Plasma-exchange and immunosuppressive therapy in a patient with mild haemophilia A and inhibitors complicated by severe muscular bleeding and compartment syndrome

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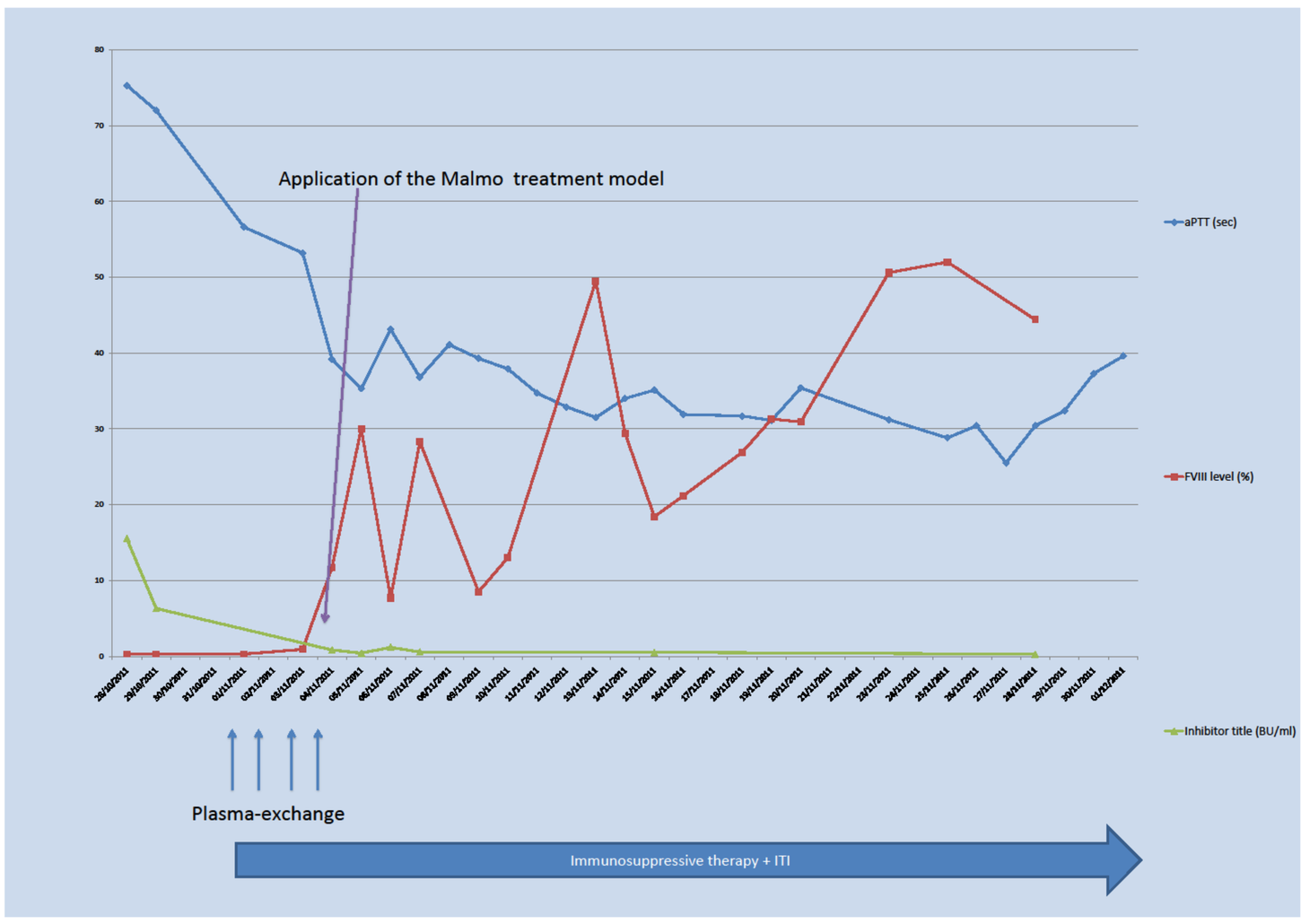
Background: The control of bleeding in haemophilic subjects with inhibitors and haemorrhagic shock is still a therapeutic problem to resolve in emergency. We describe the case of a young mild haemophilia A (MHA) patient, who developed high titer inhibitors after infusion of rFVIII because of traumatic spleen rupture and a life-threatening lower limb hemorrhage despite the use of bypassing agent.

CLINICAL HISTORY: A 19 years old man with MHA (FVIII 18 U/dL, gene mutation Val2251Ala), never infused with FVIII concentrates, on 10/02/2011, after a car crash, showed a spleen traumatic rupture requiring surgery in emergency. Full haemostasis has been achieved with B-domain deleted rFVIII infusions during the surgery and the consecutive 7 days (total dose 18.000U). On 10/09 he has been vaccinated for Streptococcus Pneumoniae, Haemophilus Influenzae and Neisseria Meningitidis.

COMPLICATIONS: Since 10/25 the patient presented progressive prolongation of aPTT not corrected by full-length rFVIII infusion. Inhibitors against F VIII were detected (titer 15 BU/ml). On 10/29 he presented a large haematoma in the lower right limb and anemia.

CLINICAL COURSE AND THERAPIES:
rFVIIa 90 mcg/kg administered every 3 hrs was ineffective to stop bleeding. On 11/01 hemoglobin dramatically fell to 6 g/dl, associated with compartment syndrome requiring fasciotomy complicated by persistent bleeding and haemorrhagic shock. 24 hrs after the patient started treatment with plasma exchange that was effective to clear the inhibitor; then we applied the Malmo treatment model (modified). The bleeding stopped within few days and detectable FVIII to haemostatic levels was observed. He was discharged on 12/03 on ITI schedule with 100 U/Kg/day of PD FVIII. No recurrences of bleeding neither neurovascular damage on his lower right limb occurred. The patient stopped ITI on June 2012, with full recovery of FVIII infused.



Conclusion. The patient presented risk factors for appearance of F VIII inhibitors such as intensive treatment with B-domain deleted rFVIII, splenectomy followed by vaccination. rFVIIa was ineffective to stop life-threatening haemorrhages; plasma exchange, followed by immunosuppression and ITI, was able to reduce inhibitor titer and to stop the severe bleeding, saving the life and the lower limb functions of this young patient.

The Malmo treatment model applied to our patient (40 Kg bw)		
Plasma exchange (four courses)		
Neutralization and replacement with factor concentrates (Emoclot- Kedrion 5000 U every eight hours)		
Cyclophosphamide **Methylprednisolone**	500 mg intravenously for two days 80 mg daily for five days	Then orally 80 mg for two days Then 40 mg daily
Intravenous gammaglobulin	40g intravenously for the first two days 16 g for other two days	

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