NOTE *Pathology*

Unusual Metastasis of Malignant Aortic Body Tumor to *Multiple* Bones in a Dog

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ABSTRACT. Unusual metastasis of malignant aortic body tumor to *multiple* bones was detected in a 5-year-old female English Setter dog. Radiographs exhibited an abnormal mass in the base of heart and osteolytic lesions in the bodies of T11 and L2 vertebrates, body of right femur, right proximal humoral epiphysis and *infraspinous* fossa near to the neck of right scapula. At necropsy, multiple tumor masses of various sizes were observed also in the bones as well as the heart base and tracheobronchial lymph node. Tumor masses of L2 and T11 protruded into the vertebral canal and compressed corresponding sites of spinal cord, leading to paraplegia. Histopathologically, the tumor cells, arranged in sheets or nests, were polyhedral, lightly eosinophilic, finely granular cytoplasm with mostly round to oval nucleus and had scattered bizarre giant cells. Ultrastructural study revealed the characteristic findings that tumor cells contained a large number of small, electron-dense, membrane-limited secretory granules in cytoplasm. This is thought to be an extremely rare case having multiple bone metastases of a malignant aortic body tumor.

KEY WORDS: aortic body tumor, canine, multiple bone metastases.

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Nodular, encapsulated tumors at the base of the heart arise usually from aortic body tissue, ectopic thyroid, or ectopic parathyroid [2, 4, 5]. Since these tumors had similar properties of gross and histopathology, it should be differentiated [2, 4, 5]. Ultrastructural characteristics may help to accurately differentiate aortic body tumors, ectopic parathyroid gland tumors, and ectopic thyroid gland tumors originating from tissues at the base of the heart in dogs [2, 4, 7]. Although malignant aortic body tumors often invade blood vessels, metastasis to the other organs occurs infrequently in dogs [2, 4]. As far as we known, multiple bone metastases of malignant aortic body tumor are extremely rare in dogs [1, 3, 6, 7, 9].

Here we report *an* unusual case of malignant aortic body tumor *with metastasis* to *multiple* bones in an adult female English Setter dog.

A 5-year-old female English Setter dog was referred to Chonnam National University Veterinary Teaching Hospital with a history of progressive hindlimb paresis, lethargy and decreased appetite for a four-week duration. Physical examination revealed abnormally accentuated heart sound, mild dehydration, and muscle atrophy of both hindlimbs. Results of the neurologic examination indicated the presence of thoraco-lumbar spinal lesions. Biochemistry and hematology findings were unremarkable. Radiographs of the thorax and spinal column demonstrated a soft tissue mass in the cranial mediastinum displacing the trachea to the right and dorsally, a mild bulging of the left auricle and moth-eaten osteolytic lesions in the L2 vertebrae. A destructive lesion in the right scapula was suspected on the thoracic radiographs, and radiographs of the right shoulder joint were retaken. Osteolytic lesions in the *infraspinous* fossa near to the neck of right scapula and proximal humoral epiphysis were detected. Pain was not elicited on palpation of the lytic region. Myelography performed via a cisternal puncture showed thinning of the dye columns at the level of T11 and L2, consistent with extradural compressive lesions laterally (Fig. 1). By echocardiography, abnormal masses were detected in the cranial mediastinum and base of heart. Because a poor prognosis was given, the dog was euthanatized and necropsied.

At necropsy, five tumor masses (2.0 × 2.0 × 1.0 cm to 2.5 × 3.0 × 3.0 cm) connected by fibrous connective tissues each other were attached between the ascending aorta and pulmonary artery, and embedded in the adipose connective tissue between these major vascular trunks (Fig. 2). On the cut surface, the tumor masses were flesh colored, coarsely

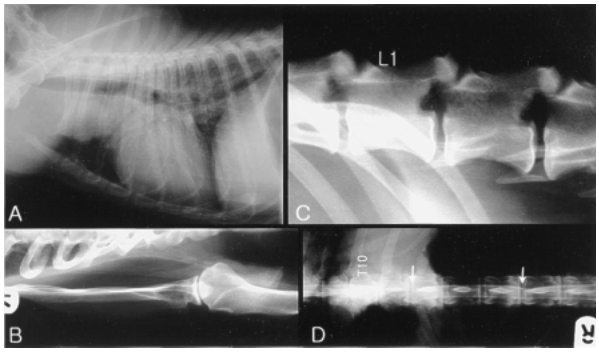

Fig 1. (A) Lateral thoracic radiograph showing a soft tissue mass in the cranial mediastinum that *displaced* the trachea dorsally. (B) Lateral view of the thoraco-lumbar vertebrae and (C) caudo-cranial view of the right shoulder joint demonstrationg the bone lysis in the L2 and right scapula, respectively. (D) Myelogram after cisternal puncture indicating the extradural spinal cord compression at the level of T11 and L2 (arrows).

