Primary Hemangiosarcoma of the Humerus in a Maltese Dog

Yuichi HIDAKA1), Mitsuyoshi HAGIO1)*, Kazuyuki UCHIDA2) and Yae HARA2)

Departments of 1)Veterinary Surgery and 2)Veterinary Pathology, Faculty of Agriculture, University of Miyazaki, 1–1 Gakuen Kibanadai Nishi, Miyazaki City, Miyazaki 889–2192, Japan

(Received 15 February 2006/Accepted 19 April 2006)

ABSTRACT. A 14-year-old intact male Maltese dog was presented with a history of pain and swelling of the left upper forelimb and lameness for 3 weeks. Hematological and radiographical examinations showed regenerative anemia and osteolysis of the humerus. Fine-needle aspiration biopsy detected epithelioid- and fibroblast-like anaplastic cells with blood components. A hemorrhagic and osteolytic malignant tumor was suspected, and the affected forelimb was amputated. Histopathologically, the dog was diagnosed with primary hemangiosarcoma of the humerus. Thereafter, metastatic lesions appeared in the skin, and the dog was euthanized 1 month after the operation.

KEY WORDS: hemangiosarcoma, humerus, Maltese.

Hemangiosarcoma (HS) arises in any tissue with blood vessels, and the most common sites in dogs are the spleen, heart, skin, and liver [7, 15, 17]. Primary HS of bones is rare, and the incidence is less than 5% of all primary canine bone tumors [1, 7, 10, 15, 17]. This tumor is predisposed to medium-sized and large breed dogs, including German Shepherds, Great Danes, and Boxers, with a median age of 6 years [1, 3, 7, 16]. The proximal humerus, rib, femur, and vertebrae are the bones most commonly involved [1, 3, 10, 17].

Recently, we encountered primary HS of the humerus in a Maltese dog. There are eight clinical articles available on primary HS of canine bones in America and England [2–6, 9, 12, 13]. Although there is one report of a dog with HS attributed to an aneurysmal bone cyst [14], osseous HS seems to be extremely rare in Japan. Furthermore, occurrence is uncommon in toy breed dogs, although a case has been reported of a West Highland White Terrier with primary HS of the radius [13].

In this paper, we describe the clinical and pathological findings of this case and review the clinical literature concerning primary HS of canine bones.

A 14-year-old intact male Maltese dog weighing 2.9 kg was presented with a history of lameness and pain in the left upper forelimb for 3 weeks. Rheumatoid disease was suspected by a private practitioner because of no significant radiographical changes in the bone. At presentation, physical examination revealed marked swelling and hardening of the upper forelimb. Regional and other superficial lymph nodes were not enlarged. A cardiac systolic murmur (Levine IV/VI) was auscultated. Echocardiography demonstrated that the murmur was caused by mitral valve regurgitation, and there were no other changes in the heart. Radiographs showed a diffuse, mottled, “moth-eaten” appearance of the humerus without periosteal osteogenesis.

Lytic change was predominant in the proximal humerus, especially in the region of the greater tubercle (Fig. 1). There were no abnormal findings found in other long and axial bones or in the thoracic and abdominal cavities by survey radiographs. Routine blood work revealed regenerative anemia (erythrocytes, 2,790,000/µl; hemoglobin, 7.2 g/dl; hematocrit, 24%), thrombocytopenia (42,000/µl), and leukocytosis (31,100/µl). Blood smear showed anisocytosis with mild poikilocytosis and neutrophilia. Plasma alkaline

*Correspondence to: HAGIO, M., Department of Veterinary Surgery, University of Miyazaki, 1–1 Gakuken Kibanadai Nishi, Miyazaki City, Miyazaki 889–2192, Japan.

Fig. 1. Radiophotograph of the humerus in the present case at first presentation. A “moth-eaten” appearance indicating osteolysis was observed in the whole humerus. Lysis was more prominent in the region of the greater tubercle. Periosteal osteogenesis was not observed.
Phosphatase (ALP) activity was 208 U/l. Since the clinical findings suggested a malignant tumor or infection of the forelimb, a biopsy was recommended; however, the owner did not give consent. An antibiotic (Viccillin, Meiji Seika Kaisha Ltd., Tokyo, Japan) was prescribed, but the dog’s condition did not improve.

