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What Is Your Diagnosis?

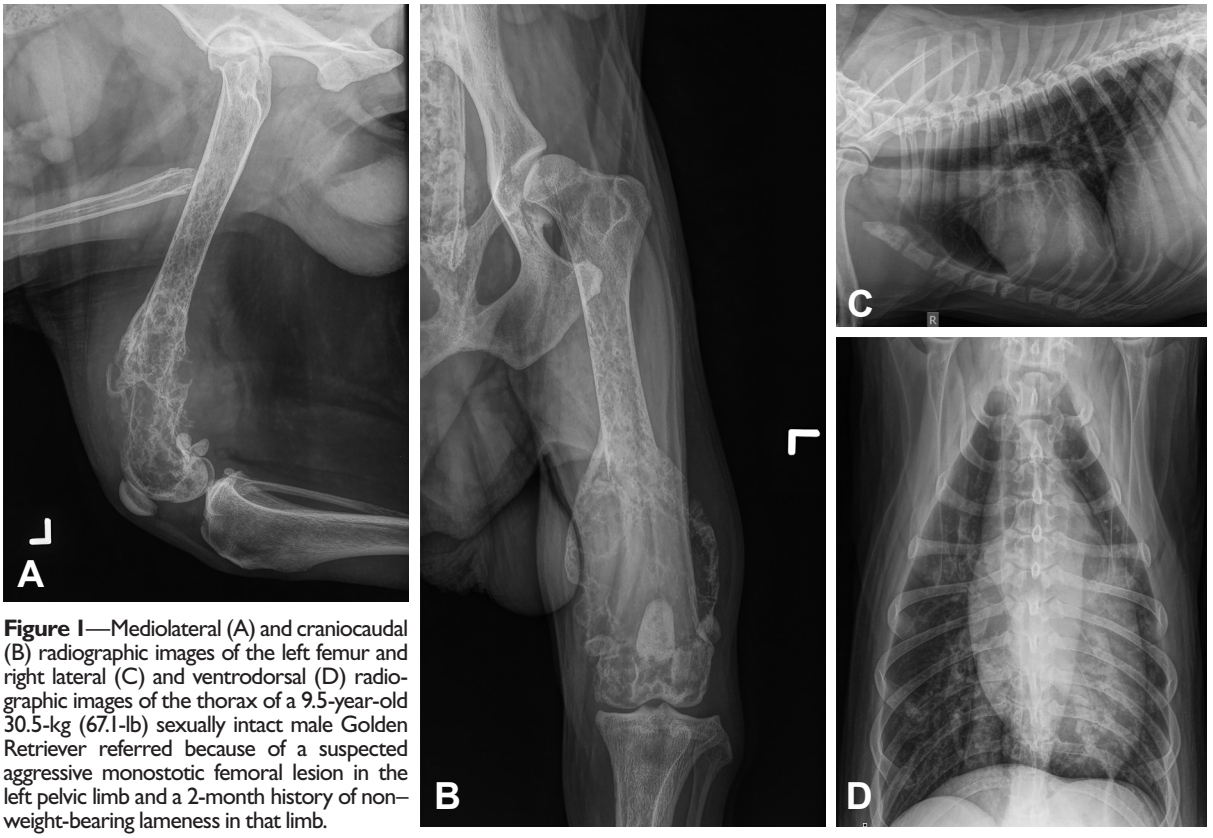

Figure 1—Mediolateral (A) and craniocaudal (B) radiographic images of the left femur and right lateral (C) and ventrodorsal (D) radiographic images of the thorax of a 9.5-year-old 30.5-kg (67.1-lb) sexually intact male Golden Retriever referred because of a suspected aggressive monostotic femoral lesion in the left pelvic limb and a 2-month history of non–weight-bearing lameness in that limb.

History

A 9.5-year-old 30.5-kg (67.1-lb) sexually intact male Golden Retriever was referred because of a 2-month history of non–weight-bearing lameness of the left pelvic limb; the referring veterinarian suspected an aggressive osteolytic lesion and pathological fracture of the left femur on the basis of radiographic findings (not shown). In addition, the dog had a 1-year history of persistent hyperglobulinemia and had had a prescapular mass removed 2 years before the present referral.

On referral examination, the dog was non–weight-bearing on the left pelvic limb, showed signs of pain on palpation of that limb, and had substantial muscle atrophy over the left femur. In addition, the dog had a large (approx 4.8 X 5.6 X 4.2-cm) subcutaneous mass in the left prescapular region; however, no signs of pain were elicited on palpation of the mass. The dog's right testicle was subjectively smaller and firmer than its left testicle. The remainder of findings from physical examination were unremarkable.

