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**Peri-interventional control of hemostasis in a patient
with combined coagulation factor V- and factor
VIII-deficiency and anaphylaxis to fresh frozen plasma –
a rare indication for recombinant factor VIIa**

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Peri-interventional control of hemostasis in a patient with combined coagulation factor V- and factor VIII-deficiency and anaphylaxis to fresh frozen plasma – a rare indication for recombinant factor VIIa

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4 **Letter to the Editor:**
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8 **Peri-interventional control of hemostasis in a patient with combined**
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10 **coagulation factor V- and factor VIII-deficiency and anaphylaxis to**
11 **fresh frozen plasma – a rare indication for recombinant factor VIIa**
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30 Running head: Recombinant FVIIa in a patient with F5F8D
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33 Keywords: factor V deficiency, factor VIII deficiency, recombinant activated factor VII,
34 fresh frozen plasma, allergy, surgery
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6 Combined deficiency of coagulation factors V (FV) and VIII (FVIII) (F5F8D) is a rare,
7
8 autosomal-recessive disease [1]. FV and FVIII antigen and activity levels are usually
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10 between 5 and 30% of normal. Underlying molecular mechanisms include mutations in
11
12 two genes, *LMAN1* and *MCFD2*, both of which encode proteins facilitating the
13
14 transport of FV and FVIII from the endoplasmatic reticulum to the Golgi apparatus.
15
16 Bleeding symptoms are usually mild, but severe bleeding complications can occur after
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18 trauma or surgery. Targeted replacement is not achievable since a FV concentrate is not
19
20 available. Reports on the clinical management of F5F8D patients are rare. However,
21
22 FVIII concentrates and fresh frozen plasma (FFP) are the therapeutic cornerstones
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24 perioperatively or in case of bleeding.
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32 We report on a 64 year-old male patient with F5F8D. His history included peritoneal
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34 hemorrhage, multiple episodes of multilocular hemarthrosis, macrohematuria,
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36 intramuscular hematomas and recurrent epistaxis. Management of bleeding episodes
37
38 was based on substitution of FFP and FVIII. From 2004 on, the patient was on long-
39
40 term treatment with FVIII and FFP for recurrent bleeding from anal fissures. During
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42 that time, signs of unspecific, cutaneous allergic reactions following administration of
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44 FFP emerged. In 2005, following surgery of the loosened socket of a right-sided total
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46 hip arthroplasty, the patient experienced nausea, hypertension and eventually
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48 anaphylactic shock in response to FFP despite pretreatment with antihistaminics and
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50 corticosteroids, so that FFP treatment had to be discontinued.
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58 Two months later, the patient was readmitted for orthopedic surgery of his left ankle
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60 (packing of a hemarthrotic subtalar joint cyst with bone allograft, followed by
arthrodesis). As FFP was regarded contraindicated because of recent anaphylaxis, it was

1
2
3 replaced by recombinant activated factor VII (rFVIIa; NovoSeven®; NovoNordisk,
4 Denmark) while administration of FVIII was retained. Preoperatively, the patient
5
6 received 4000 IU FVIII (Helixate Nexgen®, CSL Behring, Austria) and 90 µg/kg
7
8 rFVIIa followed by 60 µg/kg rFVIIa every 6 hours and 2000 IU Helixate® twice daily.
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11 rFVIIa was stopped on day 5, while FVIII was given until day 12. Pharmacological
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13 thromboprophylaxis was not given. The postoperative course was uneventful and
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In 2007, the perioperative regimen described above was applied again for surgical repair of the right-sided total hip arthroplasty and removal of osteosynthesis material from his right ankle joint, and few months later for non-surgical repositioning of his dislocated right hip after trauma. Clinically relevant bleeding or thromboembolism did not occur at any time.

Data on allergic reactions in response to FFP are scarce, the overall incidence being described to be as high as 3% [2]. Life-threatening events however are very rare.

According to The Serious Hazards of Transfusion (SHOT) scheme, 306.444 units of FFP were issued during 2007, but only 20 cases of FFP-related acute transfusion-reactions were reported, 5 of which were severe and 7 anaphylactic [3]. Acute transfusion reactions are defined as those occurring up to 24 hours excluding reactions due to incorrect components being transfused, haemolytic reactions, transfusion related acute lung injury or bacterial contamination. Urticaria are considered benign reactions and impose only a relative contraindication against repeated application. In rare cases, urticarial reactions may aggravate over the course of repeated transfusions and hence be the first sign of more serious transfusion reactions.

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3 Since FFP is the only source of FV, alternative means to control hemostasis are limited
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5 in patients with FV deficiency. Our therapeutic approach was based on evidence
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7 suggesting that rFVIIa is effective and safe in patients with FV deficiency [4] or
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9 hemophilia A with an inhibitor [5]. rFVIIa in supraphysiological doses directly activates
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11 factor X and prothrombin on the surface of activated platelets, bypasses the action of the
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13 deficient factors thereby improving impaired hemostasis. This is the first report to show
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15 that rFVIIa in addition to FVIII substitution is effective to prevent bleeding in the
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17 periinterventional management of patients with F5F8D.
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