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CASE ANECDOTES, COMMENTS AND OPINIONS

Successful treatment of intracardiac thrombosis in the presence of fulminant myocarditis requiring ECMO associated with COVID-19

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Coronavirus disease 2019 (COVID-19) is associated with myocardial injury and an increased thrombosis risk. In a meta-analysis of adult hospitalized patients with COVID-19 the odds of mortality were 74% higher with a thrombotic event (TE).[1] Despite thromboprophylaxis, both adult and pediatric patients are at risk for developing a TE.[2,3] COVID-associated myocardial injury can increase risk of intracardiac thrombus and may require extracorporeal membrane oxygenation (ECMO) in severe cases, but optimal treatment and anticoagulation strategies in these situations have not been established.

We report the case of a 17-year-old female with symptomatic COVID-19 who presented in cardiogenic shock and was cannulated to veno-arterial ECMO via the neck. Initial goal ECMO flows were 3 L/min with a cardiac index of 2.3 L/min/m^2 and good end organ perfusion. She was supported with epinephrine and milrinone. Due to severely diminished ventricular function and near ventricular akinesis, no antegrade flow was seen across the aortic valve. As the left ventricle was not distended and there was no pulmonary edema, a left ventricular vent was not pursued. For anticoagulation, we followed our institution's standard of practice and used unfractionated heparin (UFH) with goal activating clotting (ACT) time of 180 to 220 sec and anti-Xa of 0.3 to 0.7 IU/mL. Despite achieving these therapeutic ranges, on ECMO day 2 a large thrombus was noted in the left ventricular apex, extending toward the aortic valve (Figure 1). There was no additional evidence of deep venous thrombus. Given the concern for thromboembolism, continuous systemic high-dose alteplase (tPA) infusion (0.1 mg/kg/h) was initiated, and UFH at the above ACT and anti-Xa goal range was continued. Laboratory studies were monitored every 2-6 hours; she was supported with cryoprecipitate and transfusions to maintain fibrinogen and platelet goals of >125 mg/dL and >100,000 per μL, respectively. A 20-fold increase in D-dimer levels and serial echocardiograms indicated thrombolytic effect. After 22 hours of thrombolysis, tPA was discontinued as the LV thrombus had diminished in size and the patient developed cannulation site bleeding and a hemothorax. UFH was also subsequently discontinued. That same day a new thrombus was noted by echocardiogram in the right ventricle (Figure 2). As bleeding improved, she was transitioned to bivalirudin (starting dose 0.15 mg/kg/hour with goal dilute thrombin time of 40-50 sec) for systemic anticoagulation. The LV and RV thrombi resolved by ECMO day 4 and 7, respectively (Figure 3) and she underwent thoracotomy and decortication. Cardiac function recovered by day 11, allowing for separation from ECMO. She was discharged without any neurologic deficits 25 days later.

The coagulopathic derangements associated with COVID -19 pose significant challenges in the setting of fulminant myocarditis. In this case, the COVID-19 related coagulopathic state likely increased risk for a TE in the setting of severely diminished ventricular function. There is limited evidence regarding TE prevention in COVID-19 patients. In adults there is controversy regarding the utility of systemic anticoagulation in the acute setting.[2] In a multicenter study amongst children with COVID-19 or multisystem inflammatory syndrome in children, more than two-thirds of TE's occurred in those already receiving thromboprophylaxis.[3] Thus, the most appropriate anticoagulation approach for patients with COVID-19 is not yet clear.

Recommendations regarding management of intracardiac thrombi during ECMO are also limited. There have been reports regarding the use of tPA in patients on ECMO

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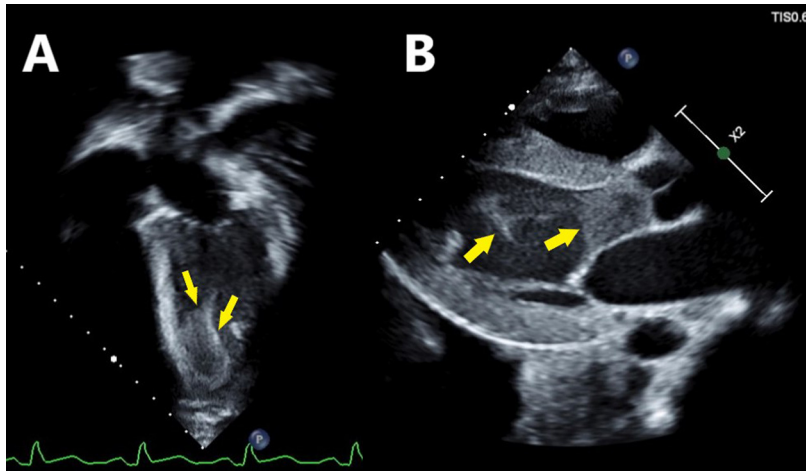

Fig. 1 Large thrombus extending from the left ventricular apex (A) to the aortic valve (B).