A week later, the affected forelimb became reddish in color and hotness and fluctuation were palpated. The dog’s anemia progressed (erythrocytes, 1,630,000/µl; hemoglobin, 4.6 g/dl; hematocrit, 17%), and plasma ALP activity increased slightly (304 U/l). Radiographs suggested a pathologic fracture at the proximal region of the humerus. Fine needle aspiration (FNA) biopsy was performed at the site, and its smear was chiefly composed of blood components with a small aggregation of epithelioid- and solitary fibroblast-like anaplastic cells (Fig. 2). These were large cells that had ovoid to round nuclei and abundant cytoplasm that frequently had vacuoles. Since an osteolytic and hemorrhagic malignant tumor, likely HS, was suspected on the basis of these findings, amputation was recommended. The owner agreed to the surgery, but the dog’s condition did not improve in spite of treatment, including fluid therapy, blood transfusion, and tranexamic acid (Transamin, Daiichi Pharmaceutical Co., Ltd., Tokyo, Japan). ALP activity was strikingly elevated (1342 U/l), and the left axillary lymph node was mildly swelled during hospitalization. On the 14th day in hospital, forequater amputation was performed with elimination of the left axillary lymph node. The dog was premedicated with atropine sulfate (Fuso Pharmaceutical Industries, Ltd., Osaka, Japan) and flunitrazepam (Silece, Eisai Co., Ltd., Tokyo, Japan). Anesthesia was induced by intravenous injection of ketamine hydrochloride (Ketalar, Sankyo Co., Ltd., Tokyo, Japan) and maintained with isoflurane in oxygen. Surgery and recovery were uneventful. Histopathological examination revealed HS of the humerus. The sarcoma tissue was derived from the subperiosteal region and protruded to the adjacent muscle through the periosteum (Fig. 3).

The dog recovered day by day and was discharged 1 week post operation (PO). At 20 days PO, however, dark red, rice-sized, hematoma-like nodules with purpura appeared in the skin (Fig. 4). FNA biopsy was performed in the nodules, and anaplastic cells were detected as previously seen in the humerus. Although metastatic lesions were not detectable...
in thoracic radiographs, the dog deteriorated again. The owner did not wish any further laboratory tests or treatment including chemotherapy. Upon request from the owner, the dog received euthanasia at 1 month PO.

Necropsy demonstrated hematomatous lesions in the heart, lung, greater omentum, small intestine, kidney, and adrenal gland. Histopathologically, they were regarded to be metastasis from the primary affected humerus.

In the present case, the disease originated in the left upper forelimb, and radiography indicated severe osteolysis only in the humerus. Physical examination, radiography, and echocardiography showed no findings associated with splenic, hepatic, and cardiac HSs. We also speculated that subcutaneous HS secondarily infiltrated the humerus. However, histopathological observation of the amputated forelimb suggested that the sarcoma tissue was derived from the subperiosteal region of the humerus. These findings indicated that the humerus was the primary site, and it is necessary to distinguish osseous HS from telangiectatic osteosarcoma, which is characterized by osteolysis, many blood filled spaces, and osteoid formation [8, 16]. These findings are very similar to those of HS in bones, but without osteoid formation [8, 16]. In our case, osteoid formation was not found in the sarcoma tissue, and therefore telangiectatic osteosarcoma was also excluded.

