RECOMBINANT HUMAN FACTOR VIII (rhFVIII) TREATMENT FOR SEVERE GINGIVAL HEMORRHAGE AND DENTAL SURGERY IN A DOG WITH HEMOPHILIA A

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Background

Hemophilia A (HA), a genetic coagulation factor VIII deficiency, commonly causes spontaneous bleeding. Recombinant human factor VIII (rhFVIII) is administered to treat bleeding in HA human patients, but was not reported in hemophilic dogs.

Case presentation

A 7-year old intact male poodle dog was admitted with marked oral hemorrhage of 4-days duration. HA was diagnosed 3 years before (5% factor VIII activity), and the dog was previously hospitalized several times due to significant bleeding episodes and was treated with pRBC and FFP. Two months prior, loose molar and pre-molar teeth were extracted due to severe ongoing gingival hemorrhage and dental disease, and major intra- and post-operative hemorrhage occurred despite pre-operative cryoprecipitate, tranexamic acid (TXA) and desmopressin treatment, requiring 4 FFP units and 1 packed RBC unit post-op.

Physical examination showed pale mucous membranes, marked gingival hemorrhage, tachycardia and a left apical systolic murmur. PCV was 21% (reference interval 37-55%). Oral examination under anesthesia revealed bilateral oronasal fistulas in both maxillary teeth. Due to ongoing bleeding, dental extractions were planned.

Treatment: immediately prior to induction, an IV bolus of **rhFVIII** (Advate®, 1000 IU, Baxter AG, Austria, 5 mg/kg, Figure 4) was administered, followed by a 20-hour IV constant rate infusion (CRI; at 4 mg/kg/hour). TXA was administered upon induction (30 mg/kg slow IV, followed by 3-hour CRI at 30 mg/kg/hour). During the procedure 5 teeth were extracted (2 canine, 2 premolar, 1 incisor), 1 unit of matched pRBC was administered, and absorbable gelatin foam was locally placed.

Thromboelastometry (TEM), performed prior to treatment, revealed intrinsic-pathway hypocoagulability (Figure 1a), typical of HA, with compensatory extrinsic hypercoagulability (Figure 1b), which improved upon repeated TEM, 4 and 12 hours post commencing rhFVIII therapy (Figures 1c-f and Figure 2). Citrated plasma samples from the dog and 2 control dogs taken before, during and after treatment were sent to a human laboratory for quantification of factor VIII activity; however, failed to document a measurable increase (Figure 3).

The dog recovered uneventfully, with no evidence of bleeding, and was discharged 36 hours post initial therapy with rhFVIII

New or Unique information:

This first report of successful treatment with **human-recombinant factor VIII** for **Hemophilia A** induced clinical bleeding supports this therapy in hemophilic dogs.

Figure 1: intrinsic and Extrinsic Thromboelastometry curves prior to and during treatment with rhFVIII