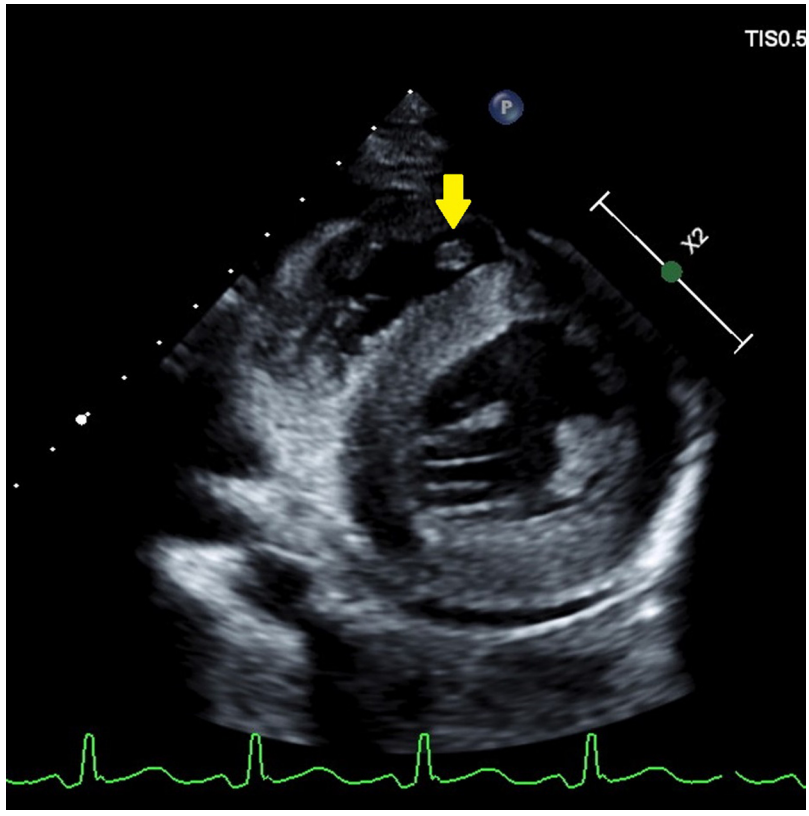

Fig. 2 Thrombus in the right ventricle.

without known COVID-19 disease. Systemic tPA has been used to address right atrial and right ventricular thrombi, while localized administration has been used for left ventricular thrombosis and coronary lesions.[4-6] Adverse events in these cases ranged from mild systemic bleeding to fatal intracranial hemorrhage. This patient experienced bleeding complications that were successfully managed with surgical intervention. This case demonstrates that, with careful monitoring, systemic tPA can be used to provide life-saving therapies with excellent neurological outcomes. Further studies are needed to develop guidelines regarding administration of systemic tPA during ECMO.

Disclosure statement

The authors have no financial conflicts of interest with regards to the present manuscript. Dr. Rossano is a consultant for Bayer, Myokardia, Abiomed, Merk, and Cytokinetics. This did not support the work presented here.

Author contributions

Drs. Erika J. Mejia, Matthew J. O'Connor, Benjamin J. Samelson-Jones, and Katsuhide Maeda collected the data

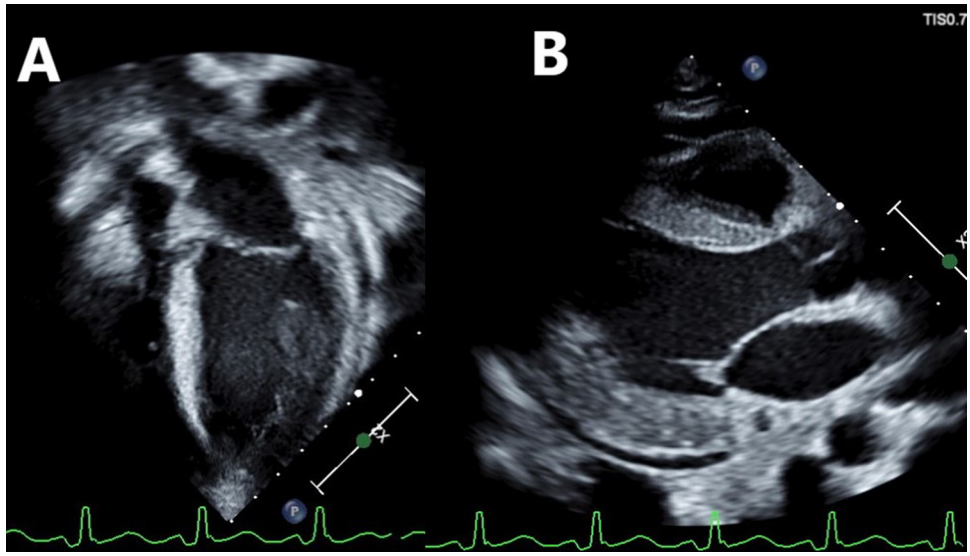

Fig. 3 Resolution of the thrombus previously noted in the left ventricular apex (A) and below the aortic valve (B).

and drafted the manuscript. All authors revised the manuscript for critical and intellectual content.

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