NOTE *Pathology*

Humeral Chondrosarcoma in a Hokkaido Brown Bear (*Ursus arctos yesoensis*)

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ABSTRACT. Humeral chondrosarcoma was found in an 18-year-old male Hokkaido brown bear (*Ursus arctos yesoensis*). Necropsy revealed a large firm mass under the left superficial pectoral muscle at the axillary region. The mass involved the left shoulder joint and peripheral muscles, and connected to the head of the humerus with osteolysis. Histopathologically, the mass was composed of irregularly shaped myxomatous to cartilaginous tumor lobules. The tumor cell showed moderate nuclear atypia with a relatively high mitotic index, especially in the edges of the myxomatous lobules. The tumor cells were positively immunostained with vimentin and S-100 protein. Based on these findings, the tumors were diagnosed as chondrosarcoma. Metastases were found in the left axillary lymph node, lungs, liver and kidney.

KEY WORDS: brown bear, chondrosarcoma, humerus, metastasis.

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Hokkaido brown bear (*Ursus arctos yesoensis*) belongs to the genus *Ursus*, and lives in Hokkaido, Japan. There have been few reports of neoplasms in the Ursidae family. These include osteoma [11], osteosarcomas [7, 12], squamous cell carcinoma [9, 13], biliary carcinoma [2, 8], thyroid carcinoma [3], hepatocellular carcinoma [4, 6], lymphosarcoma [1, 16] and mammary carcinoma [10]. To the best of our knowledge, there are no reports of chondrosarcoma in bears.

Chondrosarcoma is a malignant tumor characterized by production of chondroid and fibrillar matrix by the tumor cells [15]. In this paper, we describe a case of humeral chondrosarcoma in a Hokkaido brown bear (*Ursus arctos yesoensis*).

An 18-year-old male Hokkaido brown bear (*Ursus arctos yesoensis*), housed in a zoo (Sahoro Resort Bear Mountain), showed difficulty in loading to the left forelimb after emerging from hibernation. Under general anesthesia, clinical examination including palpation was carried out. However, there was no obvious macroscopic abnormality at that time. In spite of antiphlogistic analgetic and antibiotic treatment, the symptoms were not improved and progressed to lameness. The bear also showed anorexia and gradual weight-loss (287 kg to 257 kg), and died 3 months after clinical manifestation.

Necropsy revealed a large firm mass, 28 × 24 × 21 cm in size, under the left superficial pectoral muscle at the axillary region (Fig. 1). The mass involved the left shoulder joint and peripheral muscles, and was connected to the head of humerus with osteolysis. On the cut surface, the mass was white to whitish yellow and showed connective tissue-like hardness with multifocal areas of necrosis and bone formation (Fig. 2). The left axillary lymph node was mildly enlarged. In the thoracic cavity, there was a moderate amount of bloody pleural effusion. On the surface of both lungs, similar clear white to whitish yellow nodules, 2 to 5 cm in diameter, were observed (Fig. 3). Similar large nodules were also found in left cranial lobe, 7 × 5 × 5 cm in size, and right cranial lobe, 7 × 7 × 6 cm in size, respectively. Similar nodules, up to 4 cm in diameter, were scattered throughout the remaining lung lobes. The cut surfaces of the nodules were similar to those of the left axillary mass with calcification. Adjacent to the large nodules, massive necrosis with hemorrhage was also seen in the caudal half of both posterior lung lobes. In extrathoracic organs and tissues, whitish discrete nodules were also observed in the liver (4 × 4 × 3 cm in size) and left kidney (5 mm in diameter).

For histopathological examination, the masses and major organs and tissues were fixed in 15% neutral buffered formalin and embedded in paraffin wax. Paraffin sections were stained with hematoxylin and eosin (HE). Selected sections were also stained with toluidine blue (pH 7.0) and alcian blue (pH 2.5), and immunostained with anti vimentin rabbit polyclonal antibody (DakoCytomation, Tokyo, Japan) and anti S-100 rabbit polyclonal antibody (DakoCytomation).

