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Successful Management of Severe Bleeding After Redo Cardiac Transplantation with Recombinant Activated Factor VII

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Abstract

Heart transplant recipients who are on a prior aggressive anticoagulant or antiplatelet treatment may experience severe post-operative bleeding. We describe a case of bleeding after cardiac transplantation which was refractory to standard treatment and was eventually managed with the off-label use of recombinant activated coagulation factor VII. The relevance of this approach in terms of patient survival as well as graft preservation is discussed.

Introduction

Bleeding complications after major surgery are an important cause of morbidity and mortality in hospitalised subjects. Cardiac surgery requiring cardiopulmonary bypass is particularly prone to these complications. Large surveys have shown that the risk of significant bleeding following cardiac surgery is around 3%-11%, while the excess lethality associated with these complications is extremely high, and may reach 22% of cases [1-3].

Management of severe post-operative bleeding includes transfusion of blood products, administration of crystalloids or colloids and diverse pharmacological interventions [4]. In refractory cases, surgical re-intervention is mandatory, although afflicted by a three to four-fold increase in mortality, a considerable rise in morbidity as well as increased costs [1]. Novel strategies, such as administration of recombinant activated coagulation factor VII (rFVIIa), have been successfully applied in diverse clinical conditions, including cardiac surgery [5]. However, very little experience exists regarding the use of rFVIIa in the heart transplant setting, where the risk of bleeding is especially high.

In this article, we report a case of successful control of bleeding with rFVIIa after emergency redo cardiac transplant.

Clinical Summary

A 48 year old woman underwent heart transplant for end-stage post-ischaemic dilated cardiomiopathy in 2004. Her previous clinical history was remarkable for the presence of hyper-cholesterolaemia, hyper-homocysteinemia (25 µmol/L), family history of ischaemic heart disease, 13 pack-year cigarette smoking as well as pro-thrombotic risk factors. She was homozygous for the C677T 5, 10 methylene-tetrahydrofolate reductase gene mutation and heterozygous for the G20210A prothrombin gene mutation.

After transplant, patient diet as well as lifestyle were changed, and she was put on statin and acetylsalicylic acid (150 mg od) treatment along with the immunosuppressive regimen based on cyclosporin A, mycophenolate mofetil and prednisone. Notwithstanding, three months after transplant, coronary angiography disclosed a 40% stenosis of the left anterior descending.

Follow-up angiographies showed progressive worsening of graft coronary artery disease, which required stenting of the left anterior descending nine months after transplant and initiation of clopidogrel, 75 mg once daily, in addition to acetyl-salicylic acid.

Three months after starting the dual anti-platelet regimen, the patient presented with new-onset dyspnoea requiring hospitalisation. Over the following 12 hours, she progressed to develop pulmonary oedema. Repeat coronary angiography showed severe three vessel disease. The patient was put on the emergency waiting list and was re-transplanted within 12 hours.

Although the surgical procedure was carried out without complications, as soon as the patient came out of the operating room significant bleeding was observed. During the first six hours post-surgery, blood losses from thoracic drainage tubes reached an average of > 600 ml per hour. Figure 1 depicts the hourly amount of blood losses and the relevant blood product infusions done. Overall, the patient lost about 3650 ml from drainage tubes and received a total of 4150 ml of blood products, including 1750 ml of packed red blood cells, 1200 ml of fresh-frozen plasma and 1200 ml of platelet concentrate. In addition, 1000 IU of human pro-thrombin complex were administered.

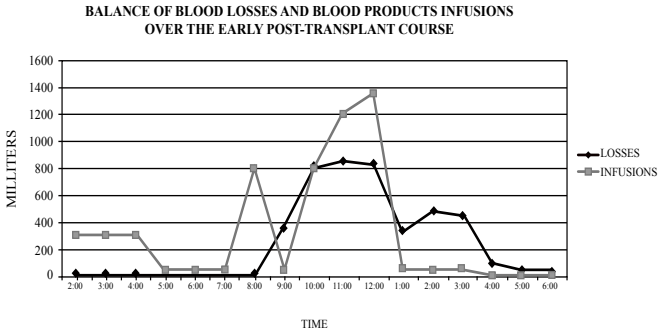

Figure 1: Balance of blood losses and blood product infusions over the early post-transplant course. The black line (⟷) indicates the amount of blood lost every hour. The grey line (⟷) shows the amount of blood products administered. The grey bar (▬) indicates the duration of the surgical procedure. The vertical black arrow (↓) shows the time when recombinant activated factor VII (rFVIIa) bolus was administered, at the dose of 70 µg/kg.

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Nonetheless, she remained hypovolemic and progressed to a condition of haemorrhagic shock. Therefore, we decided to administer a 70 μg/kg body weight bolus of rFVIIa (Novoseven, Novo Nordisk). Following administration, blood losses went down to about 50 ml per hour, and there was no need for further dosing. Patient clinical conditions improved rapidly in the absence of any thrombo-embolic complication, and she was discharged from the intensive care unit two days later.

Discussion

Emergency cardiac surgery in patients on dual anti-platelet treatment bears a major risk of bleeding. Heart transplant is often performed in these conditions. However, as yet there is very little experience of the use of rFVIIa in the emergency heart transplant setting [5].

In our case, off-label treatment with rFVIIa was safely employed to control post-operative bleeding. Several reasons supported the decision to withheld any further surgical exploration to control the bleeding: i) the sutures had been correctly performed and there had been no specific technical hurdles; ii) at the end of the transplant procedure, diffuse bleeding was already present, as the patient was on continuing dual anti-platelet treatment; furthermore, severe thrombocytopenia occurred during the extra-corporeal circulation, such that the patient was in an inherent pro-hemorrhagic state; iii) the redo surgery would have been a third sternotomy, representing a very significant risk factor for sternal wound infection; indeed, being a second transplant, the patient had already been put on an aggressive immune suppressive protocol. Therefore, by avoiding a very high-risk surgical revision, rFVIIa treatment allowed to save the patient life while preserving all human and financial resources employed for the emergency transplant. Interestingly, rFVIIa administration did not induce any thrombo-embolic complications, despite the significant pro-thrombotic risk profile of the patient. This is in line with previous observations [5] showing no increased thrombotic effect of rFVIIa. Furthermore, no effect of rFVIIa on the immunosuppression regimen was observed.

Conclusion

In conclusion, our experience suggests that rFVIIa administration may have potential successful application in the treatment of severe bleeding after heart transplant. rFVIIa may be particularly useful in this setting, where most patients present a severe, drug-induced impairment of their haemostasis which cannot be corrected in advance.

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