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Hemophilia B (factor IX deficiency) in a Labrador retriever dog

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Abstract

A 3-month-old intact male, Labrador retriever was presented with the history of coagulopathy and anemia. The results of initial screening tests of the hemostatic system yielded a tentative diagnosis of hemophilia. Activated partial thromboplastin time (APTT) was distinctly prolonged (106 seconds) and prothrombin time (PT) was not detected due to markedly prolonged test time. Whole blood transfusions (20 me l/kg body weight) were carried out prior to assays of coagulation factor. After transfusion, the patient recovered well and hemorrhage ceased. Blood samples were assessed for coagulation factor activity. The patient showed markedly low factor IX coagulation activity (5%, reference range: 7～140%) and was diagnosed with hemophilia B. After recovery, the patient was discharged from the hospital. However, 4 months later the patient was re-hospitalized for recurrence of the initial symptoms. The owner did not want to pursue further treatment and the patient died of respiratory distress two days later.

Key words : Hemophilia B, Factor IX, Coagulopathy, Dog

INTRODUCTION

Hemophilia is a group of hereditary genetic disorders with sex-linked recessive inheritance that causes severe bleeding disease in males. It causes hemostatic disorders resulting from abnormal blood clotting or coagulation. Aberration or functional deficiency of coagulation factor IX causes hemophilia B (Biggs et al, 1952). In veterinary medicine, hemophilia B is rare in comparison with hemophilia A. Clinical signs of hemophilia B are related to the degree of factor IX deficiency and are severe when factor IX coagulation activity is less than 1%, but may be less severe if the activity value is between 1% and 25% (Brooks, 1999). Symptoms include subcutaneous hematomas, hemarthrosis, and excessive bleeding from wounds and are more severe in large dogs and young dogs. These clinical signs may cause bleeding crisis and can be life threatening. Although the patient may be discharged from hospital after recovery, many patients can have relapse. To author's knowledge, this is the first case report in veterinary medicine of Korea.

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CASE REPORT

A 3-month-old intact male Labrador retriever dog was presented to the Chonbuk Animal Medical Center because of protracted bleeding after being hit by a deer's foot. On physical examination, the dog was depressed and tachycardic. There were uncontrolled nasal bleeding and subcutaneous hematoma (Fig. 1, 2). The owner reported no history of exposure to anticoagulant rodenticides.

A complete blood count (CBC) indicated mild leukocytosis and non-regenerative anemia (Table 1) and abnormal

Fig. 1. Presence of nasal bleeding. Nasal bleeding was uncontrolled and protracted continuously.

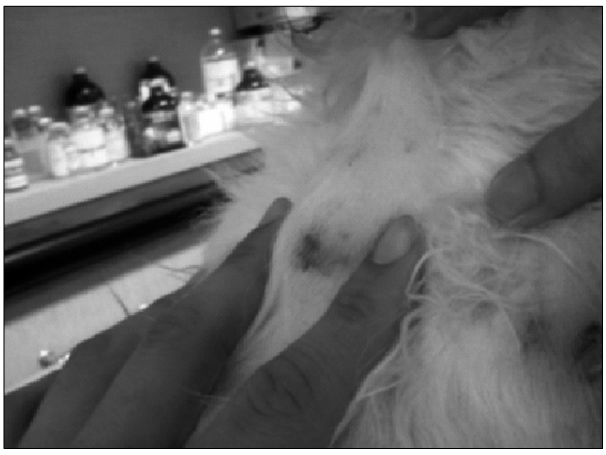

Fig. 2. Presence of subcutaneous hematoma. The diameter of the subcutaneous hematoma was about 5 cm.

platelet count. Serum biochemistry results showed increased phosphate and decreased total protein and globulin levels (Table 2). A coagulation screening test was then performed. Activated partial thromboplastin times (APTT) were distinctly prolonged (106 seconds; reference range: 60～93 seconds). Prothrombin time (PT) was not detected due to the markedly prolonged time (reference range: 11～14 seconds). Coagulation factor VIII and IX analyses were performed at commercial laboratory (Samkwang lab, Seoul, Korea). Pending the results of coagulation factor analyses, blood transfusions (20 ml/kg body weight) were initiated. The patient´s condition improved rapidly and the hemorrhage ceased. The results of coagulation factor analyses are presented in Table 3. Factor assays revealed that factor VIII activity is greater than 150% (reference range: 70～100%) and factor IX activity is 5% (reference range: 70～140%). The patient was diagnosed with hemophilia B based on markedly low factor IX coagulation activity. The patient recovered and was discharged from the hospital. However, 4 months later, the patient again presented with excessive bleeding and was re-hospitalized. The owner opted not to pursue further treatment at that time. Two days later, the patient died of respiratory distress.

