Recombinant Factor VIIa in Severe Uremic Bleeding

Dear Sir,

Activated recombinant factor VII (rFVIIa) has been successfully employed to control bleeding in haemophilia patients with inhibitors to factor VIII or IX (1) and in patients with thrombocytopenia (2). It has also been used for the treatment of a patient with abnormal platelet function (3). Until recently, repeated three-hourly doses were administered for a period of 2 to 3 days. Recent data seems to indicate that 1-3 injections of rFVIIa could adequately control moderate bleeding in haemophiliacs with inhibitors (4).

A 12-year-old girl with a history of traumatic rupture of both renal arteries, resulting in terminal renal insufficiency, was admitted for unilateral kidney transplantation. The donor was known to be CMV positive. Six weeks after the transplantation she developed abdominal pain and on CT scan a haematoma and an aneurysma of the renal artery was found. During laparotomy the aneurysma was removed with revision of the arterial sutures. In the following week, while still on immunosuppressive therapy, she developed severe CMV pneumonitis for which high dose gancyclovir and CMV hyperimmunoglobulin therapy was started. She was intubated because of respiratory insufficiency. Shortly after intubation fulminant pulmonary bleeding occurred. Platelet count at that time was 199 x 10^9/l. APTT (Boehringer) and PT (Organon) were normal, urea was 38.1 mmol/l (N: 2-7 mmol/l). Additional haemostatic investigations revealed normal levels of factors I, II, V, VII, VIII, IX, X, and vWF. No fibrin split products could be detected. Bleeding time was, however, longer than 15 min. In vitro platelet aggregation studies showed deficient aggregation with ADP, adrenaline and ristocetin and reduced aggregation with collagen.

With the institution of high positive end expiratory pressure (PEEP) ventilation, the transfusion of platelets and fresh frozen plasma the bleeding was stopped. The cause of the bleeding tendency was thought to be uremic platelet dysfunction and she received repeated platelet and red blood cell transfusions, keeping the haematocrit >0.30. Three days later, during routine suctioning another massive pulmonary bleeding occurred. Desmopressin was considered but not given as the patient already had a large fluid overload due to renal insufficiency and there was some controversy as to the starting of dialysis. A concentrate of factors VIII and vWF (Haemate P) was also given but the bleeding only stopped after high-frequency oscillation ventilation. The mechanism of the bleeding tendency in uremic patients is not fully understood and is thought to be due to a combined effect of uremia and CMV pneumonitis. The prompt effect of rFVIIa administration is most probably due to local generation of thrombin on the exposed subendothelial surface and on the surface of vessel-wall attached, activated platelets. The latter process may happen even in the absence of tissue factor and may provide a fast and effective way to control severe bleeding (6). Thus, a single dose of 90 µg rFVIIa may be effective in controlling the severe bleeding tendency occasionally observed in uremic platelet dysfunction.

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References


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