In primary HS of canine bones, radiographs reveal massive destruction, with often a pathologic fracture [10, 16, 17]. The tumor expands proximally and distally along the medullary cavity and is expressed as a soap-bubble-like expansile growth in radiographs [10]. It is believed that the manner of expansion is less painful and that symptoms may not develop until a pathologic fracture occurs [11, 16]. However, our dog suffered from pain and swelling of the forelimb before pathologic fracture. In addition, HS of bones has no or minimal periosteal new bone formation [1, 3, 10, 11, 16, 17], as seen in the present case. The reason for this poor periosteal reaction in osseous HS is unknown. We surmise that regional ischemia as a result of severe hemorrhage from the sarcoma may prevent the reaction leading to osteogenesis. Differentiation of the osseous HS from commonly occurring osteosarcoma seems to be difficult in radiographs. However, Ling et al. [11] pointed out that the pattern of spread of HS and the osteoblastic pattern aid in differentiation because the clinical signs appear later and early radiographic changes are rarely observed.

Definitive diagnosis of HS is subject to histopathological examination. Cytology by FNA biopsy has not been available for HS because samples mostly consist of blood with only a few to moderate numbers of spindle shaped cells with the features of malignant mesenchymal cells [16]. In our case, fortunately, clumps of epithelioid- and solitary fibroblast-like cells were found in the smear. Erdem and Pead [6] also observed epithelial cells in smears obtained from primary HS of the scapula in a dog by FNA biopsy. FNA biopsy may allow diagnostic of HS in bones by detecting these cells and large amounts of blood, simultaneously.

To date, treatment of osseous HS in dogs has been unrewarding (Table 1) [2–6, 9, 12, 13]. Amputation is a palliative measure, and the median survival time after surgery is less than 5 months [7, 17]. Amputation was also conducted for our dog, and the dog was euthanized at 1 month PO. Chemotherapy was not performed in this case. Although Crow [4] described that a mixed breed dog treated with doxorubicin and cyclophosphamide survived for 13 months PO, the effect of chemotherapy in prolonging survival time is also uncertain in primary HS of bones [7].

We conclude that primary HS of bones should be suspected in dogs with hemorrhagic and osteolytic disease. However, even if HS could be diagnosed, clinicians and owners would be troubled by the therapy and prognosis.

REFERENCES


Table 1. Review of clinical reports concerning primary hemangiosarcoma of canine bones

<table>
<thead>
<tr>
<th>Authors</th>
<th>Dogs</th>
<th>Sites</th>
<th>Treatments</th>
<th>Prognosis (survival time)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barber et al. [2]</td>
<td>3 F</td>
<td>Basset Hound</td>
<td>Antibiotics, prednisone</td>
<td>Euthanasia (53 days*)</td>
</tr>
<tr>
<td>Bingel et al. [3]</td>
<td>2 SF</td>
<td>Irish Setter</td>
<td>Exploratory surgery</td>
<td>Euthanasia (11 days PO)</td>
</tr>
<tr>
<td>Crow [4]</td>
<td>3 F</td>
<td>Mixed</td>
<td>Amputation, chemotherapy</td>
<td>Euthanasia (13 months PO)</td>
</tr>
<tr>
<td>Dueland et al. [5]</td>
<td>8 M</td>
<td>Boxer</td>
<td>Nothing</td>
<td>Euthanasia (—)</td>
</tr>
<tr>
<td>Erdem and Pead [6]</td>
<td>13 F</td>
<td>Collie cross</td>
<td>Nothing</td>
<td>Euthanasia (—)</td>
</tr>
<tr>
<td>Jennings et al. [9]</td>
<td>22/3</td>
<td>Belgian Malinois</td>
<td>Drainage, antibiotics, Exploratory surgery</td>
<td>Euthanasia (18 days*)</td>
</tr>
<tr>
<td>Parchman et al. [12]</td>
<td>11/3</td>
<td>Cocker Spaniel</td>
<td>Cage rest, glucocorticoid, Methylprednisolone</td>
<td>Euthanasia (3 months*)</td>
</tr>
<tr>
<td>Quigley et al. [13]</td>
<td>6 F</td>
<td>Terrier cross</td>
<td>Amputation</td>
<td>Euthanasia (3 months PO)</td>
</tr>
<tr>
<td></td>
<td>8 F</td>
<td>WHWT*</td>
<td>Amputation</td>
<td>Euthanasia (10 months PO)</td>
</tr>
</tbody>
</table>

*After development of clinical symptoms associated with hemangiosarcoma of the bone.