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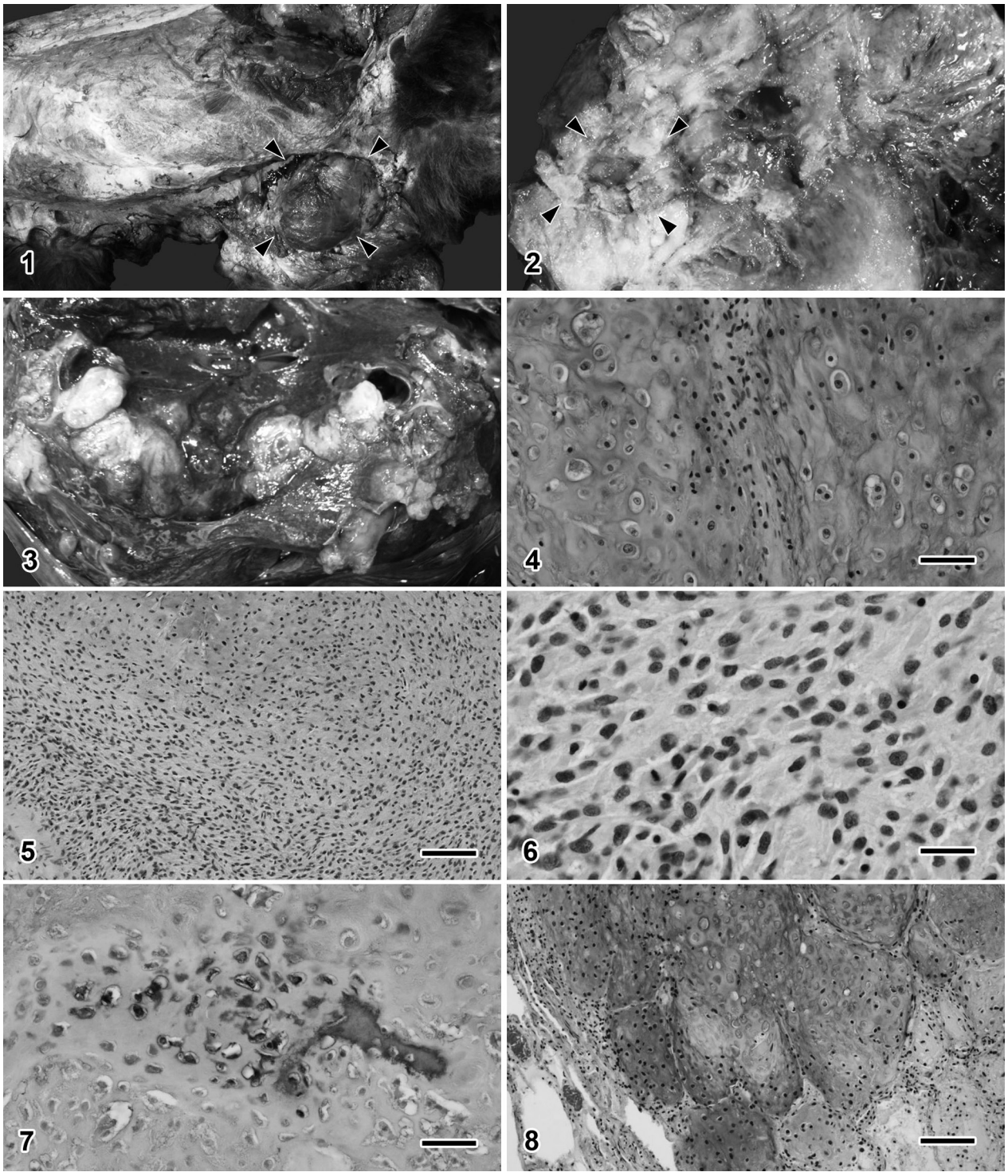

