Hemophilia B in a Crossbred Maltese Dog

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ABSTRACT. A crossbred Maltese dog, 6-year-old, male, was presented to us for examination due to coagulopathy. On examination of blood coagulation screening tests, activated partial thromboplastin time (APTT) was markedly prolonged (63.6 sec). Therefore, a defect in the intrinsic pathway of coagulation was suspected. An additional serum test was also examined and APTT was returned to within the normal range. Furthermore, factor IX coagulation activity was markedly low (2.3%). On the basis of these results, the dog was diagnosed with hemophilia B. The dog has since been presented to us because of hemorrhage problems again after 5, 10, and 16 months, but blood transfusions have maintained good control of its coagulopathy for more than two years.

KEY WORDS: canine, hemophilia B, Maltese.

Hemophilia B is caused by aberration or functional deficiency of coagulation factor IX [8]. This disease is rare in comparison with hemophilia A (factor VIII deficiency), which is a commonly inherited coagulopathy in the dog. Hemophilia B has been reported in a variety of purebred dogs, and there are few reports of it in toy or small size breed dogs [1, 2–4, 7, 10, 11]. Generally, it is considered that the clinical signs are more severe in large size and young dogs. In this paper, the authors report about a crossbred Maltese dog, 6 years old, diagnosed with hemophilia B.

A 6-year-old male crossbred Maltese dog, weighting 5.6 kg, was referred to the Nihon University Animal Medical Center from a private veterinary hospital because of coagulopathy. The first hemorrhage episode was bleeding from the gums at the loss of the deciduous teeth at 6 months of age. From around 5 years of age, the dog had repeated subcutaneous hematoma and pain of unknown origin. The dam of the dog was a Maltese and the sire was a crossbreed of a Maltese and Pomeranian. Its littermates were a female and young dogs, not including this dog.

At first presentation, no abnormal findings were observed in a physical examination. On examination of complete blood counts, the platelet count was sufficient (557,000/µl) and normal platelet granules were confirmed in a blood smear preparation. Platelet aggregation examined by a lumi-aggregometer (NBS Hema Tracer 601, Niko Bioscience, Tokyo, Japan) was normal. On examination of blood coagulation screening tests, the prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen concentration, fibrinogen/fibrin degradation products (FDPs), and antithrombin III (AT III) activity were examined and APTT was markedly prolonged (63.6 sec; reference range, 12.0 to 18.0 sec); the values of all other tests were normal (Table 1). The buccal mucosal bleeding time, examined using a Simplate device (Organon Teknika Corp., NC, U.S.A.), was within the normal range (2.7 min; reference range, 2.0 to 5.0 min), and the concentration of factor VIII related antigen, measured by rocket immunoelectrophoresis, was also normal (102%; reference range, 60 to 172%).

The serum of a healthy beagle dog, containing factors IX, XI, and XII but not factor VIII, was added to the patient’s plasma (4 times dilution; serum:patient plasma=1:3), and APTT was measured again immediately afterwards. As a result, APTT was returned to within the normal range (12.5 sec). Therefore, factor VIII deficiency (hemophilia A) was excluded, and a deficiency in the other intrinsic clotting pathway factors (IX, XI and XII) was suspected. In addition, the factor IX, XI, and XII coagulation activities were measured using human deficiency plasma (George King Bio-Medical, Inc., KS, U.S.A.). The factor XI and XII coagulation activities were 84 and 79%, respectively, but the factor IX coagulation activity was markedly low (2.3%). From these results, the dog was diagnosed with factor IX deficiency (hemophilia B).

Five months after initial presentation, the dog was referred to us again with pain and lameness in the left hind-limb. These symptoms were caused by an intramuscular hematoma (Fig. 1A). There were several abnormal findings from blood examination, mild anemia, a prolonged APTT (68.6 sec), and an elevated level of C-reactive protein (12.0 mg/dl; reference range, <1.0 mg/dl). The dog received a blood transfusion (40 ml, whole blood), and meloxicam (0.1 mg/kg, whole blood).

Table 1. Results of screening tests for blood coagulation at first presentation in this case

<table>
<thead>
<tr>
<th></th>
<th>Patient</th>
<th>Reference</th>
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<tbody>
<tr>
<td>PT (sec)</td>
<td>8.1</td>
<td>6.0–8.5</td>
</tr>
<tr>
<td>APTT (sec)</td>
<td>63.6</td>
<td>12.0–18.0</td>
</tr>
<tr>
<td>Fibrinogen (mg/dl)</td>
<td>313</td>
<td>200–400</td>
</tr>
<tr>
<td>AT III (%)</td>
<td>120</td>
<td>85–150</td>
</tr>
<tr>
<td>FDPs (µg/ml)</td>
<td>&lt;2.5</td>
<td>≤2.5</td>
</tr>
</tbody>
</table>

mg/kg) was administered for anti-inflammatory and pain control. After the treatment, the prolonged APTT shortened by 24.8 seconds, the swelling and pain improved, and the intramuscular hematoma disappeared (Fig. 1B). Ten and 16 months after initial presentation, the dog received transfusions because of similar coagulopathy. The dog is eight years old at present and is still alive.

Hemophilia B has been reported in approximately twenty purebreds and a few crossbred dogs [5, 6, 9]. This disease is an inherited recessive and X-chromosomal trait, so bleeding tendencies are primarily observed in males [8]. Females are carriers of hemophilia B, and most carriers have reduced factor IX activity (40 to 60%) [8]. Our case was male crossbred dog, but the dam was a purebred Maltese. We believe that the Maltese dog is a carrier breed. However, the mother of this patient was unavailable for coagulation examination. There have been no reports of hemophilia B in Maltese dogs.

Clinical signs, such as subcutaneous and intramuscular hematomas and prolonged bleeding from wounds are commonly seen in affected dogs [8]. These tend to be more severe in large breeds and young dogs. However, this patient was a small breed dog and was older compared with previous reports on hemophilia B [2–6, 10–13]. Although factor IX activity was markedly low, our dog did not show severe clinical signs until it was five years old. This might be related to factors, such as small size of the breed, weight, playfulness and indoor breeding.

Bleeding in hemophilia A can be improved by infusion of desamino-D-arginine vasopressin (DDAVP) in addition to transfusion [8]. On the other hand, the treatment for hemophilia B is usually transfusion of whole blood or fresh frozen plasma [8]. The patient was transfused with approximately 8% of the whole blood volume, and the treatment shortened prolonged APTT and improved clinical signs. Affected dogs with factor IX activities of 2 to 5% are moderate [8]. Furthermore, bleeding in patients with hemophilia B is reportedly improved by transfusion of at least over 5% of the whole blood volume. Thus, we were able to stop the bleeding of the dog by transfusion with 8% of the whole blood volume.

In conclusion, this case was diagnosed as hemophilia B. Since the mother of the patient was a Maltese dog, it was recognized that the Maltese dog is a carrier of hemophilia B. The patient has been maintained in good condition with a good quality of life (QOL) over a long period using only transfusions. To our knowledge, this is the first case report on a dog with hemophilia B in Japan.

REFERENCES