Hematologic evaluation revealed mild nonregenerative anemia (Hct of 38% [reference range, 41% to 58%] with a reticulocyte percentage of 0.4% [reference range, 0.2% to 1.5%]) and hyperproteinemia (8.6 g/dL; reference range, 5.5 to 7.2 g/dL), characterized by hypoalbuminemia (2.3 g/dL; reference range, 3.2 to 4.1 g/dL) and hyperglobulinemia (6.3 g/dL; reference range, 1.9 to 3.7 g/dL). Urinalysis revealed proteinuria (2+) and a urine specific gravity of 1.030. Results of cytologic examination of a fine-needle aspirate sample from the prescapular mass indicated plasma cell tumor. Radiography of the thorax and left pelvic limb was performed. **(Figure 1)**.

Formulate differential diagnoses and treatment strategies from the history, clinical findings, and Figure 1—then turn the page →

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Diagnostic Imaging Findings and Interpretation

The distal region of the left femur had evidence of severe, locally extensive permeative and moth-eaten lysis with a long zone of transition that extended to the proximal aspect of the diaphysis **(Figure 2)**. In addition, the left femur had severe thinning to complete loss of the cortices circumferentially; evidence of an expansile, solid, relatively smooth periosteal reaction; and a pathological fracture in the distal aspect of the diaphysis with mild craniocaudal displacement. The surrounding soft tissue was moderately and focally swollen.

On thoracic radiography, the first sternebra had evidence of locally extensive, moth-eaten lysis and a faint amorphous periosteal reaction (Figure 2). In the caudoventral area of the left caudal lung lobe, there was a small (approx 0.9 cm in diameter), well-defined soft tissue opaque nodule, and the midbody of the right eighth rib had a focal lytic lesion, characterized by cortical thinning and expansion with interrupted periosteal reaction.

Our primary differential diagnosis for the radiographic findings was metastatic neoplasia. Two scenarios were prioritized: a primary bone tumor (eg, osteosarcoma, chondrosarcoma, fibrosarcoma, or hemangiosarcoma) of the left femur with metastases or a round-cell neoplasm (eg, multiple myeloma, histiocytic sarcoma, or lymphoma) affecting multiple sites. The aggressive bone lesion of the left femur was considered most likely to have been the primary neoplasm, particularly because round-cell neoplasms are usually limited to lytic lesions rather than proliferative bony lesions. However, given the hematologic finding of hyperglobulinemia and the cytologic finding for the prescapular mass of plasma cell tumor, an atypical presentation of multiple myeloma was not excluded.

Abdominal and testicular ultrasonography were performed (images not shown) for staging purposes on the basis of our high index of suspicion for a neoplastic process. Findings included multiple small, distinctly margined, hypoechoic nodules within the renal cortices, and the sizes of both kidneys were clinically normal. The spleen contained a few small hypoechoic nodules (all ≤ 0.1 cm in diameter), and the liver contained a few small nodules, most of which were hypoechoic. The right testicle contained 4 to 5 small, hypoechoic nodules (largest, 1.8 cm in diameter), and the left testicle contained 1 small (0.7 cm in diameter) hypoechoic nodule. Results of ultrasonography were considered suggestive for metasta-