Fig. 1. Gross appearance of left axillary mass. Large mass in the left axillae (arrowheads).
Fig. 2. Cut surface of left axillary mass. The mass is white to whitish yellow with multifocal areas of necrosis and bone formation (arrowheads).
Fig. 3. Cut surface of lung. Numerous clear white to whitish yellow nodules are observed.
Fig. 4. Photomicrograph of left axillary mass. Well-differentiated cartilaginous lobules, the tumor cells are located within lacunae surrounded by basophilic amorphous chondroid matrix. At the edges of the lobules, the tumor cells have a round to polygonal pale eosinophilic cytoplasm. HE. Bar=50 μm.
Fig. 5. Photomicrograph of left axillary mass. A myxomatous lobule characterized by higher cellularity and myxoid matrix. HE. Bar=100 μm.
Fig. 6. Higher magnification of a myxomatous lobule. The tumor cells show moderate nuclear atypia with some mitotic figures. HE. Bar=25 μm.
Fig. 7. Photomicrograph of left axillary mass. Bone formation in the center of a cartilaginous lobule. Bar=50 μm.
Fig. 8. Photomicrograph of lung. In this area, lung tissue is mostly replaced by tumor tissue similar to those seen in left axillary mass. Bar=100 μm.

Histologically, most areas of the left axillary mass were massively necrotized. At the relatively well-preserved areas, there were irregularly shaped myxomatous to cartilaginous tumor lobules that were irregularly demarcated by connective tissue bands (Figs. 4 and 5). In the center of the cartilaginous lobules, the tumor cells were located within lacunae surrounded by basophilic amorphous chondroid matrix (Fig. 4). At the edges of the lobules, cellularity was relatively high, and the tumor cells had a round to polygonal pale eosinophilic cytoplasm. Binucleated tumor cells sometimes were present, though mitotic figures were rare in these areas. On the other hand, in myxomatous lobules, which were characterized by higher cellularity and myxoid matrix (Fig. 5), the tumor cells showed moderate nuclear atypia with relatively high mitotic index (2 to 3 figures per × 400 field) compared with those in well differentiated cartilaginous lobules (Fig. 6). The head of the humerus connected to the neoplastic tissues was also massively necrotized, and chondroid tumor tissues filled the marrow spaces. Though calcification and bone formation was also observed in some areas, these were mostly confined to the center of cartilaginous lobules (Fig. 7) and hyalinized hypocellular areas without obvious osteoblast-like atypical cells.

All the macroscopic nodules found in the lungs, liver and left kidney were composed of neoplastic tissues mostly similar to those seen in the axillary mass (Fig. 8). Compared to those tumors in the left axillary area, myxomatous high-cellularity areas were evident in these masses. Though mild calcification was seen in a few pulmonary nodules, bone formation was not detected in these nodules. The left axillary lymph node was massively necrotized with invasion of chondroid tumor tissues in the sinuses. In addition, massive necrosis with hemorrhage was also noticed adjacent to the large metastatic foci of the tumors of both lungs.

Both myxoid and cartilaginous matrices were stained with alcian blue and showed metachromatic stainability with toluidine blue. Immunohistochemically, the tumor cells were positive for vimentin and S-100 protein. Based on these findings, the present tumor was diagnosed as a humeral chondrosarcoma, originating from the head of humerus, with metastases to the left axillary lymph nodules, lung, liver and left kidney.

In chondrosarcoma, although tumor cells do not produce osteoid, bone formation by endochondral ossification of tumor cartilage may be present [15]. Chondroblastic osteosarcoma directly produces chondroid matrix [15]. Thus, in making a diagnosis of chondrosarcoma for a tumor with bone formation, we have to eliminate the possibility of chondroblastic osteosarcoma. In the original humeral tumor tissue of the present case, there was bone formation in some areas. However, the bone formation was mostly confined to the central areas of the tumor lobules and hyalinized hypocellular areas without obvious osteoblast-like atypical cells. Furthermore, bone formation was not found in metastatic tumor nodules. These facts support our diagnosis of humeral chondrosarcoma.

In domestic animals, flat bones such as scapula and ribs are considered to be the most common sites of chondrosarcoma, though long bones are occasionally affected [5, 14, 15]. It has been known that chondrosarcoma in domestic animals develops hematogeneous metastases to lungs, kidney, liver, heart and skeleton [15]. These biological characteristics of chondrosarcoma were compatible with those of the present case. In bears, bone tumors are rare, and osteoma and osteosarcomas are the only tumors reported in the literature [7, 11, 12]. Thus, the present case is the first reported case of chondrosarcoma in bears.

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