



Case report

Recombinant activated factor VII for a warfarinised Jehovah's Witness with an acute subdural haematoma

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Received 26 April 2007; accepted 13 May 2007

Abstract

Recombinant activated factor VII (rFVIIa) (NovoSeven; Novo Nordisk A/S, Bagsvaerd, Denmark) is a haemostatic agent first developed for bleeding associated with haemophilia and trauma, but for which the indications continue to expand. Recent reports have suggested efficacy for various types of intracranial haemorrhage and for patients with abnormalities of coagulation. We report a warfarin-anticoagulated Jehovah's Witness patient with an acute subdural haematoma for whom rFVIIa was used perioperatively. The haematoma was surgically evacuated without excessive blood loss and the patient eventually made a good recovery, returning to independent self-care.

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Keywords: Recombinant activated factor VIII; Acute subdural haematoma; Surgery; Anticoagulation; Warfarin; Jehovah's Witness

1. Introduction

Recombinant activated factor VII (rFVIIa) (NovoSeven^R; Novo Nordisk A/S, Bagsvaerd, Denmark) is a haemostatic agent first developed for bleeding associated with haemophilia and trauma, but for which the indications continue to expand. Pharmacological doses activate factor X directly on the surface of activated platelets, localised to the site of injury where tissue factor is also present, giving rise to formation of factor Xa and subsequently thrombin and a stable fibrin clot.

We report an anticoagulated Jehovah's Witness patient with an acute subdural haematoma for whom rFVIIa was used perioperatively with good outcome.

2. Case report

A 74-year-old woman on warfarin for atrial fibrillation was brought by ambulance to the emergency department.

She had complained of a worsening headache, associated with slurred speech and left-sided weakness. She had become progressively unconscious, with a Glasgow Coma Scale (GCS) score of 7. She was intubated and ventilated, and a CT scan of her brain showed a large right acute subdural haematoma (ASDH) with mass effect and midline shift (Fig. 1). Her International Normalised Ratio (INR) was 3.7 and haemoglobin 104 g/L. There was no history of trauma and no external injury.

Reversal of the warfarin with fresh frozen plasma (FFP) was planned; however, after administration of a small volume, it was determined that the patient was a Jehovah's Witness, refusing all blood products even for life-saving indications. The FFP was ceased and rFVIIa 3.2 mg was given. She was taken to the operating room for craniectomy and evacuation of the haematoma. Intraoperative blood loss was not excessive and the INR measured 4 h after administration of rFVIIa was 1.0.

Two days following surgery, her haemoglobin was 92 g/L and INR 1.0 but her conscious state was not improving. A CT scan showed a re-accumulation of blood in the extra- and subdural spaces (Fig. 2) and this

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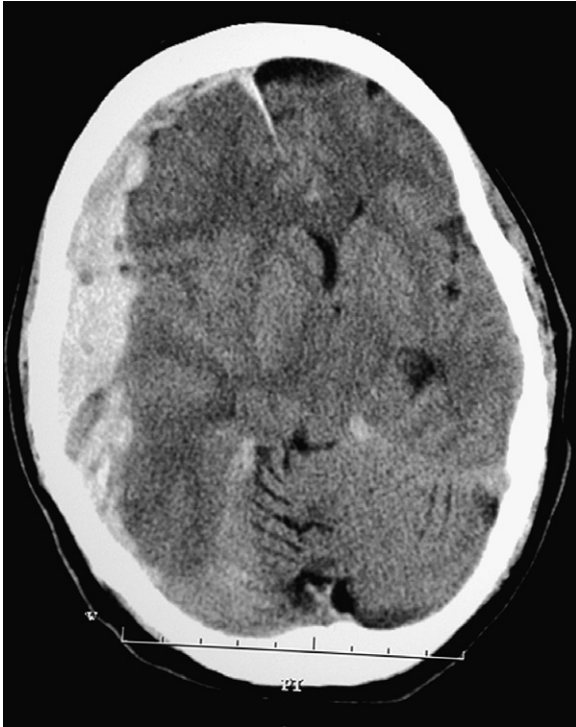


Fig. 1. Axial CT scan of the head at presentation showing a right acute subdural haematoma with 2 cm of midline shift.