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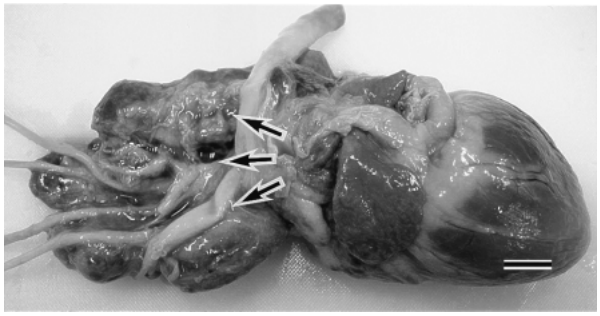

Fig. 2. Malignant aortic body tumor (arrows) embedded in the adipose connective tissue between the major vascular trunks in the heart base. Bar = 0.57 cm.

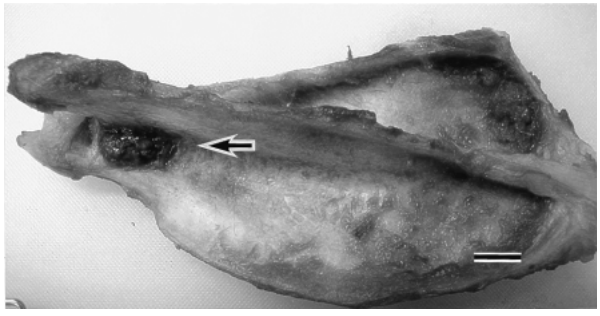

Fig. 3. Metastasis of malignant aortic body tumor into the right *infraspinous* fossa (arrow) near *the neck* of scapula. Bar = 0.6 cm.

roughed, encapsulated and irregularly lobulated. There were small flesh round tumor masses (maximum 1.0 cm diameter) in the walls of left atrium and ventricle, respectively. A regional tracheobronchial lymph node near to the tumor masses was enlarged and flesh colored. Multiple bone metastasis of tumor were detected in the vertebral bodies of T 11 (1.1 × 0.8 × 0.4 cm) and L2 (1.8 × 1.3 × 0.5 cm), body of right femur (2.0 × 1.0 × 1.0 cm), and right *infraspinous* fossa (2.2 × 1.8 × 1.0 cm) near the neck of scapula (Fig. 3). The prominent gross evidence of osteolysis due to the metastasized tumor mass was observed in these bones. Tumor masses of L2 and T11 protruded into the vertebral canal and compressed corresponding sites of spinal cord.

For histology, tissues were fixed in *neutral buffered 10% formalin*, processed routinely for paraffin embedment, sectioned, and stained with hematoxylin and eosin (H&E). For the morphological evaluation of bone tissues, formalin-fixed bone tissues were decalcificated by Plank-Rychlo's solution [8], embedded in paraffin, sectioned, and stained with H&E. Microscopic examination of multiple cross sections of the tumor masses revealed that tumor cells were arranged in sheets or nests separated by the fine fibrovascular connective tissue (Fig. 4). The cytoplasm of the tumor cells was polyhedral, lightly eosinophilic, finely granular, and occasionally vacuolated. The cytoplasmic boundaries were usually indistinct, but occasionally distinct. Nuclei

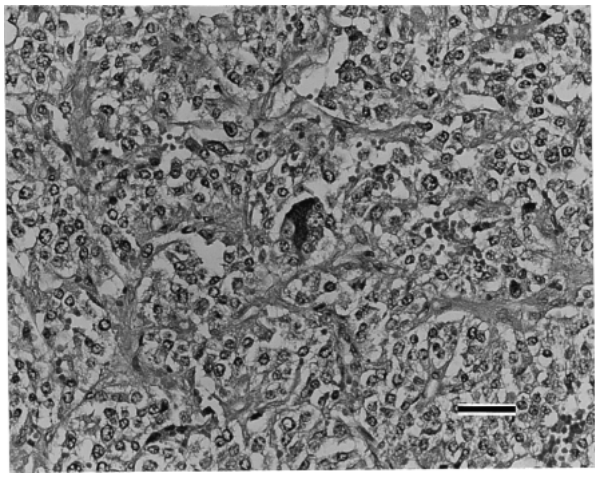

Fig. 4. Malignant aortic body tumor cells were arranged in nests which were separated by fine fibrous connective tissue. Note a bizarre giant cell among tumor cells. H&E stain. Bar= 65 μm.

