CASE REPORT

Haemophilia A in a major trauma patient

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SUMMARY

Haemophilia A is a coagulopathy with an absence or functional deficiency of coagulation factor VIII. The disease can be subdivided into a congenital form (incidence 1:10 000–1:20 000) and an acquired form (incidence 1:1 000 000). Both forms present an increased risk of bleeding even in low-impact trauma in severe cases of haemophilia A. The course of a man with haemorrhagic shock after a fall from a height of more than 3 m is described. After the secondary survey in the intensive care unit, several interventions (laparotomy, mass transfusion) were performed to stop the bleeding. A history of haemophilia was belatedly reported by relatives. The activity of factor VIII was determined, and substitution was initiated. No recurrent signs of bleeding occurred. The patient survived in good condition and presented for follow-up 3 years later with no disabilities.

BACKGROUND

Haemophilia A is a coagulopathy with an absence or functional deficiency of coagulation factor VIII. A subdivision of haemophilia A is the congenital form (incidence 1:10 000–1:20 000), which is associated with the recessive X chromosome.¹ In the acquired form of haemophilia A (incidence 1:1 000 000), antibodies interact with factor VIII and neutralise its function. This process can be triggered by malignant tumours, lymphoproliferative disorders, pregnancy or drug interactions (penicillin, ampicillin, trimethoprim/sulfamethoxazole, methyl dopa, clopidogrel, phenytoin and phenothiazine derivatives).²

Approximately 50% of haemophilia A cases are idiopathic.^{3 4} Haemophilia A is divided into a severe form with residual activity of factor VIII <1%, a moderate form with residual activity of factor VIII between 1% and 5%, and a minor form with residual activity of factor VIII between 5% and 25%. The minor form of haemophilia A is often diagnosed as an incidental finding. Haemophilia is suspected in cases of increased, inadequate or spontaneous bleeding after low-impact trauma, minor surgical procedures or tooth extractions. Factor VIII deficiency results in a prolonged blood coagulation time, measured as the activated partial thromboplastin time (aPTT). In the minor form of haemophilia, depending on laboratory measures, aPTT can be unaffected. The bleeding time and international normalised ratio (INR) are unaffected. The definitive diagnosis requires a separate determination of the factor VIII activity level.

The treatment of congenital haemophilia A consists of the administration of virus-inactivated and

genetically engineered clotting factor concentrates. The therapy in case of acquired haemophilia is different from the functional treatment of congenital haemophilia and consists of the administration of recombinant factor VIIa (rFVIIa), activated prothrombin concentrate, prednisolone and cyclophosphamide as an immunosuppressant or, in an emergency, plasmapheresis.^{2 3}

CASE PRESENTATION

A middle-aged man was admitted to the emergency department after a fall from more than 3 m.

INVESTIGATIONS

After a secondary survey in the intensive care unit, several interventions (laparotomy, mass transfusion) were performed to stop the bleeding. The history of haemophilia was belatedly reported by relatives.

TREATMENT

The minor form of haemophilia A with a moderate increased risk of bleeding after trauma explained the recurrent bleeding episodes (table 1). The activity of factor VIII was determined, and substitution was started.

The substitution was stopped on day 7 at a level of 107%; 24 h later, the patient started to bleed again, in the urinary bladder. Accumulating blood in the bladder eventually developed clots and led to bladder tamponade even though the bladder had been sutured after rupture on day 1 post-trauma. Factor VIII therapy was continued, and even though there was no invasive intervention after day 3, the substitution had to be continued for a total of 10 days.

OUTCOME AND FOLLOW-UP

Only after 10 days could the therapy be adjusted; neither severe, life-threatening bleeding nor recurrent signs of bleeding occurred. Factor VIII was administered before each of the following elective surgical procedures during the hospital course. The patient survived in good condition and presented for follow-up 3 years later with no disabilities.

DISCUSSION

Early recognition and identification of haemophilia followed by fast and accurate treatment is essential for survival. Unusual bleeding episodes, tendencies to develop haematomas, epistaxis or even muscle and joint bleeding after low-impact trauma in the family and the patient's history should be explicitly questioned. Prior to primary haemostasis, which is not impaired in haemophilia, excessive bleeding from the smallest cut or abrasions is not present.¹

