



LETTER TO THE EDITOR

Successful treatment of an injury bleeding on a patient suffering from mild von Willebrand's disease and predisposition to allergic diseases, with recombinant factor VIIA

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Patients with von Willebrand's disease (VWD) often suffer from mucocutaneous bleedings, menorrhagia, postpartum bleeding and postsurgical haemorrhage. One well known therapeutic option is the treatment with desmopressin (DDAVP) in body weight-adapted doses. The alternative option is the substitution of FVIII/von Willebrand factor (VWF) concentrates, if treatment with desmopressin is not possible or not efficacious. Bleeding tendencies in patients with VWD are different in every patient, therefore difficult sometimes to decide which treatment is reasonable and how long the treatment should take. Recombinant factor VIIa (rFVIIa) is another treatment option, in cases of insatiable bleeding [1].

A 67-year-old woman was admitted, exhibiting hip contusion and gluteal haematoma after a road accident. Distinct generation of haematoma and pain along with her anamnestic VWD type 1 led to immediate admission to intermediate care unit. A big gluteal haematoma and several painful excoriations over the patient's body were visible. The examination of heart, lungs and abdomen was unremarkable. The patient's body exhibited several haematomas and epistaxis as well as other bleedings due to minor injuries. Small surgical interventions (cleavage of abscess, coronary artery angiography, thyroidec-tomy) were accomplished without any substitution or bleeding complications.

Secondary disorders included allergic asthma, hypertensive heart disease, hypothyreosis, idiopathic osteoporosis and polyarthrosis. In addition, the patient reported abortion (1980), meningioma (2007) and an insufficiency of adrenal cortex. Her medication comprised budesonid (Pulmicort® R 2 × 1, Astra Zeneca, Wedel, Germany), verapamil (Isoptin® R 80 3 × 1, Abbott GmbH, Wiesbaden, Germany), thyroxin (L-Thyroxin® R 100 1 × 1, Henning, Flörsheim, Germany), clenbuterol (Spiropent® R 0, 02 2 × 1, Boehringer Ingelheim, Ingelheim, Germany), calcium 1000 mg and methylpred-nisolone (Urbason® R 4 mg 1 × 1, Aventis Pharma, Frankfurt, Germany). Before admission, she had been treated with antibiotics (amoxicillin 250 mg twice a day) due to a chronic infection of the urinary tract.

Laboratory diagnostics could not be carried out before treatment, but showed normal values the day after (Table 1). The activated partial thromboplastin time (aPTT) was normal (27 s, normal range 27–28 s); as well as prothrombin time (89%, normal range 80–120%). Platelet aggression-test showed normal aggregation to ADP, arachnidonic acid and ristocetin. von Willebrand parameters were at a high range, probably due to the acute phase reaction (Table 1). The VWD was diagnosed in 1989 (Table 2). Other coagulation disorders

Table 1. VW: Parameter.

aPP (sec)	PT (%)	VWF:Ag (%)	VWF:Rco (%)	FVIII (%)	CRP (mg%)
27	89	153	135	166	0.65

Table 2. VWD: laboratory findings before injury.

aPP (sec)	PT (%)	VWF:Ag (%)	VWF:Rco (%)	FVIII (%)	CRP (mg%)
28	109	66	58	110	Not done

*VWF:Ag: normal range 70–100%; VWF:Rco: normal range 70–100%.

could be excluded. Table 2 shows VWF levels from 2008 (before accident).

Furthermore, laboratory tests showed low levels of haemoglobin (9.6 g dL⁻¹, normal range 12–16 g dL⁻¹) and thrombocytes (141 nL⁻¹, normal range 150–450 nL⁻¹). Liver enzymes and renal values were within the normal range (Table 3).

Treatment with VWF concentrates was not carried out, due to acknowledged allergy against proteins. The patient rejected transfusions. Due to known intolerance to desmopressin (flush, palpitation, hypotension, nausea), the patient received tranexamic acid (3 × 1 g die⁻¹, planned for the 3 days) under regulation and control of haemoglobin and clinical status. Initially, the patient tolerated tranexamic acid therapy under concomitant corticoid treatment (Solu-Decortin® 250 mg, Merck, Darmstadt, Germany); afterwards, she developed side effects, namely rash dyspnoea and heart palpitation, which thereafter resulted in stoppage of tranexamic acid infusion. To stop bleeding, the patient was treated twice with rFVII (240 kE first dose and 60 kE 8 h later). The bleeding stopped afterwards; the patient did not show any allergic reactions and no thromboembolic side effect occurred (Table 2). Due to her stabilized condition, she could be transferred from the intermediate care to the normal ward the following day. The patient was discharged 1 week later without any further complications.

In the course of the following month, the patient underwent tooth extraction under treatment with rFVII (60 kE, 90 µg kg b.w.) without any complications (Table 4).

Table 3. Allergies and intolerance.

- Contrast medium
- Animal proteins
- Anaesthetics in exception of disoprivan
- Antibiotics
- Dust
- Medical strip
- Narcotics
- Pollen
- Some fruits
- Intolerance to desmopressin

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Table 4. Dosing recombinant factor VIIa.

- 240 kE first dose (270 µg kg⁻¹ b.w.)
- 60 kE 8 h later (90 µg kg⁻¹ b.w.)

Table 5. Blood count.

PLT (per nL)	Hb (g dL ⁻¹)	Hk (%)	MCH (%)	RBC (per nL)	WBC (per nL)
141	9.6	29.9	28.1	3.3	17.99

In the present case, the patient with VWD type 1 exhibited distinct generation of haematoma and pain after a road accident. The patient was treated with antibiotics due to chronic infection of the urinary tract. Treatment with antibiotics can lead to an impaired platelet function and therefore increase the bleeding risk in addition to that of VWD. For reasons of patient's allergy to proteins (Table 5) and intolerance of desmopressin and tranexamic acid, we decided to treat the patient with rFVII. Recombinant FVII was originally introduced in clinical practice for the prophylaxis and treatment of haemorrhage

in patients suffering from congenital or acquired haemophilia [2]. Later on, the agent had been approved for congenital FVII deficiency and Glanzmann's disease refractory to platelet transfusion. Recently, published case reports showed that administration of rFVIIa is safe and efficacious in patients with acquired and congenital VWD. No thromboembolic adverse effect has been reported except for fever (once). All cases reported an efficacy of rFVIIa in patients suffering from VWD [3,4] and our data could confirm to these. In the present case, treatment was successful and reliable in a patient with VWD, as no bleeding or thrombotic events occurred.

Mild VWD is not a licensed indication for rFVII, but as in other indications with severe bleeding tendency [5], the drug is effective in the prevention and treatment of bleeding complications. For VWD patients with allergic reactions and intolerance against VWF concentrate and/or desmopressin and tranexamic acid, rFVII might be an alternative due to the unique administration.

Disclosures

The authors declare no interests that might be perceived as posing a conflict or bias.

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