Cardiology in the Young (2018), **28**, 144–146
doi:10.1017/S1047951117001007

Brief Report

Recombinant factor VIIa as a rescue therapy in severe haemoptysis in a patient with a Fontan circulation

Thomas W. Mason,[1] Andrew Retter,[1] Gareth J. Morgan[2]

[1]*Critical Care;* [2]*Adult Congenital Cardiology, St Thomas' Hospital, Guys and St Thomas' NHS foundation trust, London, United Kingdom*

Abstract We describe the successful use of recombinant factor VIIa (rFVIIa) in the control of massive haemoptysis in a 17-year-old patient with a Fontan circulation. The patient was intubated and ventilated in the ICU with deteriorating gas exchange. Conventional methods to control the haemoptysis were ineffective, and rFVIIa was successfully administered as a rescue therapy. rFVIIa is a powerful pro-thrombotic agent, which is only licensed in haemophiliacs with acquired inhibitors to anticoagulation. It has been used off-license in the treatment of massive haemorrhage, although a Cochrane review did not show any significant benefit; however, it may have a role as a rescue therapy where alternatives options have been exhausted after careful risk–benefit analysis.

Keywords: Fontan; rFVIIa; factor VIIa; haemoptysis

Received: 7 January 2017; Accepted: 20 April 2017; First published online: 11 September 2017

Case presentation

A previously active 17-year-old young man with a Fontan circulation was admitted to our intensive care unit with massive haemoptysis. His background diagnosis was left atrial isomerisation, unbalanced atrioventricular septal defect, and pulmonary atresia. His initial palliation was with a central aorto-pulmonary shunt followed by a left modified Blalock–Taussig shunt. His fenestated Fontan-type circulation was eventually completed at the age of 10 years. The patient was chronically anticoagulated with warfarin as per our protocol to prevent thromboembolism. His baseline oxygen saturations were 85–89%, and he led an active lifestyle. He had been playing football in his back garden with his brother the night before his admission.

The patient was intubated and ventilated and transferred from his local hospital following presentation with haemoptysis and respiratory compromise. On arrival, he was hypoxic and had ongoing bleeding with oxygen saturations <70% despite an FiO_2 of 1.0. He was haemodynamically stable. His chest radiograph is shown in Figure 1. His admission international normalised ratio was 1.4. Anticoagulation was fully reversed during initial treatment. Cardiac catheterisation showed mildly elevated Fontan pressures and multiple major aorto-pulmonary collaterals to the right lung, which were embolised with coils. The patient's condition improved, and he was extubated and transferred to the ward after 48 hours. He was re-admitted to the ICU 4 days later with recurrent massive haemoptysis and required an emergency intubation. Further catheterisation was performed, but given his extensive recent procedures no new targets for occlusion were identified. Pulmonary angiogram excluded any arteriovenous malformations as an additional source of haemoptysis. He was transferred back to the ICU with ongoing haemoptysis, rising oxygen requirements, fevers, and renal failure. Supportive therapy progressively increased over the following 12 hours with ongoing blood suctioned through his endotracheal tube. He was considered too unstable for bronchoscopy or any other further interventions, and the situation was bleak.

Correspondence to: A. Retter, Critical Care, Guy's and St Thomas' NHS Foundation Trust, St Thomas' Hospital, Westminster Bridge Road, London, SE1 7EH, United Kingdom. Tel: +020 7188 7188, ext 54509; Fax: +44 2071887345; E-mail: andrew.retter@gstt.nhs.uk

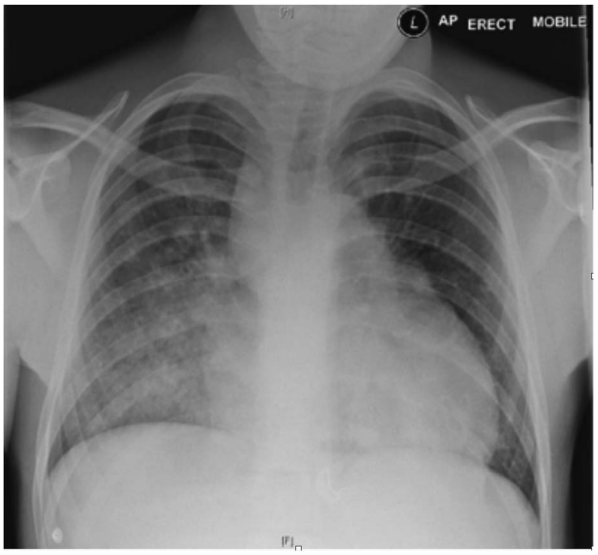

Figure 1.
Antero- posterior chest radiograph on clinical presentation. The key finding is that of diffuse patchy infiltrates predominantly in the right middle and lower lobes representing the inflammatory response to hemorrhage.

