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Diffuse Alveolar Hemorrhage Post-Primary Percutaneous Coronary Intervention Requiring V-V ECMO Support in an Out-of-Hospital Cardiac Arrest Patient

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Abstract

We present the case of a 62-year-old man who developed Diffuse Alveolar Hemorrhage (DAH) post-primary Percutaneous Coronary Intervention (PCI), following an Out-of-Hospital Cardiac Arrest (OHCA). He had severe hemoptysis resulting in poor ventilation while intubated and was treated successfully with heparin-free Veno-Venous Extracorporeal Membrane Oxygenation (V-V ECMO).

Keywords: Diffuse alveolar hemorrhage; ECMO; Out-of-hospital cardiac arrest; Anticoagulation

Introduction

A 62-year-old man, with no significant past medical history, had witnessed an OHCA and bystander Cardiopulmonary Resuscitation (CPR). The downtime was 30 min with a total of 4 defibrillation shocks for ventricular fibrillation. He was intubated and the electrocardiogram showed extensive anterior ST Elevation Myocardial Infarction (STEMI) (Figure 1). The patient was loaded with 300 mg of aspirin and 180 mg of ticagrelor.

During PCI, an intra-aortic balloon pump was inserted for hemodynamic support. The emergency coronary angiography showed acute thrombotic occlusion of proximal Left Anterior Descending artery (LAD) (Figure 2). The LAD was successfully re-canalized with 2 overlapping drug-eluting stents achieving TIMI 3 flow (Figure 2). Anticoagulation was performed with weight-adjusted intravenous heparin and 2 intracoronary weight-adjusted bolus doses (each of 6.2 ml) of Glycoprotein (GP) IIb/IIIa inhibitor (eptifibatide) were also administered due to the heavy thrombus burden.

Shortly after transferring to the coronary care unit, the patient developed severe hemoptysis with 500 ml of frank blood aspirated from the endotracheal tube. Emergency bronchoscopy revealed DAH. Reversal of heparin was done with 60 mg of intravenous protamine sulphate. Repeated bronchoscopy suction of the intra-alveolar blood was performed with adrenaline injections but subsequently abandoned due to difficult ventilation and futility. The ventilator requirements continued to increase even as adequate oxygenation was not achieved.

The patient developed hypoxic Pulseless Electrical Activity (PEA) collapse secondary to type 2 respiratory failure. The decision was made to insert V-V ECMO despite active bleeding to support his ventilation. Our strategy was to start heparin-free V-V ECMO support and change the circuit in case of clotting. The patient received total of 5 units of packed red blood cells, 1 unit of platelets and 2 units of fresh frozen plasma. The V-V ECMO was successfully explanted after 32 h with significant improvement of the arterial blood gases. Therapeutic temperature management was maintained while on V-V ECMO support at 36 degrees Celsius.

The patient continued mechanical ventilation for the next 15 days due to complications of ventilator-related pneumonia. Aspirin followed by clopidogrel was resumed step-wise over the next few days without further bleeding episodes. The intra-aortic balloon was removed on day 4, and the chest X-ray and a chest computed tomography scan performed showed the diffuse ground glass bilateral opacities (Figure 3, 4). The leftmost picture in Figure 3 shows the diffuse bilateral opacities characteristic for DAH. The middle one was taken post V-V ECMO implantation and

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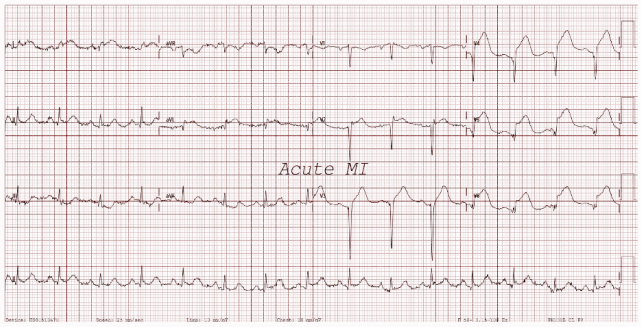

Figure 1: 12 lead ECG showing extensive anterior MI.

