Successful use of activated recombinant factor VII to control bleeding abnormalities in a patient with a left ventricular assist device

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Bleeding is the most frequent complication related to implantation of a mechanical cardiac assist device.¹ Recombinant activated factor VII (NovoSeven; Novo Nordisk, Bagsvaerd, Denmark) was developed as a prohemostatic agent. We report the successful use of recombinant activated factor VII to control bleeding abnormalities in a patient with a left ventricular assist device (LVAD).

Clinical Summary

After repeated cardiac surgery (mitral and later tricuspid annuloplasty, implantation of a mechanical mitral valve, and subsequent reimplantation of an artificial mitral valve), a 34-year-old male patient was admitted to the cardiac surgical intensive care unit with severe left ventricular dysfunction. Hemostatic disturbances were also observed, with the following initial coagulation parameters: international normalized ratio (INR) 2.22, antithrombin III 48.84%, platelet count $35 \times 10^9/L$, and a negative result of the D-dimers test ($<200 \mu g/L$).

Cardiac shock developed despite high and increasing doses of inotropic agents. To unload the failing heart and prevent the patient's condition from deteriorating into multiple organ failure, we implanted a pneumatically driven, diaphragm-type LVAD (POLVAD, Zabrze, Poland). The device was placed paracorporeally between the left atrium and ascending aorta. The pump was operating in an asynchronous mode, and it was giving a pump output of about 5.2 L/min, thereby nearly completely unloading the failing left ventricle. Cardiopulmonary bypass was not used during the implantation procedure, intraoperative blood loss equaled 2500 mL, and blood products were transfused accordingly.

During the next 6 hours postoperatively, hourly drainage exceeded 150 mL. Additionally, the patient had massive epistaxis,

requiring nasal packing, and excessive oozing from the wound, which amounted to an extra blood loss of about 800 mL. The hemostatic disturbances persisted despite the use of conventional measures. After administration of packed red blood cells, fresh frozen plasma, platelet concentrate, and tranexamic acid, slight correction of coagulation parameters was achieved (INR 1.61, antithrombin III 60.26%, platelet count $89 \times 10^9/L$, and fibrinogen 2.71 g/L), yet there was no clinical improvement.

In an attempt to achieve hemostasis, we administered recombinant activated factor VII (20 $\mu g/kg$ bolus injection given intravenously). Laboratory results after 30 minutes showed an INR of 0.97, and bleeding and oozing significantly decreased (drainage 25 mL/h). Clinical improvement lasted for 2 hours.

Four hours after the initial dose, the second, higher recombinant activated factor VII dose of 30 $\mu g/kg$ was administered. Afterward, laboratory results showed an INR of 0.89. Bleeding and oozing ceased and hourly drainage decreased below 15 mL. There were no further episodes of bleeding, and no significant side effects were observed. Close inspection of the pump chamber performed by a applying light source to the transparent LVAD walls and cannulas showed neither areas of thrombus formation nor platelet aggregation. There were no laboratory equivalents of hypercoagulability, and the D-dimer test results remained negative. Echocardiography showed no abnormalities of the mechanical mitral valve.

The patient survived 7 days with the LVAD. On the second postimplant day, continuous veno-venous hemoperfusion was instituted because of oliguric renal failure. In the following days we observed gradual recovery of kidney and liver function. However, despite the use of lung-protective ventilatory strategy (pressure-controlled low tidal volume ventilation), on the seventh postimplant day a tension pneumothorax developed, precipitating right ventricular failure. Prompt insertion of a chest tube did not stop acute circulatory decompensation, and the patient eventually died. Afterward, the device was removed and examined. It was found to be free of thrombin and platelet aggregates.

Discussion

Appropriate balancing between the dangers of bleeding and thrombosis is a difficult task in the care of the patient with an implanted mechanical circulatory support device. Risk of bleeding, particularly in the immediate postoperative period, is very high, frequently necessitating reoperation. On the other hand, because of the significant risk of thromboembolic events, introduction of anticoagulants and antiplatelet agents is indispensable.

Activated factor VII has the ability to bind to tissue factor expressed at the site of tissue injury, resulting in site-specific throm-

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bin generation. Formation of tissue factor–activated factor VII complex not only initiates coagulation cascade, but also provides the first thrombin molecules necessary for platelet activation.²

Activated recombinant factor VII was previously applied in patients with hemostatic disorders, for example, hemophilia and inhibitors to factors VIII or IX.³ Recently, it has been increasingly used to secure hemostasis in difficult clinical situations.⁴ Infusion of recombinant activated factor VII results in an immediate, short-term, local generation of thrombin at sites of tissue factor exposure, such as surgical wounds. Recombinant activated factor VII was already safely used to control refractory bleeding in patients undergoing heart valve replacement surgery.⁵ Lack of thrombotic complications after administration of activated recombinant factor VII in the presence of an artificial device is thus probably related to its site-specific mode of action.

To our knowledge, this was the first case in which activated recombinant factor VII was administered in a patient with an LVAD. Our observation suggests that activated recombinant factor

VII may be safely used to control refractory bleeding in patients with mechanical cardiac support, but further studies are required.

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