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Table 1 Patient's course

Post-trauma day	Diagnosis and complications	Interventions	Laboratory findings	Transfusion requirements, factor VIII activity
Trauma day	ISS 66; pneumothorax, blunt abdominal trauma with contusion of the urinary bladder, unstable pelvic fracture type C, suspicion of dissection of internal iliac artery, upper and lower extremity fractures, laceration wound with acute foot compartment syndrome	Chest tube insertion, external and internal fracture fixation, fasciotomy of the foot	Hb: 10.6 g/dL INR: 1.1 aPTT: 34 s Tc: 183/nL	14 units PRBCs 8 units FFPs 4 g fibrinogen
1st	Haemorrhagic shock, urinary bladder bleeding (occult rupture), bleeding from iliac artery, relatives reported the history of haemophilia and brought the haemophilia patient's card	Coiling of the internal iliac artery, explorative laparotomy, suture of the urinary bladder, abdominal packing	Hb: 9.8 g/dL; INR: 1.3 aPTT: 49 s; Tc 33/nL Fibrinogen: 156 g/dL Factor VIII: 21% vWF: Ag 96% Risto Cof: 129	2 units PRBCs 3 units Tc 40 µg desmopressin 2000 IU of PCC 4000 IE of factor VIII Factor VIII after administration: 85%
2nd	Continuous severe haematuria, near-tamponade of urinary bladder with clots	PRBC transfusion and factor VIII administration	Hb: 8.3 g/dL; INR: 1.1 aPTT: 31 s; Tc: 91/nL Fibrinogen: 310 g/dL	4 units PRBCs Factor VIII: 77% 4000 IE of factor VIII
3rd	No bleeding signs	Re-laparotomy, de-packing, suprapubic vesical fistula performed intraoperatively	Hb: 8.3 g/dL; INR: 1.1 aPTT: 35 s; Tc: 94/nL Fibrinogen: 519 g/dL	Factor VIII: 93% 4000 IE of factor VIII
4th	Spontaneous haematoma in the area of thigh and scrotum		Hb: 9.1 g/dL; INR: 1.0 aPTT: 35 s; Tc: 102/nL Fibrinogen: 624 g/dL	Factor VIII: 89% 4000 IE of factor VIII
5th and 6th	No bleeding signs, decreased sedation, weaning from mechanical ventilation, spontaneous breathing		Hb: 9.3 g/dL; INR: 1.0; aPTT: 31 s; Tc: 121/nL Fibrinogen: 649 g/dL	Factor VIII: 77% 4000 IE of factor VIII per day
7th	Haematuria	Extubation Continuous lavage via transurethral catheter	Hb: 9.3 g/dL; INR: 1.0 aPTT: 30 s Tc: 146/nL	Factor VIII: 107% No administration
8th	Continuous severe haematuria. Tamponade of urinary bladder with clots	Continuous lavage via transurethral catheter	Hb: 9.9 g/dL; INR: 1.0 aPTT: 33 s; Tc: 172/nL	2 units PRBCs Factor VIII: 103% 6000 IE of factor VIII
9th & 10th	Clots were flushed out, less haematuria	Continuous lavage via transurethral catheter	Hb: 8.7 g/dL; INR: 1.0 aPTT: 29 s; Tc: 205/nL	2 units PRBCs

aPTT, activated partial thromboplastin time; FFP, fresh frozen plasma; Hb, haemoglobin; INR international normalised ratio of prothrombin time; ISS, injury severity score; IU, International Units; PCC, prothrombin complex concentrate; PRBC, packed red blood cells; Tc, platelets; vWF, Von Willebrand factor.

An important differential consideration is an accurate drug history, if available, from the patient's card (record), especially because of new oral anticoagulants. These drugs cannot be monitored by the usual laboratory tests. Autoimmune diseases, malignancies or pregnancies might indicate an acquired haemophilia.⁵

If a suspicion of haemophilia A is present, in the case of prolonged clotting time, as measured by aPTT with normal bleeding time and unaffected INR, the determination of the activity

levels of factor VIII and factor VIII inhibitor should be considered as quickly as possible. With any unclear bleeding, despite the transfusion and administration of coagulation factors (including factor XIII) according to current guidelines, a differential diagnosis of haemophilia should be considered.

In minor forms of haemophilia, the administration of desmopressin is required to limit the bleeding signs.^{1 6} Patients affected with the moderate form, who rarely have bleeding, are substituted (with spontaneous bleeding or prior to surgery) with

factor VIII. Patients with severe haemophilia and frequent bleeding events receive long-term prophylactic therapy with the administration of factor VIII three times per week.¹

At the beginning (during the first 10 days or more), a level of 100% of FVIII:C should be achieved. The administration of 1 IE/kg body weight results in a factor VIII:C increase of approximately 2%. The therapy should be continued in low doses as a maintenance therapy because the half-life of factor VIII is 12 h.¹ Laboratory monitoring of factor VIII and maintenance of a level of 100% should be continued in severe injury patients until all invasive procedures are completed.

Therefore, the substitution should be performed twice a day. Furthermore, this case report demonstrates that substitution in polytrauma patients and the maintenance of a level of 100% should be continued not only until all invasive procedures are

completed, but also in the absence of surgical intervention for approximately 10 days or more; otherwise, bleeding events may result. Even after the completion of therapy, the patient should be examined closely for bleeding signs.

As treatment for acquired haemophilia A, the administration of 90 µg/kg of rFVIIa is recommended every 2–3 h prior to achieving haemostasis, as well as a bolus administration of activated prothrombin complex between 50 and 100 IU/kg every 8–12 h up to a maximum of 200 IU/kg/day.⁶ Unfortunately, the monitoring of rFVIIa is not possible; the decision depends on the patient's condition. Well-balanced immunosuppressive therapy should also be considered.⁵ The duration and doses of immunosuppressive drugs are also dependent on the patient's course and post-traumatic inflammation.

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Learning points

- ▶ Early recognition and identification of haemophilia followed by fast and accurate treatment is essential for survival.
- ▶ Knowing the patient's history is important to complement the treatment.
- ▶ In the case of prolonged clotting time, as measured by activated partial thromboplastin time with normal bleeding time and unaffected international normalised ratio, the activity levels of factor VIII and factor VIII inhibitor should be determined as quickly as possible.
- ▶ In the case of any unclear bleeding, despite the transfusion and administration of coagulation factors (including factor XIII) according to current guidelines, a differential diagnosis of haemophilia should be considered.

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