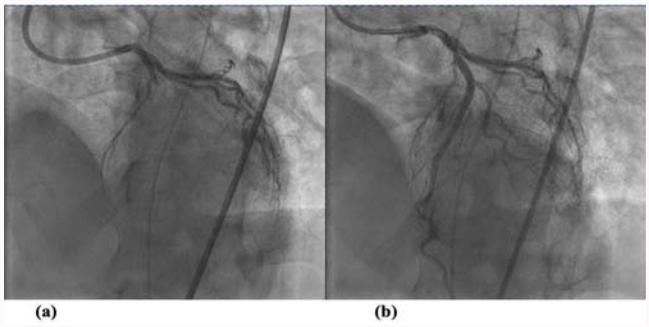

Figure 2: a) Left Anterior Oblique (LAO) cranial view showing totally occluded proximal LAD artery. b) LAO cranial view showing opened and stented LAD artery.

shows the ECMO catheters and the IABP. The rightmost picture was post-removal of ECMO, IABP and endotracheal tube. Figure 4 shows bilateral fine diffuse nodular densities characteristic of the subacute phase of DAH. The patient had full neurological recovery and was discharged to the step-down rehabilitation care facility with a cerebral performance category score of 1 on day 28.

Discussion

The limited literature of ECMO application in a DAH setting predominantly focused on causes such as silicon embolism, systemic lupus erythematosus and granulomatosis with polyangiitis. However, DAH post-PCI has been increasingly associated with various antithrombotic agents during the procedure. A retrospective analysis in 2009 suggests that GP IIb/IIIa induced DAH is likely more frequent than expected1. 292 patients received either abciximab or eptifibatide, and two patients developed significant alveolar hemorrhage diagnosed by bronchoalveolar lavage with an incidence of 0.68%. Subsequently, one died from complications [1]. Another small case series showed a

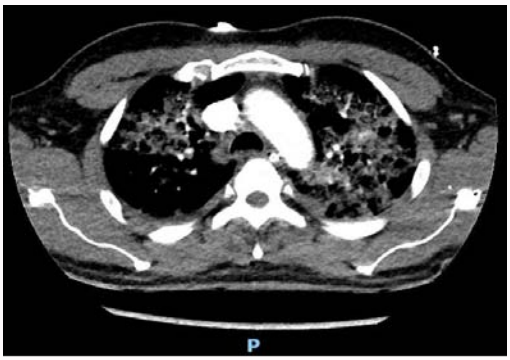

Figure 4: Cross-sectional cut of CT chest on day 9 of admission.

high mortality rate ranging from 20% to 50% [2].

Another contributing factor for DAH in our case is possibly Dual Antiplatelet Therapy (DAPT), specifically ticagrelor. A limited number of cases reports attribute DAH post-PCI to ticagrelor [2-4]. None of these cases reports required V-V ECMO and all discontinued ticagrelor, administered supplemental oxygen and continued aspirin, after which DAH symptoms improved. From the four cases reported, one died secondary to septic shock.

Unfractionated Heparin (UFH) can theoretically induce bleeding such as DAH. The fact that major bleeding was stopped by UFH reversal with protamine might point towards UFH as a potential cause. However, to our knowledge, there is no record of DAH developing solely due to weight-adjusted UFH administration.

Interestingly, Cardiopulmonary Resuscitation (CPR) is an independent risk factor for major bleeding. In a relatively extensive retrospective cohort study conducted in Vienna, 265 patients presented with acute MI and successful CPR was observed for major bleeding. Thrombolysis was administered to 132 patients in whom 13 developed major bleeding. 7 of 133 patients who did not receive thrombolysis developed major bleeding. Although the risk of bleeding was slightly higher in the thrombolysis group, it was not statistically significant. None of them presented with DAH [5].

DAPT is an established guideline-mandated pharmacotherapy during PCI for acute coronary syndrome. However, physicians should discontinue antiplatelet agents immediately upon massive spontaneous pulmonary bleeding and consider blood transfusion, particularly platelets, to overcome the lingering antiplatelet effects.

