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Successful use of recombinant activated coagulation factor VII in a patient supported with veno-venous ECMO after lung transplantation

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Editor,

We would like to describe a case of the successful use of recombinant activated factor VII (rFVIIa) to treat a bleeding complication in a patient on veno-venous (VV)-ECMO.

A 26-year old female presented for a re-do bilateral sequential lung transplantation (BSLT). Her initial BSLT was performed 12 months before for end stage respiratory failure caused by cystic fibrosis. Despite initial improvement of functional capacity she presented with worsening pulmonary function within the first year and due to chronic graft rejection and was re-listed for lung transplantation. Bronchiolitis obliterans was progressing quickly and patient had been admitted to the intensive care unit (ICU) with type II respiratory failure; unsuccessful ventilatory therapy resulted in the use of VV-ECMO as a potential bridge to BSLT. After forty days of VV-ECMO support she presented for redo BSLT.

During the surgical procedure, the VV-ECMO was changed to veno-arterial (VA) ECMO support, at a flow of 4 L min^{-1}, to provide haemodynamic stability and adequate oxygenation throughout a technically difficult surgical dissection. Due to ongoing haemorrhage (multiple adhesions after previous thoracotomy) and surgical difficulties, the VA ECMO circuit was converted to full cardiopulmonary bypass (CPB). At this moment the tranexamic acid infusion was initiated according to BART protocol [1]. After implantation of the second donor lung, the patient was weaned from CPB to VV-ECMO support to provide adequate oxygenation since the new grafts developed primary graft dysfunction. The patient continued to bleed excessively and received multiple blood products (50 units of packed red blood cells (PRBC), 28 units of fresh frozen plasma (FFP), 32 units of platelets (PLT) and 40 units of cryoprecipitate). Even with massive transfusion therapy bleeding was moderately well controlled thus patient was transferred to the ICU with VV-ECMO support and the thorax packed with sponges.

Despite further transfusion of blood products the patient continued to bleed through the chest tubes (2,575 mL per hour for the first 3 hours), requiring further transfusions of PRBC (13 units), FFP (6 units) and PLT (8 units). On the first postoperative day a decision was made to administer rFVIIa. In total 6 mg (100 μg kg^{-1}) of rFVIIa were given. An initial dose of dose of 2 mg was administered, followed by a second dose of 4 mg three hours later. She also received desmopressin 12 μg prior to the first dose of rFVIIa. Acid base status and temperature were normal before and after rFVIIa administration. Table 1 shows coagulation profile on arrival to ICU and after rFVIIa. The flows on the VV-ECMO circuit were between 2.5 and 3.5 L min^{-1}. Due to high risk of ECMO circuit thrombosis, the administration of rFVIIa was accompanied by extra vigilance for clot formation, and a second, primed ECMO circuit was immediately available in the event of thrombus formation. The patient stopped bleeding and started to form clots in the chest tubes. Chest tube drainage also decreased to 200 mL per hour the first 4 hours. The patient's hemodynamic stabilized, the transfusion rate decreased, and directed goal therapy was followed to keep Hb over 70 g L^{-1}. On postoperative day 3 the sponges were removed from the thorax and the chest was formally closed. At no time were any thrombi visualized in the ECMO circuit, the filter or the oxygenator membrane. The patient remained haemodynamically stable and adequately oxygenated via the VV-ECMO support. An intravenous infusion of heparin was restarted, with no subsequent bleeding. On postoperative day 18 the patient was successfully weaned from VV-ECMO completing 58 days of support. However, she developed ischemic retinopathy probably due to severe swelling (nevertheless thrombosis was not rule out), acute renal failure requiring haemodialysis, and sepsis; progressing quickly to septic shock with non-response to aggressive medical management dying one month after surgery.

Extracorporeal membrane oxygenation (ECMO) may be used to provide temporary oxygenation support for patients before (bridge) and after lung transplantation (primary graft dysfunction) or with refractory hypoxemia not responding to conventional treatment [2, 3]. Since 2009 H_1N_1 flu pandemic disaster ECMO became rapidly emerging technology, which is becoming introduced to many intensive care unit

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Table 1. Coagulation results before and after rFVIIa administration

Variable	Arriving ICU	Before rFVIIa administration	Two hours after rFVIIa administration
Haemoglobin (g L^{-1})	71	84	10
Platelets (G L^{-1})	116	104	62
Fibrinogen (mg dL^{-1})	180	238	217
INR	1.5	1.4	0.8
aPTT (sec.)		41	40

ICU — intensive care unit; INR — international normalized ratio; aPTT — activated partial thromboplastin time

all over the world. Its use requires systemic anticoagulation to avoid thrombi formation, circuit thrombosis or malfunctioning of the oxygenator. Typically, unfractionated heparin is administered to achieve an activated clotting time (ACT) between 160 and 220 sec., when supporting a patient with veno-venous (VV) ECMO [4]. Prolonged use of ECMO leads to profound derangements in haemostasis causing both haemorrhagic and thrombo-embolic complications. When haemorrhagic complications occur, their treatment may require partial reversal of this anticoagulation. rFVIIa has been used to treat coagulopathy and stop bleeding in multiple life-threatening situations, however its application in adults treated with ECMO has not been described [5–10]. Potentially, use of rFVIIa in patients supported by ECMO may lead to thrombus formation within the circuit with potentially fatal consequences. In this patient, aggressive perioperative transfusion therapy was necessary to maintain hemodynamic stability. In spite of fact that normal values of fibrinogen, PLT and INR were achieved, coagulopathy was persistent. Off-label use of rFVIIa has been described as a rescue therapy to stop bleeding in patients on VA-ECMO and in a few cases of paediatric VV-ECMO [11, 12]. This patient presented with a life threatening coagulopathy and as a final strategy we chose rFVIIa instead of using multiple blood products, which were ineffective. We observed significant bleeding reduction after rFVIIa administration. Clots appeared on the chest tubes but not in the ECMO circuit or oxygenator membrane. Regarding bleeding management, we considered this intervention as effective. However, there is not enough information to support use of rFVIIa on VV-ECMO as a routine procedure.

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