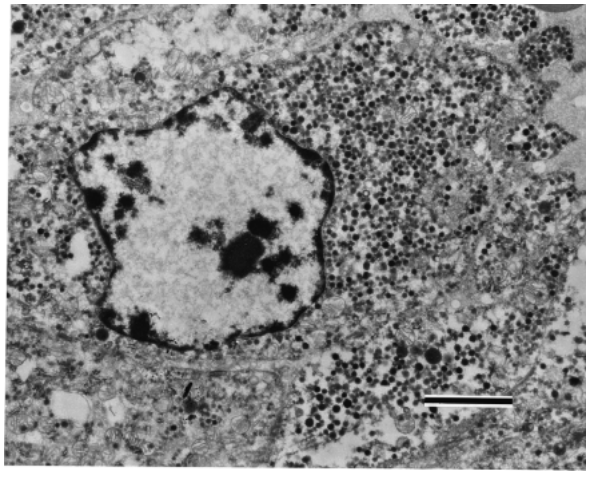

Fig. 5. Tumor *cells* contained abundant small, electron-dense, membrane-limited secretory granules in cytoplasm. Uranyl acetate and lead citrate. Bar= 2 μm.

varied in size and shape, but most were round to oval and usually centrally located. Chromatin was usually clumped. Frequently, giant cells were observed among the tumor cells (Fig. 4). These giant cells were pleomorphic and characterized by a large bizarre hyperchromatic nucleus and moderate to abundant, lightly eosinophilic fine cytoplasmic granules. Mitotic figures were uncommon. The areas of coagulative necrotic tumor cells were scattered among the tumor tissues. The histopathological characteristics of tumor masses in the myocardium, bodies of T 11 and L4 vertebrates, body of right femur, right infraspinous fossa near the neck of scapula, and tracheobronchial lymph node were identical with those of tumor masses in the heart base. In addition, the tumor masses metastasizing to each bone and lymph node produced an osteolytic lesion and cortical

atrophy, respectively. The tumor cells infiltrated into the lumbar and thorax bone marrow spaces with focal loss of spongiosa and extended into the vertebral canal but not into the dura matter and spinal cord. There was marked demyelination of white matter in spinal cord compressed by protrusion of the tumor mass. The lung exhibited diffuse moderate interstitial pneumonia with moderate congestion. There were frequent moderate to severe swelling of centrilobular hepatocytes in the liver. The significant lesions were not detected in the remaining organs and tissues.

For transmission electron microscopy, blocks of tumor masses (about 2 mm in diameter) were fixed in Karnovsky's fixative (2% paraformaldehyde, 2.5% glutaraldehyde in 0.1 M sodium phosphate buffer) for 2 hr, rinsed in 0.1 M phosphate buffer (PB), postfixed in 1% osmium tetraoxide-0.1 M PB, and embedded in Quetol (Epon 812). Ultra-thin sections were double-stained with uranyl acetate and lead citrate and examined with a JEOL JEM-1210 electron microscope. Ultrastructurally, the clusters of tumor cells were composed mainly of light granular cells with some dark granular ones. Differences between light and dark granular cells were related mainly to the number of small, electron-dense, membrane-limited secretory granules in cytoplasm, scattered in light granular but abundant in dark granular cells (Fig. 5). Cytoplasm of both tumor cells was generally abundant in amount and contained large numbers of small spherical mitochondria, a few profiles of rough endoplasmic reticulum, and moderate number of vesicles and smooth endoplasmic reticulum. The nuclei of tumor cells were oval to irregular in shape and varied in size. The nucleus frequently contained usually clumped peripheral chromatin, small prominent nucleolus, and a distinct nuclear membrane. Nuclear vesicles formed by large outpocketings of the nuclear membrane were frequent.

By the ultrastructural characteristics, the aortic body tumor can be easily differentiated from the other heart base tumors, ectopic parathyroid gland tumors and ectopic thyroid gland tumors [2, 4, 7]. The presence of electron-dense, membrane-bound cytoplasmic granules was the unique feature of the aortic body tumor cells as seen in the present case [2, 4, 7]. Therefore, the present tumor was diagnosed as aortic body tumor. In addition, the histopathological and ultrastructural findings of all tumor masses in the thorax and lumbar vertebrae, bones, and regional lymph node were identical with those of heart base aortic body tumor, reading that the lesions in the vertebrae, bones, and lymph node were thought to be metastatic from the heart base aortic body tumor.

Malignant aortic body tumor is known to prefer local invasion of the pericardium, epicardium, myocardium and walls of great vessels at the base of the heart [2, 7]. When metastasis occurs even infrequent, it may involve the regional lymph nodes, liver, and lung [2, 7]. In the present case, however, metastasis of tumor cells occurred into multiple bones as well as a tracheobronchial lymph node and the myocardium. By careful examination of multiple cross sections of the other organs and tissues, we could not find any metastasized tumor cells. As far as we known, there were only five reports about metastasis to bone [1, 3, 6, 7, 9], in which only one cited multiple bone metastases (proximal femur and 2 ribs) [1]. Therefore, it is thought that this case is an extremely rare case of malignant aortic body tumor which metastasized to multiple bones. Besides, paraplegia seen in the present case might have followed direct spinal cord compression by protrusion of tumor masses into the vertebral canal.

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