Emergency use of ECMO, while still a last-resort due to its highly invasive nature, has been successfully applied in many

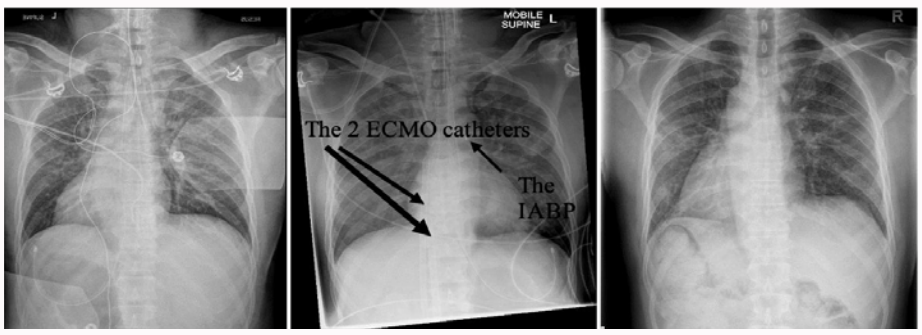

Figure 3: Antero-posterior chest X-rays.

instances of severe respiratory failure until lung recovery occurs. Application of ECMO necessitate systemic anticoagulation to prevent thrombus formation. However, systemic anticoagulation is a strong contraindication during active hemorrhage and thus not usually considered as a viable option for patients with DAH. While successful use of ECMO in cases of pulmonary hemorrhage has been reported in Acute Respiratory Distress Syndrome (ARDS), it has rarely been used post-PCI with DAH. The optimal level of anticoagulation has yet to be defined for this group.

Anticoagulation was used in a large majority of these reported VV-ECMO cases. This is due to the risk of clot formation in the oxygenator and venous thromboembolism in the patient without adequate anticoagulation which can result in mortality if left undetected. While new ECMO technologies such as biocompatible circuits with less thrombogenic modifications, centrifugal pumps and heparin-coated membranes (shorter lengths of heparin-bonded VV-ECMO tubing) are now available, it is still an evolving therapy and these solutions have not been conclusively proven to entirely eliminate the risk of circuit thrombosis [6]. Therefore, most centers seem to favor a lower therapeutic range of anticoagulation allowed for ECMO rather than withholding anticoagulation entirely [7].

We present several important clinical management measures for heparin-free V-V ECMO as a potential life-saving technology in future DAH settings with active severe bleeding. Firstly, prompt reversal of anticoagulation is essential in managing bleeding in severe DAH cases post-PCI. Throughout this period, it is essential to carry out routine evaluation of thrombotic complications within the circuit and closely monitor the patient for signs of venous thromboembolism. During a prolonged period of ECMO support, the membrane oxygenator may also have to be exchanged several times whenever circuit thrombosis occurs.

Thirdly, without the aid of anticoagulation agents, additional care must be taken to minimize the lethal triad of clot formation. Our practice was to maintain a slightly higher than normal blood flow rate to enhance flow throughout the circuit, possibly lowering the risk of stasis and subsequent thrombosis. However, this should be balanced with the fact that in the context of DAH where the patient has lost significant amounts of blood, there is a higher risk of the pump sucking down on the tubing due to inadequate venous return. It is therefore vital to maintain adequate venous return, either through transfusions to maintain sufficient intravascular volume or reducing the pump flow to decrease the suction process [8].

Our patient was successfully extubated after 32 h using the strategy outlined above. He suffered no major thrombotic complications or systemic embolization during this period. Furthermore, neurological protection of the patient was achieved through therapeutic hypothermia which was easily and rapidly controlled through the ECMO circuit.

Trauma records the first experience of initially heparin-free ECMO in severe trauma patients with coexisting bleeding shock [9]. There are no randomized controlled trials comparing anticoagulation to no anticoagulation for V-V ECMO-supported DAH. A clinical trial has outlined the successful use of anticoagulation-free V-V ECMO for up to 5 days without thrombotic complications [10].

Further studies are required to sufficiently support the observation that withholding anticoagulation in V-V ECMO is safe and feasible, and especially in investigating the optimal combination, duration and dosage of therapeutic anticoagulation agents.

Conclusion

We conclude that heparin-free V-V ECMO can be considered as a viable life-saving measure for critically ill DAH patients with hypoxemic respiratory failure refractory to all other supportive care. This is especially true as ECMO circuit technologies continue to advance and allow for lower anticoagulation levels.

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