The patient had received extensive blood product support throughout, and his clotting parameters were within normal limits: international normalised ratio <1.5, activated partial thromboplastin time ratio <1.5, and platelet count 110×10^9/L. He received tranexamic acid 1 g quater die sumendum. After careful consideration, 40 μg/kg of recombinant factor VIIa (rFVIIa) was administered in an attempt to reduce or terminate the haemoptysis. After administration of rFVIIa, the haemoptysis reduced to 50 ml over the following 12 hours and had virtually ceased at 24 hours. The patient remained intubated for a further 5 days but was extubated uneventfully and discharged to the ward 7 days later. He returned home ~3 weeks after his admission and has returned to college and everyday activities. Anticoagulation has not been re-started. In recent months, his overall functional status and ventricular function have declined, and he is currently being considered for cardiac transplantation.

Discussion

Haemoptysis is a recognised complication of a Fontan circulation[1] and may be secondary to major aorto-pulmonary collaterals or pulmonary arteriovenous malformations. Previous cases have been treated with coil embolisation, extracorporeal membrane oxygenation, and lobectomy.[2] In this case, coil embolisation was performed on three occasions without sustained resolution of haemoptysis. Given the ongoing, large-volume haemoptysis, the anticoagulation required for extracorporeal membrane oxygenation was deemed to be an absolute contraindication to its use. Given the poor prognosis, rescue therapy with rFVIIa was attempted. The major risk was that the rFVIIa would cause extensive clotting throughout the Fontan circuit, leading to reduced cardiac output and death; however, the desperation of the situation justified this risk. To our knowledge, this is the first case report to document the use of rFVIIa in a patient with massive haemoptysis related to a Fontan circulation.

rFVIIa is only licensed for use in haemophiliacs with acquired inhibitors to anticoagulation. It has been used off-license in the setting of uncontrollable haemorrhage, notably in the case of a 19-year-old Israeli soldier who suffered a gunshot wound to the inferior caval vein, which continued to bleed despite surgical attempts to achieve haemostasis.[3] The American Society of Thoracic Surgeons and the Society of Cardiovascular Anaesthesiologists recommend the use of rFVIIa in patients with uncontrollable non-surgical bleeding who have undergone cardiac procedures on bypass.[4] A Cochrane review evaluating the use of rFVIIa in the control of haemorrhage in patients without haemophilia has been performed.[5] In the setting of therapeutic use of rFVIIa, there was no significant difference in mortality, red cell transfusion requirements, or total number of thromboembolic adverse events. There were non-significant trends towards reduced mortality and increased thromboembolic events in patients treated with rFVIIa, and alarmingly there was a significant increase in the total number of arterial thrombotic events. At present, expert opinion recommends that off-license use of rFVIIa in patients without haemophila be restricted to clinical trials.[5]

In conclusion, where conventional options for haemostasis have been exhausted, the use of rFVIIa as a rescue therapy in extremis may be considered after carefully assessing the risk–benefit profile. Significant haemoptysis in the setting of a Fontan circulation may be indicative of deteriorating haemodynamics; successful treatment of the acute situation may only provide temporary relief in the setting of a failing Fontan circuit.

Acknowledgement

None.

Conflicts of Interest

None.

Ethical Standards

The contents of this report meet the ethical standards of Guys and St Thomas' NHS foundations trust.

References

1. McRae ME. Long-term issues after Fontan procedure. AACN Adv Crit Care 2013; 24: 264–288.
2. Bedard E, Lopez S, Perron J, et al. Life-threatening hemoptysis following the Fontan procedure. Can J Cardiol 2008; 24: 145–147.
3. Kenet G, Walden R, Eldad A, Martinowitz U. Treatment of traumatic bleeding with recombinant factor VIIa. Lancet 1999; 354: 1879.
4. Ferraris V, Brown J, Despotis G, et al. Update to The Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists, blood conservation clinical practice guidelines. Special report: STS workforce on evidence based surgery. Ann Thorac Surg 2011; 91: 944–982.
5. Simpson E, Lin Y, Stanworth S, Birchall J, Doree C, Hyde C. Recombinant factor VIIa for the prevention and treatment of bleeding in patients without haemophilia. Cochrane Database Syst Rev 2012; issue 3: CD005011.

https://doi.org/10.1017/S1047951117001007 Published online by Cambridge University Press