BRIEF COMMUNICATION

Factor VIII Deficiency in a Cat

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Classical hemophilia is an inherited bleeding disorder characterized by a deficiency of Factor VIII (FVIII), a major procoagulant protein of the blood. Factor VIII circulates noncovalently bound to von Willebrand factor (vWF), a large multimeric protein required for normal platelet interaction (adhesion) at sites of vessel damage. The plasma FVIII/ vWF complex plays a critical role in both primary hemostasis (the initial platelet/vascular response) and secondary hemostasis (the reinforcement of the primary plug with fibrin). Hemophiliacs tend to have normal platelet responses but bleed excessively because of poor fibrin generation and inadequate stabilization of the hemostatic seal (1, 2).

Factor VIII deficiency is the most common inherited coagulation factor deficiency seen in dogs. The clinical severity varies with the size of the animal and the degree of FVIII deficiency (3, 4). Large breeds and/or dogs with severe FVIII deficiencies (plasma levels $<1\%$ of normal) are usually presented with a severe spontaneous hemorrhagic diathesis. Factor VIII deficiency has also been reported in horses and Hereford cattle, in both of which it is a severe clinical disease (5, 6). Only a few cases of classical hemophilia have previously been described in cats (3, 7). The purpose of this report is to describe a case of feline FVIII deficiency and to illustrate the insidious nature of the disease in this species.

A male domestic short-haired cat had first been seen by a veterinarian (JCM) at five months of age at which time it had been examined and vaccinated. One week following this initial examination, the cat was reexamined because of a complaint that the cat had not used its right hind leg since it had been given the intramuscular injection. Although the cat would not bear weight on the leg, there was no evidence of swelling, or pain on manipulation. Radiographic examination of the pelvis and hindlimb revealed no abnormalities which might account for the lameness. Suspecting a vaccination reaction, the attending veterinarian advised keeping the cat indoors, and monitoring by the owner. Only after a further two weeks was the cat reported to have started to use his leg again. Over the next two months the owner reported that the cat experienced short periods of shifting lameness apparently involving both hind legs.

When presented for neutering and declawing at eight months of age, the cat appeared clinically normal. Surgery was uneventful. The spermatic cords were ligated with absorbable sutures and the forepaws sutured with nonabsorbable sutures and bandaged. The cat bled profusely from both feet and the scrotum in the initial postoperative period. By 8 h postsurgery, the bandages had been changed several times and the cat was pale and very weak. At this time, the scrotal incision was sutured, the feet rebandaged, and a transfusion of 20 mL of fresh feline blood administered. The hematocrit after transfusion was 0.25 L/L.

The next day the cat was bright and alert, however both foot bandages were blood-soaked. When the the bandages were changed, both feet began to bleed freely. Over the next eight days, the cat continued to bleed periodically from its feet, particularly when the bandages were changed.

On the ninth day postsurgery, the cat was referred to the Ontario Veterinary College for evaluation of the apparent hemostatic defect. On presentation the cat was bright and alert, although reluctant to walk. Both foot bandages were blood-soaked.

A citrated blood sample was collected using a jugular venipuncture. Activated partial thromboplastin time (PTT), prothrombin time (PT), and thrombin clotting time (TCT) tests were performed. These screening tests were normal, with the exception of the PTT which was prolonged by 3.5 times (Table I).

Specific factor assays revealed normal levels of plasma Factor IX (FIX) and Factor XI (FXI), but a severe deficiency of FVIII ($<1\%$ of normal). Plasma vWF antigen (vWF:Ag) was elevated at 294% of normal. Plasma from the cat supported ristocetin-induced aggregation of fixed washed human platelets to a greater degree than did normal feline control plasma. Quantitation of plasma ristocetin cofactor activity (an index of the functional activity of vWF), indicated that the plasma level was elevated (Table I).

On the basis of history, clinical signs, and laboratory data a diagnosis of classical hemophilia was made. Euthanasia of the cat was elected. An attempt to identify the parents of the cat was only partially successful with the location of the queen. The owner of the queen indicated that her cat had had three previous litters and that a number of the kittens had "bled to death". A recommendation was made that the dam be tested and/or be neutered as soon as possible.

