USE OF HIGH DOSES FVIII/ VON WILLEBRAND FACTOR CONCENTRATE IN A PATIENT WITH TYPE III VON WILLEBRAND DISEASE AND HIGH TITER INHIBITOR .

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Introduction:

Patients with type III Von Willebrand disease (VWD) can develop alloantibodies to Von Willebrand factor in about 8-14%, especially in carriers of null mutations , which may lead to complex-mediated, life-threatening anaphylactic reaction, as a consequence of replacement therapy. Concentrates containing VWF are generally contraindicated at first. There are only a few reported cases with different options of management but no considering concentrates containing VWF. We report the case of a patient with type 3 VWD and anti-VWF alloantibodies who has been managed with high doses FVIII/ VWF concentrate(Haemate P; CLS Behring).

Clinical case:

A 21-year-old male patient with type III vWD (FVIII 2%, vWFAg 2% %,vWF:RCo 1%), developed alloantibodies against vWF for the first time about 1 year ago. The causative mutation is located in exon 28 of VWF gene and gives rise to a TAG stop codon in the codon 1311, which normally encodes glutamine. Therefore, due to the mutation Q1311X (3931C> T), the two alleles of the patient generated a truncated protein in the A1 domain of VWF *(figure 1*). The patient has gipsy ethnian origin, lives with bad social conditions, comes to hospital from time to time since childhood and usually produces a lot of problems with health assistance personal. He was admitted to Emergency Department with a spontaneous muscle haematoma of the left thigh , being imminent a compartment syndrome despite his usual dosage.(Four months ago he had needed therapy during 15 days for an elbow haemarthrosis after a police raid).The initial titer of inhibitor (modified Bethesda assay , VWFAg and VWF : RCo measurement by inmunoturbidimetric assay, IL) was 17 BU/ml. We decided to continue treating with the same concentrate but with closer infusion of FVIII/vWF concentrate, 2000 UI/4h, as he had not developed any anaphylactic reaction ,and because his family´s fear to accept any change in treatment and not evident clinical worsening. He had good clinical response and levels of FVIII 68%,VWFAg 50%, VWF: RCo not detected, after 2 days with this scheme. On the 5th day , having into account the good clinical response and maintained FVIII 77% VWFAg 52%, VWF RCo 18% , we decided to reduce doses progressively to 3000 UI/6h, 4000UI/8h in a week, 5000 UI/12h another week and then little by little to 4000UI/12h, 4000UI/24h until completed a month. He also received local ultrasound treatment. The titer of inhibitor increased until peak of 168 BU/ml after a month without spontaneous bleeding, then in a month to 225 BU and decreased to 79 UB/ml after 5 months and to 7 BU in 7 months. He has been treated after this episode and the inhibitor detection with isolated doses of 4000 UI FVIII/VWF concentrate for minor bleedings and without any inmune reaction and maintaining good hemostatic response.

Graphics:

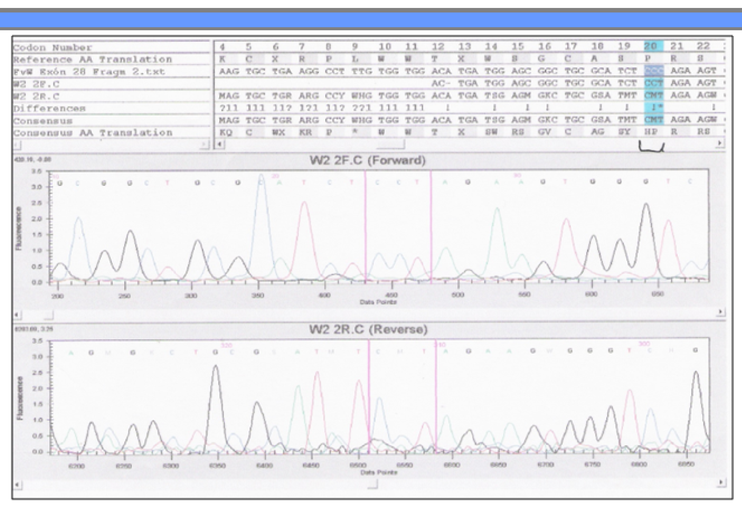
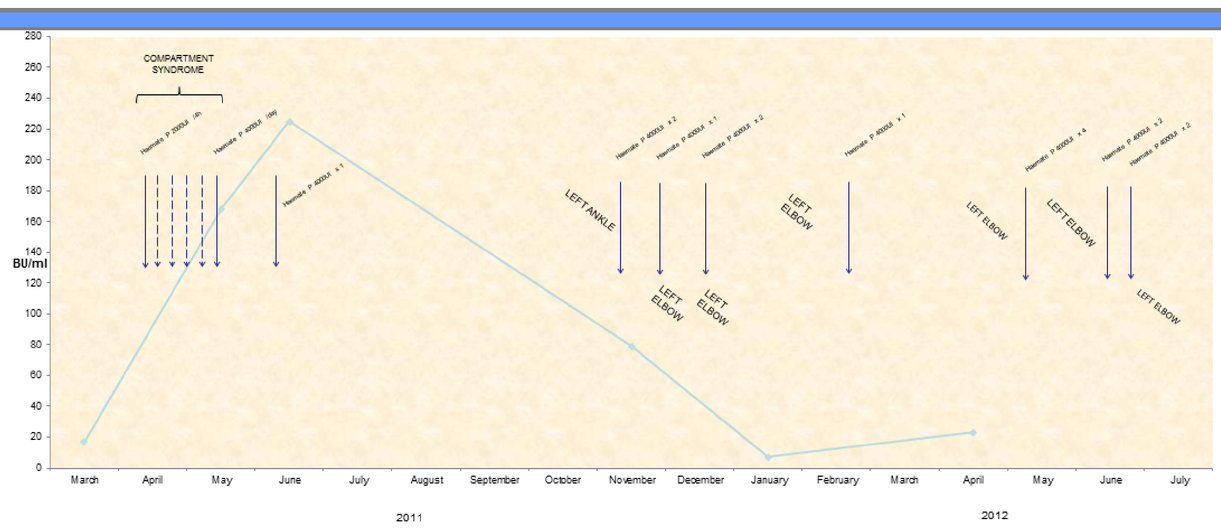


Figure 1



Conclusions:

Therapy with FVIII/VWF concentrate was clinically effective in our patient without any immune reaction and with high level of inhibitor. This is not usually described in these cases. The consequent rise inhibitor did not carry more bleedings. The inhibitor decreased in accordance with the lack of treatment. We suppose the inhibitor could really develop months ago in our patient as inadequate clinical response developed then but we did not think of it due to the usual bad patient`s behaviour. We think there must be different types of antibodies to VWF, possibly someones with more complex kinetics as in hemophilic patients with type 2 inhibirtors and perhaps with spontaneous eradication of inhibitor . Likely in relation with the type of causative mutation. These patients represent a real challenge regarding the management of hemorrhagic events. More studies are necessary to clarify this important question.

References:

Haemophilia 2002;8.607-21.Haemophilia 2008,14,645-6. Haemostasis 1996;26(suppl1):150-154.Thromb Haemost 2000 ;83:633-4.

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