History

An adult, 29.6-kg spayed female mixed-breed dog that was dead on presentation to its primary veterinarian was evaluated. Earlier that day, it underwent surgery to remove masses from the ventral aspect of the neck, caudal region of the left flank, and inner right aspect of the stifle joint. The dog recovered well from anesthesia and was discharged to the owner but died an hour later. The dog was reportedly current for vaccinations against *Bordetella bronchiseptica*, canine distemper virus, hepatitis virus, parvovirus, parainfluenza virus, and rabies virus and was negative for heartworm antigen and fecal parasites.

Clinical and Gross Findings

At necropsy, the dog had a cutaneous incision apposed with suture material at the right side of the stifle joint, left flank, and base of the neck. Both eyes were mildly exophthalmic.

The lungs were dark red and firm, and oozed dark red, nonviscous fluid when sectioned. Petechia were scattered across the tracheal mucosa and green-brown mucus covered mucosal surface. Similar fluid was present throughout the esophagus and in the stomach where there was also partially digested food material. The serosa of the pyloric antrum was reddened. The pancreas was also dark red and edematous.

Protruding from the external surface of the parietal and frontal bones, compressing the temporalis muscles, was a 9 X 5 X 4-cm, firm, pale tan, gritty mass. The mass bulged into the cranial cavity, compressing the frontal lobes of the cerebrum (Figure 1).

Formulate differential diagnoses, then continue reading.

Histopathologic Findings

Representative sections of the calvarial mass, brain, cerebellum, lungs, trachea, a randomly selected lymph node, spleen, portion of the temporalis muscle that bordered the mass, pancreas, heart, kidneys, small intestines, large intestines, and urinary bladder were fixed in neutral-buffered 10% formalin and processed routinely for histologic examination.

The mass was expansile and infiltrative and comprised of numerous, well-demarcated lobules containing cells that were differentiated along several lines and separated by prominent fibrous septa. Lobules were comprised of proliferating mesenchymal cells resembling fetal osteoblasts that formed well-differentiated nonmineralized and mineralized osteoid and chondroid matrices (Figure 2). Associated osteocytes and chondrocytes were embedded within lacunae within the lobules. Anisocytosis and anisokaryosis were moderate with no mitoses observed in 2.37 mm² (equivalent to 10, FN22/40X fields). Few lobules were necrotic and adjacent myofibers were compressed and atrophied.

Various collagen types were observed in sections of the neoplasm after application of a picrosirius red histochemical stain and examination with filtered, polarized light microscopy. Primarily, type I collagen was observed within the fibrous septa and mineralized osteoid matrix (changing from red to yellow with polarization); nonmineralized osteoid or chondroid matrix had more prominent type II or III collagen (blue-green appearance with polarization [Figure 2]).

Mild hemorrhage expanded the leptomeninges, and the gyri of the cerebral frontal lobes were

Figure 1—Photographs of a mass in the frontal and parietal bones of a dog that died suddenly after anesthesia for removal of several skin masses. The mass measured 9 X 5 X 4 cm. A—The skull mass has expanded outward from the calvarium, pushing against the temporalis muscles, and inward into the cranial cavity. B—Notice the irregular thickening of the inner surface of the calvarium, which had resulted in severe compression of the dorsal portion of the cerebrum (frontal lobes).
Multilobular tumor of bone is an uncommon, slow-growing, locally invasive neoplasm that most frequently arises in the bones of the skull. Although this tumor type has no sex or breed predilection in dogs, it frequently affects middle-aged to older dogs (median age, 8 years) of medium to large breeds (median weight, 29 kg). The name of this tumor has changed often in the past but the term MTB is now preferred because it encompasses the tumor’s variable histologic morphologies and its potential to be benign or malignant.

Results of diagnostic imaging of these neoplasms are often characteristic or strongly suggestive of MTB. Radiographically, this neoplasm has a common, so-called popcorn ball appearance that is characterized by a well-delineated, multilobulated, expansile growth from the underlying bone with typical mineral or bone opacity. Although radiographic findings may be strongly indicative of MTB, noncontrast CT may be used to evaluate the extent of calvarial invasion.

Like most neoplasms, histologic examination of specimens is required for a definitive diagnosis. The tumor has a complex pattern of lobules separated by fibrous septa. The appearance of the lobules can vary considerably within a spectrum of well-defined cartilaginous matrix with chondrocytes to bony trabeculae with osteocytes. Use of a grading scheme developed by Straw et al. based on the histologic appearance of the tumor provides a baseline for predicting the tumor’s behavior in dogs. The grading scheme incorporates whether the tumor is invasive or expansive, size of the tumor lobules and their cellular organization, number of mitotic figures, pleomorphism of cells, and presence of necrosis. On the basis of those characteristics, a grade of I to III can be assigned to the tumor. Tumor grade has been associated with time to recurrence, metastatic rate, and survival time. Lower grades are associated with longer median times to recurrence or metastasis and survival time. In the present case, the tumor was considered grade 2, indicative of a mean survival time of 18 months with an approximately 10-month interval to metastasis, if that were to occur.