Fig. 2. Axial CT scan 2 days postoperative, showing a recollection of the haematoma in the extra- and subdural spaces. Despite the large haematoma, there is less midline shift and compression of the ventricles due to the craniectomy.

was again surgically evacuated. Postoperatively, her haemoglobin was 88 g/L. Five days postoperatively, a marked neurological improvement was noted and she be-

gan to obey commands. Her haemoglobin became normal. After a prolonged period of rehabilitation and an autologous cranioplasty, she returned to independent self-care at home.

3. Discussion

Recombinant activated factor VII was initially developed for the treatment of spontaneous and surgical bleeding in patients with haemophilia and has been widely used for severe trauma. Pharmacological doses activate factor X directly on the surface of activated platelet localised to the site of injury where tissue factor is also present, giving rise to formation of factor Xa and subsequently thrombin and a stable fibrin clot. Evidence from its extensive use in the haemophilic population demonstrates that it enhances haemostasis at the site of injury, with less systemic activation of the coagulation cascade. Because of its mode of action, rFVIIa has the therapeutic potential for haemostasis in bleeding disorders associated with liver disease and oral anticoagulant treatment (in which endogenous FVII levels may also be low). Additionally, it may be used in conditions characterised by reduced platelet surface thrombin generation, including thrombocytopenia, platelet disorders, intracerebral haemorrhage and diffuse bleeding triggered by surgery.^{1,2}

There have now been many reports of the use of rFVIIa for treatment of non-haemophilic bleeding, including in patients with intracerebral haemorrhage (ICH). Early haematoma growth is the major cause of neurological deterioration after ICH, and may be amenable to early intervention.³ A multicentre randomised controlled trial investigated rFVIIa for ICH and found that early treatment (within 4 h) limited haematoma growth, reduced mortality and improved functional outcomes despite a small increase in the frequency of thromboembolic events.⁴ A second trial has recently been completed, but results are yet to be published. Additionally, there have been reports of successful use of rFVIIa to control bleeding during neurosurgical procedures for resection of intracranial tumours⁵ and to prevent rebleeding after aneurysmal subarachnoid haemorrhage without increasing the risk of cerebral infarction – a complication commonly associated with older antifibrinolytic agents.⁶ Thus, there is emerging evidence that rFVIIa may be used successfully for the treatment of various types of intracranial bleeding, including reports of a small number of patients on warfarin anticoagulation.^{7,8}

Factor VII may be the coagulation factor most affected by oral vitamin K antagonists. It thus follows that replacement of factor VII may control bleeding induced by routine or over-anticoagulation. In animal models, treatment with rFVIIa in rats anticoagulated with warfarin reduced both the bleeding times and amount of blood lost. In human studies, rFVIIa has been shown to normalise the INR in anticoagulated volunteers.⁹ Several features make rFVIIa ideal for reversal of coagulopathy

in intracranial haemorrhage. It acts almost immediately, requires a negligible volume for infusion, poses no risk of transfer of blood-borne pathogens, and has few apparent complications.¹⁰

The reported patient is unique: a warfarin anticoagulated Jehovah's Witness with a life-threatening subdural haematoma requiring immediate evacuation and thus normalisation of coagulation. Blood products, most commonly FFP, could not be used to reverse the coagulation abnormality. After administration of rFVIIa the INR returned to normal within a few hours, and surgery proceeded without unusual blood loss, as indicated by the small decrease in postoperative haemoglobin. The postoperative haematoma recollection may be an indication of ongoing coagulation abnormalities, although this was not evident on laboratory tests, but may also occur in patients with a normal coagulation profile.

rFVIIa has been reported for the treatment of intracranial haemorrhage in a Jehovah's Witness with severe haemophilia A and factor VIII (FVIII) inhibitors.² Patients with this condition are usually treated with FVIII bypassing agents, namely prothrombin complex concentrates or their activated derivatives. Human plasma-derived FVII concentrate has also been used. None of these products is acceptable to Jehovah's Witnesses, as all are derived from human blood. However, non-blood and recombinant alternatives are acceptable.¹¹ The patient reported here illustrates the usefulness of rFVIIa in this difficult group of patients, the anticoagulated Jehovah's Witness with life-threatening bleeding.

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