Table 1. Hematologic outcome for the patient at initial presentation

Hematology	Values	Reference range
WBC	18.2	6.0～17.0
RBC	2.06	5.40～7.80
HGB	4.5	13.0～19.0
HCT	13.3	37.0～54.0
PLT	121	160～430
MCV	65	64～74
MCH	21.9	22.0～27.0
MCHC	33.8	34.0～36.0
RDW	17.4	14.0～17.0
MPV	10.0	6.7～11.1

Table 2. Serum biochemistry profile of the patient at initial presentation

Serum biochemistry	Values	Reference range (units)
ALB	2.9	2.5～4.4 (G/DL)
ALP	85	20～150 (U/L)
ALT	21	10～118 (U/L)
AMY	521	200～1,200 (U/L)
TBIL	0.2	0.1～0.6 (MG/DL)
BUN	23	7～25 (MG/DL)
CA	9.4	8.6～11.8 (MG/DL)
PHOS	7.7	2.9～6.6 (MG/DL)
CRE	0.3	0.3～1.4 (MG/DL)
GLU	118	60～130 (MG/DL)
NA+	139	138～160 (MMOL/L)
K+	4.5	3.7～5.8 (MMOL/L)
TP	4.3	5.4～8.2 (G/DL)
GLOB	1.3	2.3～5.2 (G/DL)

Table 3. Results of coagulation factor analysis

Factor	Values	Reference range
Factor assay VIII	>150	60～150 (%)
Factor assay IX	5	60～150 (%)

DISCUSSION

Hemophilia is the most common inherited coagulation disorder in humans and dogs. Among the hemophilias, hemophilia B is a blood clotting disorder caused by a mutation of the factor IX gene, leading to a deficiency of factor IX. It is the less common form of hemophilia, rarer than classic hemophilia (hemophilia A). The severity of bleeding in affected animals depends on the degree of factor deficiency (Chao et al, 1999). Hemophilia B is a disturbance of coagulation. Clinical signs and coagulation tests suggest problems in the intrinsic clotting pathway, similar to classic hemophilia (hemophilia A). Therefore, most hemophilia A and B patients have prolonged APTT and normal PT. For the definitive diagnosis of hemophilia A and B, the activities of factors VII and IX must be measured.

In our case, the patient presented with uncontrolled nasal bleeding resulting in anemia as a result of excessive bleeding. And laboratory examinations indicated decreased platelet number and a hematocrit. Anemia was severe and the hematocrit was 13.3%. Additional laboratory studies demonstrated prolonged APTT and PT. The cause of prolonged PT was thought to be result from the consumption of coagulation factors due to severe bleeding. In addition to these results, the anemia was non-regenerative. The best-known treatment for hemorrhage in cases of true hemophilia is transfusion with fresh blood or with concentrated materials prepared from the fibrinogen fraction of normal fresh plasma (Feldman et al, 1995). In this patient, whole blood transfusions were performed to induce increase in factor IX, red blood cells, and platelets.

Hemophilia is treated well with transfusion therapy. To prevent life-threatening bleeding in the future due to sustained trauma, hemophilia patients must have restricted activity levels. This dog underwent one more trauma after discharge from the hospital in 4 months and same clinical sings appeared like bleeding and non-regenerative anemia. Finally the patient was euthanized because the owner did not want treatment anymore.

Hemophilia B has been reported in a variety of pure bred dogs (Biggs et al, 1952; Verlander et al, 1984; Villiers and Blakwood, 2005; Nakata et al, 2006; Nelson and Couto, 2009). This case, however, is the first report of canine hemophilia B in veterinary medicine of Korea.

In conclusion, This patient had some clinical sings including protracted nasal bleeding and pale mucous membrane. The results of coagulation time test and coagulation factor analysis indicated hemophilia B. Whole blood transfusions were performed and the patient recovered immediately. Four months later the patient was re-hospitalized because of same cause of initial hospitalization. However the patient died because client did not want to treat anymore. To authors' knowledge, this is the first case report of canine hemophilia B in Korea.

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