

Quick Correction of Hemostasis in Two Patients With Fulminant Liver Failure Undergoing Liver Transplantation by Recombinant Activated Factor VII

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IT IS WELL KNOWN that reducing blood loss is an important goal for the liver transplant surgeon; however, the surgeon's technical skills and experience, along with other factors (eg, extent of patient's pretransplant coagulopathy, basic disease, intraoperative hypothermia, and acidosis) may increase blood losses and transfusion needs.¹⁻⁴

Fulminant liver failure (FLF) is often associated with severe coagulopathy and is very difficult to correct using conventional replacement therapy with transfusions of fresh frozen plasma, cryoprecipitate, and platelet concentrates and if necessary AT-III and antifibrinolytic drug administration. According to King's College Hospital (KCH), the lack of a spontaneous correction of prothrombin time is one of the main indicators of the need for orthotopic liver transplantation (OLTx); therefore, replacement therapy should not be performed until this is achieved.⁵ In most cases, correction of hemostasis for safe performance of OLTx is still possible; however, a significant number of patients will not respond well for even extensive replacement therapy, which increases the risk of uncontrollable intraoperative blood loss.

We report here the first (to our knowledge) experience with the treatment of severe pretransplant coagulopathy by

recombinant activated factor VII (rFVIIa) in two children with FLF in whom no correction of hemostasis was achieved by standard methods. rFVIIa is very effective for patients who have hemophilia A or B and circulating anticoagulants. We have also used rFVIIa to treat patients for coverage of major abdominal surgery with a very good hemostatic result. It has been also reported, in the treatment of severe acquired prothrombin complex deficiency.^{6,7}

MATERIALS AND METHODS

Two boys; a 2.5-year-old weighing 16 kg and a 6-year-old, weighing 21 kg, were admitted to our institute with symptoms of FLF caused by NANB hepatitis. Both boys were scheduled for OLTx after fulfilling KCH criteria; however, it was not possible to correct their coagulation before transplantation despite large amounts of FFP, cryoprecipitate, platelet concentrate, and peripheral red blood cell

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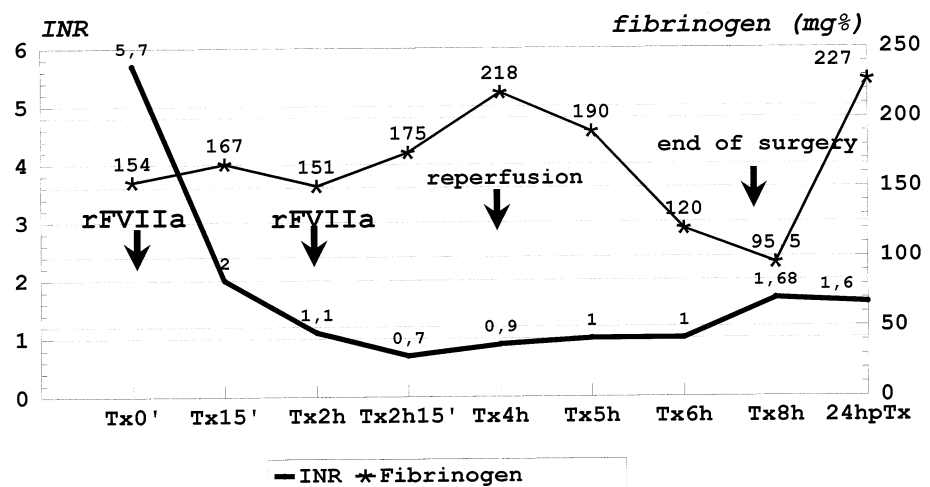


Fig 1. Patient # 1, reduced liver graft, intraoperative coagulation.

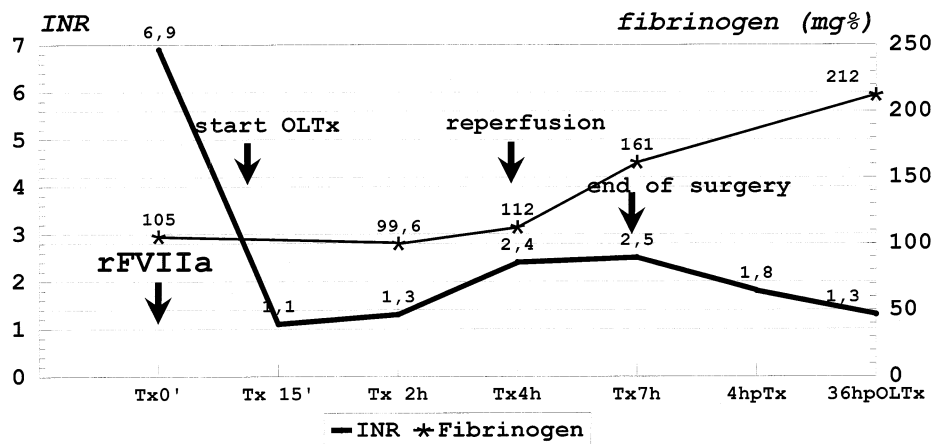


Fig 2. Patient # 2, whole liver graft, intraoperative coagulation.

(PRBC) transfusions. One of the patients was actively bleeding from his gastrointestinal and urinary tracts. Before OLTx, their INRs were 5.7 and 6.9, respectively, so we administered rFVIIa (NovoSeven, Novo Nordisk S/A, Denmark). In the first patient, two doses (100 μ g/kg body mass) were administered 5 minutes before skin incision and 2 hours after, resulting in immediate (hyper)correction of INR which remained within the normal range (0.7 to 1.1) until the end of surgery (Fig 1). In the second patient, only one dose of rFVIIa was administered just before OLTx started, and INR was 1.1 to 2.4 during the operation (Fig 2). Both patients were given also single doses of tranexamic acid simultaneously with the first dose of rFVIIa. Clinically blood loss was minimal. Blood transfusion amounted to 600 mL (reduced graft) in the first case and 300 mL in the second case (whole liver graft). No postoperative bleeding or any thromboembolic complications occurred in either patient.

DISCUSSION

Severe, uncorrected coagulopathy, especially in a patient who has FLF, correlates with increased intraoperative blood loss, morbidity, and mortality after OLTx. An additional risk of disease transmission due to large amounts of blood products being transfused cannot be omitted.^{1,4,8}

The unique characteristics of rFVIIa depend on its mode of action. It is well documented that an excess of activated FVII enhances the intermediate steps of coagulation cascade through direct activation of factor X, even without the presence of tissue factor and most prothrombin complex factors. As the activation of factor X takes place mostly on the surface of activated platelets, hemostasis is achieved in the sites of active bleeding and there is no tendency for generalized coagulation, especially since rFVIIa has very short clinical activity time (about 2 hours).

Our initial experience with the use of rFVIIa in the liver transplant patients showed striking improvement of hemostasis despite severe depletion of coagulation factors. Liver transplant surgery was performed in both cases without any excessive blood loss as in elective patients, thus, without an increased risk of postoperative complications. INR seems to be a good indicator of rFVIIa effects allowing for dosage adjustment without increasing risk of overcorrection of hemostasis, especially when the new liver starts its own synthesis of clotting factors.

The other potential usage of rFVIIa in patients with FLF may include coverage of liver biopsy and intracranial pressure transducer placement, which may be followed by severe bleeding if performed without good patient hemostasis.⁷⁻⁹

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