The few reports of FVIII deficiency in cats to date, suggest that the disease in this species is commonly a clinically mild spontaneous bleeding diathesis which is exacerbated by surgery or physical trauma. Like the cat in question, most of the other cases have been diagnosed as a result of the investigation of the cause of severe postoperative hemorrhage (7).

Classical hemophilia is a sex-linked recessive trait so it is usually the hemizygous male who is clinically affected. Heterozygous females are usually asymptomatic carriers of the hemophilia defect. Female hemophiliacs (homozygotes) can occur with certain matings; most likely, a het-

TABLE I
Hemostatic Test Results for a Cat with Factor VIII Deficiency

	Patient	Normal Reference Plasma[a]
Partial thromboplastin time (s)	62.9	18.3
Prothrombin time (s)	22.4	21.7
Thrombin clotting time (s)	7.4	6.7
Factor VIII coagulant activity (%)[b]	<1	100
Von Willebrand factor antigen (%)	294	100
Ristocetin cofactor activity (%)	272	100
Factor IX (%)	95	100
Factor XI (%)	102	100

[a]Plasma pooled from three clinically normal cats.
[b]Percentage of the activity of the reference plasma.

erozygous female:hemizygous male breeding. This mating arrangement is unlikely to occur in larger animals with FVIII deficiency because affected males usually show signs of a bleeding disorder and are diagnosed before they reach breeding age. In smaller animals (small breeds of dogs, and cats), or where the FVIII deficiency is less severe, the possibility of the hemizygous male reaching sexual maturity undiagnosed is much greater and thus the chance of the affected male:carrier female mating is also greater (4). The cat in this report could easily have sired kittens if he had not undergone elective surgery and been recognized as a "bleeder'. Although hemophilia is usually expressed clinically in the male, female feline hemophiliacs must be anticipated.

The clinical expression of classical hemophilia ranges from mild to severe depending primarily on the size of the animal and the degree of FVIII deficiency. Dogs with plasma FVIII levels of 10-20% of normal do not show the same tendency towards spontaneous bleeding (particularly joint bleeding) as do similar sized dogs with FVIII levels of <1% of normal, but do bleed if stressed by injury or surgery (3, 4). Small sized animals are less prone to spontaneous bleeding probably because there is less stress on weight-bearing surfaces to predispose to bleeding. Excessive bleeding associated with tissue trauma is a typical form of expression of FVIII deficiency. This cat had no history suggestive of spontaneous bleeding. It is possible that the major episode of lameness in the cat was associated with vaccination-induced injury. Intramuscular injections are potentially dangerous in animals with severe bleeding diatheses because of the risk of intramuscular bleeding and hematoma formation. Vaccination with a live-virus vaccine commonly produces quantitative and/or qualitative platelet abnormalities two to seven days postvaccination. In the healthy animal, the degree of platelet depression rarely produces detectable signs, however, in the animal with compromised hemostasis, the additive effect of the vaccine may be sufficient to trigger excessive bleeding (5). The lameness in this cat may have been due to the development of a hematoma subsequent to the intramuscular administration of the vaccine. Unfortunately, a postmortem examination was not performed.

The normal PT and TCT but prolonged PTT suggested an abnormality of the intrinsic pathway particularly involving FXII, FXI, FIX and/or FVIII (1). Factor XII was considered unlikely as FXII deficiency is usually not associated with a hemorrhagic diathesis (8, 9). Factor XI and FIX deficiencies are associated with an increased bleeding tendency but were ruled out on the basis of normal plasma levels of these clotting factors. Two diseases may be associated with FVIII deficiency, classical hemophilia and von Willebrand's disease (vWD). In classical hemophilia, plasma FVIII activity is reduced while vWF is normal or increased. Von Willebrand's disease is characterized by a deficiency of vWF with normal or subnormal FVIII activity. The elevated vWF-antigen (quantitative measurement of the vWF protein) and ristocetin cofactor (functional activity of the vWF protein) ruled out vWD in this cat (2, 4).

Hemophilia must be considered in any cat (particularly males) with signs of protracted bleeding associated with surgery or physical injury. Although whole blood is frequently administered because of the emergency situation, fresh plasma is a superior therapy as it provides more FVIII per unit volume and avoids the possibility of red cell sensitization. Although euthanasia was elected in this case, cats with hemophilia may live a reasonably normal life requiring only periodic therapy. Affected animals should be neutered however to prevent dissemination of the genetic abnormality.

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