

Disordini emorragici acquisiti: aspetti diagnostici e clinici

VARIABLE CLINICAL RESPONSE TO RECOMBINANT PORCINE FVIII IN ACQUIRED HAEMOPHILIA A: A TWO CASE EXPERIENCE WITH LABORATORY SUPPORTED MONITORING

A.M. Pizzini[1], M. Bovara[2], M. Sebastiani[2], A. Fusco[1], C. Fantoni[1], M. Silingardi[1], R. Mancini[2], A. Coppola[3]

[1]Ambulatorio Emostasi & Trombosi, Dipartimento Medico - Ospedale Maggiore Bologna, Italy; [2]Laboratorio Unico Metropolitano - Ospedale Maggiore Bologna, Italy; [3]SDD Centro Hub Emofilia e MEC, Azienda Ospedaliero-Universitaria di Parma, Italy

Background. Recombinant porcine factor VIII (rpFVIII, Susoctocog α – Obizur®) is used to treat bleeding in patients with Acquired Haemophilia A (AHA). rpFVIII may represent a valid alternative for bleeding control, especially in case of bypassing agents (BPAs) failure. Disadvantages to BPAs include the inability to monitor response with standard laboratory assays, inconsistent haemostatic efficacy and increased thrombotic risk. Susoctocog α allows laboratory monitoring of FVIII activity with calibrated one-stage assays, which may reduce thrombotic risk. However, the response is variable and depends not only on the inhibitor titre (human or porcine), but also on poorly defined pharmacokinetic variables.

Materials and Methods. We collected two cases treated with rpFVIII in June 2025 and January 2026. In the first case, rpFVIII was used for bleeding control in a patient with coronary artery disease and AHA (FVIII 0%, Inhibitor 4.07 BU/mL) who developed severe thrombocytopenia during sepsis (platelets 20 000/mmc). In the second case, rpFVIII was used after BPAs failure to stop femoral arterial bleeding following removal of the embolization introducer in a recently diagnosed AHA patient (FVIII 0.8%, Inhibitor 27.98 BU/mL). Clinical and laboratory findings are summarized in the *Table*. FVIII activity was measured using three assays: one-stage FVIII:C with Actin® (Siemens) calibrated with human plasma; chromogenic FVIII assay (Siemens) calibrated with human plasma; and the reference method for rpFVIII, a one-stage FVIII assay with Actin® FS (Siemens) calibrated with a dedicated Obizur® curve. The anti-porcine FVIII inhibitor was quantified using a mixing Bethesda assay adapted for rpFVIII: patient plasma was heat-inactivated at 56 °C for 45 minutes, mixed 1:1 with Obizur-spiked normal plasma, incubated for 2 hours at 37 °C, and residual FVIII activity measured using the Actin® FS Obizur-calibrated assay.

Results. Bleeding control was achieved in both cases and no adverse events related to rpFVIII were observed. The initial bolus of Susoctocog α was 100 U/kg in both cases with a variable response. In the first case the response was less long-lasting and additional doses were required in the first 24 hours to maintain FVIII >50% (another 100 U/kg in boluses 50–30–20 U/kg). In the second case the response was more prolonged (over 24 hours), without further doses to maintain FVIII >50% and bleeding stop. This difference may be partially explained by the increase in human inhibitor titre (15 BU/mL) during sepsis in the first patient. However, since neither patient developed rpFVIII inhibitors, other factors may underlie these differences (age? pharmacokinetic variables?). The calibrated one-stage FVIII assay (Actin® FS with Obizur calibration) correlated with FVIII:C measured using Actin®, while the chromogenic assay underestimated rpFVIII recovery.

Conclusions. Susoctocog α proved effective and safe in AHA, also at lower than recommended dosage. However, rpFVIII pharmacokinetics can be highly variable and require active laboratory monitoring. Plasma FVIII:C provides an alternative estimation of rpFVIII recovery. A larger case collection could help clarify the heterogeneous response and the factors influencing it (age? rpFVIII inhibitors? pharmacokinetic variables?).

	Case 1				Case 2		
Sex	Female				Female		
Age (Years)	62				76		
Weight (Kg)/Height (cm) Body Mass Index (BMI)	48 Kg/152 cm BMI 20.77				78 Kg/160 cm BMI 30.46		
Cause of AHA	Rheumatoid Arthritis				Autoimmune Thrombocytopenia		
Co-morbidities	Chronic ischemic heart disease, Hypertension and type 2 diabetes mellitus; chronic renal disease (II)				Hypertension, type 2 diabetes mellitus, dyslipidemia; chronic renal disease (III); autoimmune thyroiditis		
Antiplatelet/Anticoagulant	YES				NO		
at diagnosis	Aspirina 100 mg and Ticagrelor 90 mg bis in die						
Bleeding site	Extensive hematoma of the right lower limb complicated by necrotizing fasciitis				Retroperitoneal haematoma and right inguinal haematoma after embolization		
Surgery during AHA	Limb amputation				Inguinal haematoma evacuation		
VIII at diagnosis (%)	0%				0.8%		
Inhibitor Titer (BU/ml)	4.07				27.98		
Therapy before rpFVIII	aPCC/Tranexamic Acid				aPCC/Tranexamic Acid		
Loading dose rpFVIII (UI/kg)	100 U/Kg				100 U/Kg		
Laboratory data	after 1 hour	after 12 hours	after 24 hours	after 48 hours	after 1 hour	after 24 hours	after 72 hours
FVIII chromogenic (%)	85%	21%	32%	4.3%	113%	24%	0.8%
FVIII: C (%)	164%	48%	56%	8.8%	198%	51%	3%
FVIII Obizur® (%)	126%	36%	51%	9%	189%	44%	4.2%
		+ 100 U/Kg in fractionated boluses (50-30-20 U/Kg)				No additional boluses	
Subsequent doses rpFVIII (UI/Kg)	100 U/Kg in fractionated boluses (50-30-20 U/Kg) in 36 hours for platelets 20 000/mmc				Another bolus 12 days later (100 U/Kg) for rectal bleeding and anemia		
Infusion doses frequency	3				1 dose repeated		
Duration rpFVIII treatment (days)	3 consecutive days				1 days + 1 days		
Immunosoppressive therapy	Corticosteroids/Rituximab				Corticosteroids/Cyclophosphamid		
Transfusion (bags)	3 U				8 U		
Inhibitor rpFVIII (BU/ml)	None				None		
Outcome	Limb amputation				Death from pulmonary sepsis and Candidemia		
VIII Inhibitor Eradication	Yes (66 days from diagnosis)				Yes (42 days from diagnosis)		
Follow up duration	Ongoing (10 months)				70 days		
Therapy	Prednisone 5 mg die				-		

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