The histologic origin of MTB is still uncertain, but most cases of MTB appear to develop in the dermocranium or viscerocranium layers of the skull. Some cells in the calvarial periosteal cambium are able to produce cartilage as well as bone. One hypothesis suggests that changes in the regulatory signals in the cambium of the dermocranium or viscerocranium may lead to the unique histologic structure seen in MTBs. This tumor type typically expands from the bone and compresses the local soft tissues. Although MTB does not frequently invade other tissues, it has been shown to occasionally spread to the lungs late in the disease process. Fortunately, metastases also appear to have a slow growth-rate and dogs do not frequently have signs associated with clinical disease in the lungs.

Multilobular tumor of bone is most

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**Figure 2**—High magnification photomicrographs of sections of the mass. A—The cells are organized into lobules of unmineralized osteoid (asterisk) and mineralized osteoid, and cartilage (arrow), separated by fibrous septa (F). H&E stain; bar = 200 μm. B—Following picrosirius red histochemical staining, polarized light highlights the fibrous septa (F), osteoid (asterisk), and mineralized osteoid and cartilage (arrow). Picrosirius red histochemical stain; bar = 200 μm.

Variably flattened with fine vacuolation of the cortical neuroparenchyma and numerous microglial cells. Other histologic findings included tracheal hemorrhage with aspirated material. Alveoli were diffusely expanded by edema, and the large airways contained abundant mucus. Mild lymphoplasmacytic gastritis and pancreatic hemorrhage were also present.

**Morphologic Diagnosis and Case Summary**

Morphologic diagnosis and case summary: grade 2 calvarial multilobular tumor of bone (MTB) in a dog.

**Comments**

The cause of death for the dog of the present report was most likely secondary to aspiration of gastric contents following anesthesia for the removal of several skin lesions. Aspiration of gastric contents was supported grossly and histologically by the presence of feed material in the tracheal lumen and acute tracheitis. Furthermore, mild gastritis was evident histologically, which may have additionally contributed to regurgitation and aspiration. No cause of the underlying gastritis was determined. Anesthetic procedures may predispose animals to regurgitation and vomiting leading to aspiration pneumonia if preanesthesia food withholding is not optimal. The preexisting MTB may have been an additional stimulus to vomit in this dog. Slight increases in intracranial pressure during anesthesia may have contributed to compression of the cerebrum, which may have stimulated the vomiting centers in the caudal portion of the brainstem. Other causes of death for this dog, such as cardiopulmonary failure or electroconductive disturbances (eg, 1 or more acute arrhythmic episodes) could not be entirely ruled out; however, no histologic changes associated with myocardial disease or congestive heart failure were detected.
common in dogs, but these neoplasms in humans, cats, a horse, and a ferret have also been reported.8,9 Clinical signs depend on the tumor’s location and size.1 Multilobular tumors of bone often present as a firm, immovable mass on the skull, most frequently involving the calvarium, maxilla, mandible, orbit, zygomatic arch, and tympanic bulla.1,10,11 However, there have been cases where a mass was not evident during physical examination, as evidenced in the case described in the present report.7 Tumors of the calvarium can cause neurologic signs through compression of the brain, cranial nerves, or cervical portion of the spinal cord.2 Because MTBs grow slowly without invading the nearby soft tissues, they generally have to grow to a considerable size before clinical signs are evident.1 In this dog, there were no reported neurologic signs even though the cerebrum was compressed. From the tumor’s location, expected clinical signs would include onset of dementia, loss of the dog’s recognition of its owner, difficulty with training, compulsive pacing, circling, and seizures, all of which may have been confused with effects of advanced age in a dog.1,2

The treatment of choice for MTBs is complete surgical excision with margins.3 Surgery can prove difficult due to a tumor’s location, but it can result in long-term remission from disease.3,6 Cisplatin chemotherapy with and without radiation therapy represent attempted treatments.1,5 However, given the slow growing nature of this type of tumor, it is likely to be resistant to radiation therapy. Moreover, tumor progression and metastasis have occurred despite administration of chemotherapeutics.5 Compared with tumors excised with complete margins, tumors excised with incomplete surgical margins are 11 times as likely to recur.1 Overall, recurrence rates are high, ranging from 47% to 58%.1,5 It should be noted that not all tumors will recur or metastasize, but those that do recur also seem to be more likely to develop pulmonary metastases.2 Median recurrence intervals for MTBs in dogs range from 420 to 797 days.1,5

Acknowledgments

No third-party funding or support was received in connection with this study or the writing or publication of the manuscript. The authors declare that there were no conflicts of interest.

References