23]. In the meta-analysis conducted by Sanjeev Kharel *et al*^[24] it was shown that the efficacy and safety of urokinase in thrombolysis were not inferior to those of alteplase. The 2019 Chinese Stroke Association guidelines indicate that urokinase is still a safe and effective thrombolytic agent^[25]. Therefore, in this case, urokinase was used for thrombolysis.

Urokinase is extracted from human urine and is without antigenicity. It acts directly on the endogenous fibrinolytic system to drive the conversion of fibrinogen into fibrinolytic enzyme, thereby rapidly dissolving fresh thrombi. Following 24 h of thrombolytic therapy in our patient, the thromboelastogram showed a hypocoagulable

state, and bedside echocardiography showed that the thrombus had decreased. At the same time, fibrinogen degradation product and D dimer initially increased and then decreased, while fibrinogen did not significantly decrease. As there was thrombus dissolution at this time, rather than coagulation activation, thrombolysis was considered effective. However, 34 h after thrombolysis, hemorrhage occurred at the catheter site. Following treatment measures such as local compression which were ineffective, urokinase was stopped, argatroban anticoagulation was continued, and the bleeding was controlled. Seventy-two hours after thrombolytic therapy, the left ventricular thrombus had disappeared. At that time, we were also worried that the thrombus would break off and cause embolism in other areas. However, no clinical manifestations of embolism were observed, and no obvious signs of vascular embolism were seen on head, chest and abdominal CT. The patient recovered and was discharged from hospital.

CONCLUSION

The cornerstone of left ventricular thrombosis prevention in ECMO is systemic anticoagulation and prevention of left ventricular dilation. Systemic thrombolysis with urokinase is a treatment option following the formation of left ventricular thrombus.

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