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Recombinant human activated factor VII in postpartum hemorrhagic shock: the dark side

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Sir: A 38-year-old woman (gravida 2, para 3) was referred to our hospital because of intractable postpartum hemorrhagic shock. During this gemelli pregnancy she was admitted to the hospital three times for vaginal blood loss. Ultrasonography revealed a hematoma and a placenta close to the cervical ostium. Coagulation and platelets were normal. Because of fetal distress during spontaneous labor at 34 weeks an emergency

cesarean section was performed. Vaginal hemorrhage began after abdominal closure. Management consisted of uterotonic drugs, intravenous fluids, red blood cells, and fresh frozen plasma without effect. Supravaginal hysterectomy was deemed necessary. Because of pelvic oozing the abdomen was closed after packing of the pelvis. She was still in hemorrhagic shock. Recombinant human activated factor VIIa (rFVIIa; NovoSeven) was administered twice as a 7.2-mg intravenous bolus at an interval of 120 min, but bleeding continued from almost all orifices. The next day she was referred. Hemodynamic instability persisted, and multiorgan failure developed. Angiography of the pelvic arteries resulted in coiling of three small arteries, but hemostasis was not achieved. On the third day tranexamic acid was added and, after lack of effect, a 9-mg intravenous bolus of rFVIIa (90 µg/kg). Coagulation parameters improved and for several hours the hemoglobin level was stable, but she developed blistering of arms, fingers, and feet with slow

capillary refill. Toes, heel, and sole of the right foot became black and cold. On laparotomy packings and 9 l blood and cloths were removed. Afterwards there was no bleeding. The ischemia worsened in a few days and spread to the fore foot (Fig. 1) resulting in amputation of the lower extremity. Necrosis also developed on the dorsal side of the left fore arm. Other acra were cyanotic but did not become necrotic. Since delivery she had received 48 U red blood cells, 30 U fresh frozen plasma and 17 U five donors each of platelets. Multiorgan failure improved, and 19 days after admission the patient was discharged to the ward.

rFVIIa use has been reported for severe postpartum hemorrhage [1, 2]. Immediately after administration of the third dose of rFVIIa hemostasis was indeed reached. However, severe thromboembolic complications occurred. Although there seems to be a relationship in time between the onset of complications and moment of drug administration, it is hard to confirm this relationship. rFVIIa overdosing or sepsis may also play a role. However, there was no positive confirmation of infection.

The incidence of thrombotic complications in licensed use is 1–2%. Most thromboembolic events have followed off-label use of rFVIIa [3]. Off-label rFVIIa is used principally in desperate situations. However, to make a balanced choice, even then we need to have an impression of the complication rate. Safety and efficacy in off-label use must be studied [4]. Pregnant and postpartum women should receive special attention in these studies because of their particular coagulation condition.



Fig. 1 Right foot of the patient

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