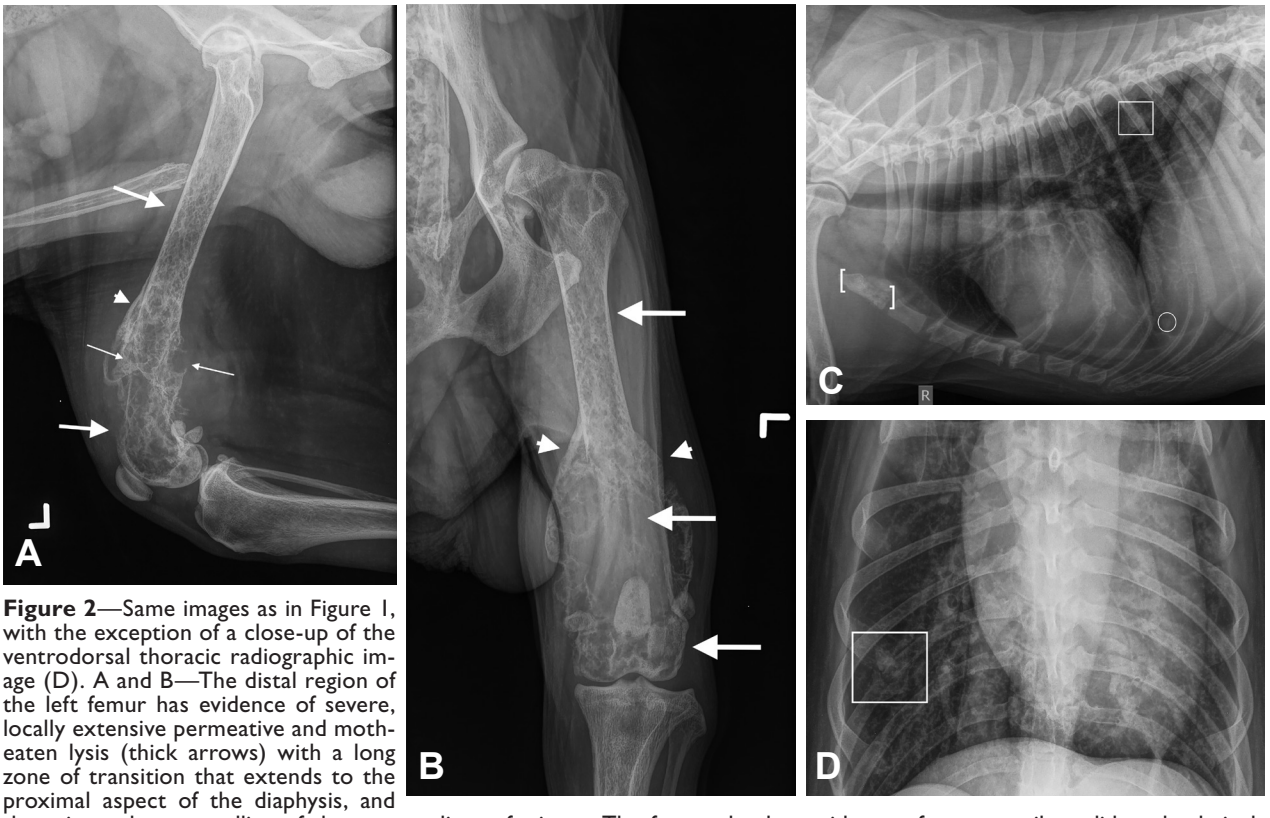

Figure 2—Same images as in Figure 1, with the exception of a close-up of the ventrodorsal thoracic radiographic image (D). A and B—The distal region of the left femur has evidence of severe, locally extensive permeative and moth-eaten lysis (thick arrows) with a long zone of transition that extends to the proximal aspect of the diaphysis, and there is moderate swelling of the surrounding soft tissue. The femur also has evidence of an expansile, solid, and relatively smooth periosteal reaction (arrowheads) distally and a pathological fracture (thin arrows) in the distal aspect of the diaphysis with mild craniocaudal displacement. C and D—The first sternebra has evidence of locally extensive, moth-eaten lysis and a faint amorphous periosteal reaction (brackets). There is a well-defined nodule (circle) in the area of the left caudal lung lobe. The proximal aspect of the right eighth rib has a focal lytic lesion with cortical thinning and expansion with interrupted periosteal reaction (square) evident on the ventrodorsal projection (D) but difficult to appreciate on the right lateral projection (C).

ses; however, the primary neoplasm had not yet been confirmed cytologically.

Treatment and Outcome

The dog underwent amputation of the left pelvic limb and removal of the left prescapular mass. Histologic examination of tissue sections from the amputated limb revealed fibroblastic osteosarcoma at the fracture site in the distal aspect of the femur in conjunction with plasma cell infiltrates that replaced normal bone marrow and caused a microfracture of the cortical bone, consistent with multiple myeloma, in the proximal aspect of the femur. Histologic results for the prescapular mass indicated that it was the superficial cervical lymph node effaced by a malignant round-cell neoplasm, most suggestive of a malignant plasma cell tumor owing to its strong nuclear immunoreactivity to immunohistochemical staining to detect MUM1 protein. Serum electrophoresis revealed a monoclonal gammopathy with high β-globulin concentration (3.56 g/dL; reference range, 0.83 to 1.79 g/dL), and results of cytologic examination of an ultrasound-guided fine-needle aspirate sample of one of the nodules in the right renal cortex indicated a plasma cell tumor.

