J. Comp. Path. 2014, Vol. 150, 8–17

Available online at www.sciencedirect.com

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NEOPLASTIC DISEASE

Occurrence of Tumours Metastatic to Bones and Multicentric Tumours with Skeletal Involvement in Dogs

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Summary

The skeletons of 110 dogs with malignant tumours of different origins were examined by necropsy examination over a 3-year period to identify bone metastases. Twenty-one cases of metastatic or multicentric tumours with bone involvement were recorded. In general, more female dogs presented with bony metastases; however, when the dogs with mammary tumours were omitted, the gender distribution of the cases was approximately equivalent. The mammary gland was the primary site of most of the metastatic bone lesions, followed by the musculoskeletal system and the respiratory system. The majority (77%) of metastases were grossly visible and present in multiple bones. However, in 23% of the cases, the metastases could be diagnosed only at the microscopical level. The vertebrae and the humerus were the most frequently affected bones regardless of the primary site and the histogenesis of the tumours. The results of this study revealed a high prevalence of bone metastases and/or bone involvement in dogs with multicentric tumours.

Keywords: dog; oncology; pathology; skeletal metastasis

Introduction

In veterinary medicine, information available about bone metastases and the bone involvement of multicentric tumours is limited to the description of individual cases and restricted to a small number of more comprehensive studies, which are relatively old (Misdorp and Den Herder, 1966; Goedegebuure, 1979; Cooley and Waters, 1998). Thus, most of the current clinical and pathological veterinary information on this subject concerns comparisons with human studies (Lester and Keller, 2003).

Bone metastases are a frequent and serious complication in human patients with advanced cancer (Lipton, 2004; Akhtari *et al*., 2008). They are more prevalent than primary bone tumours and are often associated with severe bone pain, pathological fractures and compression of the adjacent muscular structures and nerves, as well as spinal cord compression in the case of vertebral involvement (Berettoni and Carter, 1986; Riccio *et al*., 2007; Hofbauer *et al*., 2008).

Detection of bone metastases has prognostic and therapeutic significance for human patients (Boxer *et al*., 1989) and diagnostic imaging methods such as standard radiography are useful techniques for the early detection of metastases, particularly in cases where structural bone changes have occurred (Riccio *et al*., 2007). Furthermore, inspection of the skeleton at necropsy examination, although time consuming and requiring meticulous work, is an accurate method of detecting bone metastases (Resnick and Niwayama, 1995).

In man, the skeleton is the third most common site of metastasis after the lungs and liver. Bone metastases have been observed in approximately 60–70% of patients who die from disseminated cancer and

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0021-9975/$ - see front matter
http://dx.doi.org/10.1016/j.jcpa.2013.07.002

whose bodies are submitted for autopsy (Jaffe, 1958; Lichtenstein, 1972; Berettoni and Carter, 1986; Lester and Keller, 2003; Virk and Lieberman, 2007).

In most cases, bone metastases occur via the haematogenous route, are multiple and involve the bone regions that contain large amounts of active bone marrow (Berettoni and Carter, 1986; Resnick and Niwayama, 1995; Coleman, 2006). Although virtually any malignancy can metastasize to bones, carcinomas of the breast, the prostate, the lungs, the kidneys and the thyroid gland account for approximately 80% of those metastases in man (Berettoni and Carter, 1986; Riccio *et al*., 2007).

In contrast to man, bone metastases are considered to be unusual in dogs and less common than primary bone tumours (Thompson and Pool, 2002; Rosol *et al*., 2003; Chun and Lorimier, 2003). In the available studies, the prevalence of diagnoses of bone metastases within a population with tumours was 5.8% or 11.4%, depending on the detection methodology (Goedegebuure, 1979; Cooley and Waters, 1998). Compared with dogs with primary bone tumours, the dogs with metastatic bone tumours constitute a more heterogeneous group that is characterized by variable-sized and older dogs (Brodey *et al*., 1966). Metastases have been reported most frequently in the axial skeleton (particularly in the vertebrae) and in the proximal appendicular bones, such as the humerus and femur (Goedegebuure, 1979; Cooley and Waters, 1998).

Despite the possible existence of a real difference between the frequency of skeletal metastases in man and domestic animals, it is believed that bone metastases in dogs are underestimated (Brodey *et al*., 1966; Misdorp and Den Herder, 1966; Owen, 1967; Thompson and Pool, 2002). This is largely because the skeleton is rarely completely examined by radiography and necropsy examination (Thompson and Pool, 2002).

The aim of the present study was to provide new and more accurate data on the occurrence of bone metastases in dogs through necropsy examination.

Materials and Methods

This study of metastatic bone tumours and multicentric tumours with bone involvement was performed over a period of 3 years. Dogs submitted to the necropsy service of the Laboratório de Patologia Veterinária, Universidade Federal de Santa Maria that displayed gross evidence of metastasis to lymph nodes and/or other organs from tumours of different origins, gross evidence of malignancy (i.e. large infiltrative tumours or tumours accompanied by large areas of necrosis) or multicentric organ involvement were selected for the study. A specific methodology was necessary for this study, which is briefly described below.

The bones were sawed with a handsaw or a bandsaw and inspected for gross lesions. The following bones were collected from the selected cases: both humeri and femurs as well as a segment of the pelvic bones (at the pubic symphysis). The entire spine was sectioned longitudinally and evaluated grossly. In the absence of gross lesions, only the seventh and eighth thoracic vertebrae were collected. Their corresponding ribs and sternebrae were collected in all cases. The selection of these specific bones was based on the bones in which metastases are most frequently found in dogs and people (Jaffe, 1958; Goedegebuure, 1979; Lee-Parritz and Lamb, 1988; Thompson and Pool, 2002).

The long bones (humeri and femurs) were sectioned longitudinally and sections of approximately 4 mm in thickness were obtained. Sections of the proximal metaphyses were taken and, in the absence of gross lesions, only the trabecular bone was collected. In cases where gross changes were observed in the cortical regions of these bones, they were included in the samples to be processed. Sections (4 mm thick) were also obtained from the other bones.

The samples were placed into plastic cassettes for histological processing, fixed in 10% neutral buffered formalin, decalcified in an aqueous solution of formic acid and sodium citrate and processed routinely for histopathology.

Results

In the 3-year period of this study, the skeletons of 110 dogs were examined. Most of these dogs had a single primary, potentially malignant tumour. In some cases the dog had more than one tumour and for this reason 118 malignant tumours were detected in the 110 dogs included in the study (Table 1).

Multicentric ($n = 1$) or metastatic bone involvement ($n = 20$) was observed in 21 dogs (19.1%) and the epidemiological, clinical and pathological data for these dogs are summarized in Table 2.

The number of females with affected bones ($n = 16$) exceeded males ($n = 5$) by a factor of 3.2. However, when mammary gland tumours were not considered, this ratio was 1.3 affected females for each male. The age of the affected dogs ranged from 4 to 16 years, with a mean age of 9 ± 3.15 years. One third of the dogs were not of a specified breed. Among the dogs with a specified breed, rottweilers ($n = 4$) and poodles ($n = 3$) were the most commonly affected. Most of the dogs (62%) had been humanely destroyed.