Figure 1a Intrinsic, pre rhFVIII treatment

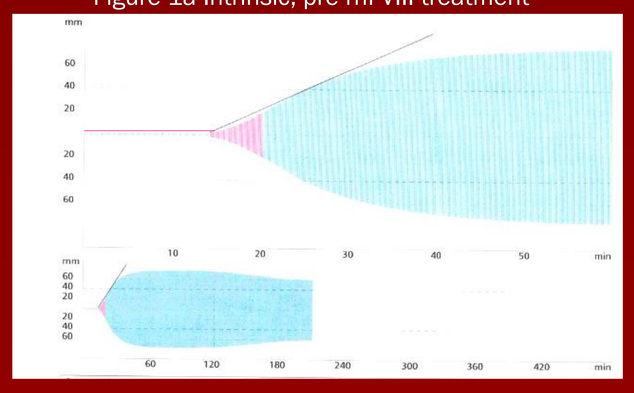

Figure 1b: Extrinsic, pre rhFVIII treatment

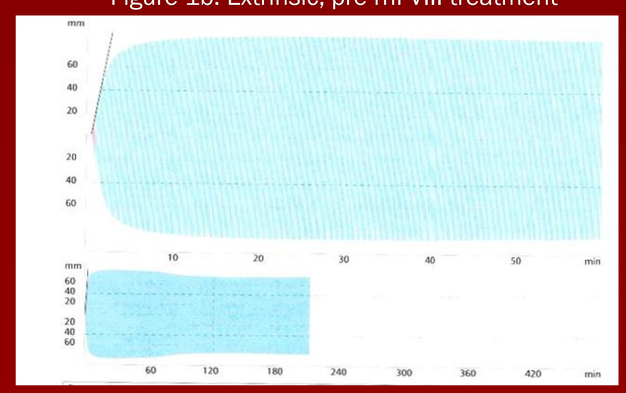

Figure 1c: Intrinsic, 4hr rhFVIII treatment

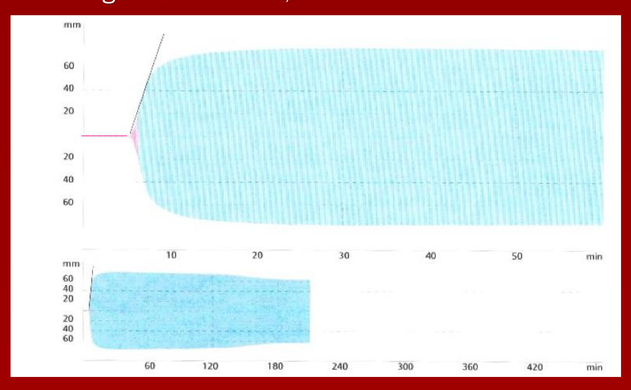

Figure 1d: Extrinsic, 4hr rhFVIII treatment

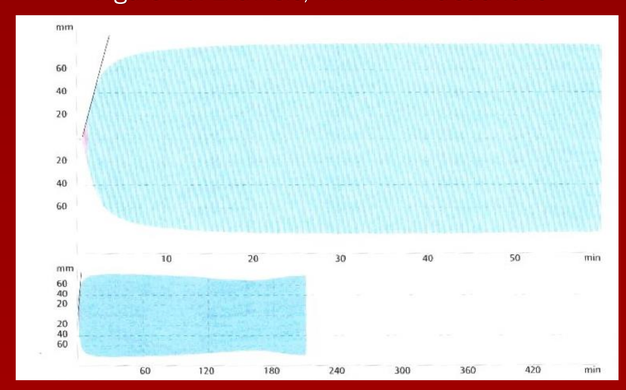

Figure 1d: Intrinsic, end of rhFVIII infusion

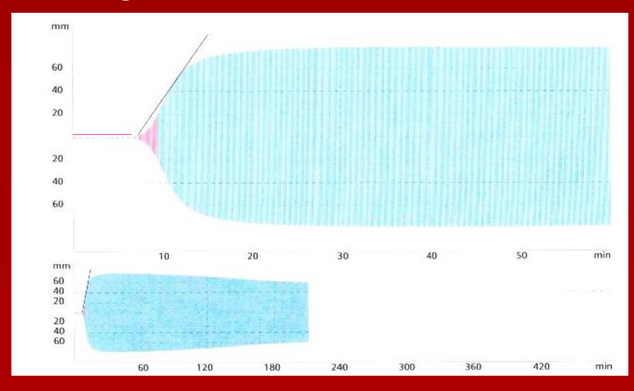

Figure 1f: Extrinsic, end of rhFVIII infusion

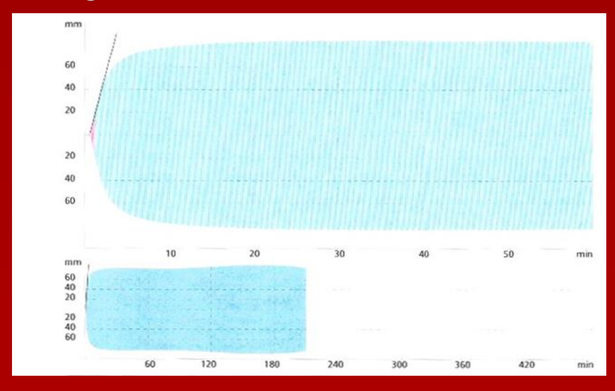

Figure 2: Selected intrinsic-thromboelstometry parameters prior to and during treatment with rhFVIII

InTEM parameter (units)	Ref interval	Pre TX	4 hrs	12 hrs
Clot time (sec)	100 – 240	860	323	438
Clot formation time(sec)	30 – 110	363	59	138
Alpha (°)	70 – 83	41	80	70
A10 (mm)	44 – 66	37	75	73
A20 (mm)	50 – 71	63	78	78
Maximal clot firmness (mm)	50 – 72	78	78	79
Maximal clot firmness-time (mm)	1726 – 2822	3610	1345	1617
Maximum velocity (sec)	4.4 – 25	5	32	17
Maximum velocity-time (sec)	112 – 255	1345	379	622

Figure 3: % activity of factor VIII before, during and after treatment with rhFVIII

	Factor VIII%	Factor VIII corrected %*
Control1	200	133
Control2	99	67
Pre-treatment	5	3.3
Post Bolus factor VIII, start CRI	5	3.3
During CRI (~6 hours)	4.1	2.7
4 hours post CRI	3.5	2.3

*% factor VIII considering average controls = 100%

Figure 4

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