Chemotherapy with alternating doses of doxorubicin (1 mg/kg [0.45 mg/lb]) and carboplatin (300 mg/m^2) was administered IV every 3 weeks for 6 treatments. The dog was also prescribed prednisone (1 mg/kg, PO, q 24 h) to reduce the malignant plasma cell tumor burden. Prior to receiving the third doxorubicin treatment, the dog developed signs of pain on palpation over the region of its caudal thoracic vertebrae, weakness in its right pelvic limb, and ataxia. Radiography of the vertebral column revealed polyostotic aggressive lesions of L2-L4, consistent with metastases of multiple myeloma or osteosarcoma already diagnosed in this dog. Because of the clinical progression of disease, additional treatment options were discussed, such as palliative radiation therapy (as an alternative to or in conjunction with chemotherapy) or altering chemotherapy to include melphalan combined with a higher dosage of prednisone. The owner did not pursue further treatment, and the dog was lost to follow-up shortly thereafter.

Comments

The dog of the present report had concurrent osteosarcoma and multiple myeloma, the combination of which, to our knowledge, had not been reported previously. Initial findings in the dog were typical of those for dogs with a primary bone tumor. Osteosarcoma is by far the most common primary bone tumor of dogs and has been reported to represent as high as 86.7% (78/90) of all malignant primary bone tumors diagnosed.[1] Most affected dogs are presented between 6 and 10 years of age, and Golden Retrievers are one of the breeds with an increased risk of developing osteosarcoma.[1] The most common locations for osteosarcoma are the proximal metaphyses of the humerus and tibia and the distal metaphyses of the radius and femur, with the front limbs affected more commonly than the hind limbs.[2] Radiographically, lesions caused by osteosarcoma commonly have periosteal reactions, long zones of transition between affected bone and normal bone, and moth-eaten to permeative lysis in affected metaphyses that can lead to pathological fractures,[3] as was evident in the dog of the present report. However, osteosarcoma cannot be distinguished from other primary bone tumors on the basis of radiographic findings alone, and definitive diagnosis requires a tissue biopsy with histologic evaluation,[4] as was performed on the limb amputated from the dog in the present report.

Our concern for an atypical presentation of a round-cell neoplasm or concurrent secondary process developed during interpretation of findings from thoracic radiography, given that multiple myeloma is typically polyostotic with purely lytic lesions and no reactive periosteal reaction, whereas osteosarcoma is usually monostotic.[2] In addition, the dog had persistent hyperglobulinemia (which with serum electrophoresis we later characterized as a monoclonal gammopathy) and recurrence of a mass in the left prescapular region (later diagnosed cytologically and histologically as plasma cell tumor). Results of ultrasonography further substantiated suspicion of a second neoplastic process owing to findings of multiple sites (spleen, liver, kidneys, and testicles) affected with lesions consistent with potential metastases. These findings, in addition to the osteolytic lesions identified radiographically, led us to a presumptive diagnosis of multiple myeloma, the clinical features of which typically include osteolytic bone lesions, Bence-Jones proteinuria, and monoclonal gammopathy. Findings on histologic examination of tissue sections from the amputated limb supported our presumptive diagnosis; however, definitive diagnosis of multiple myeloma is made by cytologic examination of bone marrow aspirates for evidence of plasmacytosis.[2]

Findings in the dog of the present report emphasized the importance of fully evaluating radiographic images to ensure that all relevant findings and differential diagnoses are identified so that all appropriate treatment options and protocols may be considered. The recognition of inconsistencies between typical signs of osteosarcoma and findings on physical, radiographic, and ultrasonographic examinations of the dog in the present report was critical to including multiple myeloma on the differential diagnosis list when the amputated limb was submitted for histologic examination and in developing treatment options and protocols.

References

1. Trost ME, Kommers GD, Brown CC, et al. Primary bone neoplasms in dogs: 90 cases. *Pesqui Vet Bras* 2012;32:1329–1335.
2. Withrow S, Vail D, Page R. Hematopoietic tumors. In: *Withrow and MacEwen's small animal clinical oncology*. 5th ed. St Louis: Saunders Elsevier, 2013;608–678.
3. Vanel M, Blond L, Vanel D. Imaging of primary bone tumors in veterinary medicine: which differences? *Eur J Radiol* 2013;82:2129–2139.
4. MacEwen EG, Kurzman ID. Canine osteosarcoma: amputation and chemoimmunotherapy. *Vet Clin North Am Small Anim Pract* 1996;26:123–133.