Canine Breed Predisposition to Cancer

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Introduction

Particularly now that pets are living longer, cancer has become a leading cause of death in dogs.[1] Cancer can affect all breeds of dogs, but there are some breeds that appear to be at higher risk to certain types of cancer. Given the similarities between many human and canine cancers, the domestic dog has been used as a model of spontaneous neoplasia.[2]

Histiocytic Sarcoma: Bernese Mountain Dog

General Information:
- Mean age of onset is 6.5 years
- Comprises 25% of cancer diagnoses in Bernese Mountain Dogs
- Average survival is 49 days[3]
- Polygenic mode of inheritance in Bernese Mountain Dogs[3,4]
- Can arise from interstitial dendritic cells or macrophages[4]

Clinical Manifestation:
- Primary tumors can occur in the spleen, lymph nodes, lung, bone marrow, meninges, skin, and joints
- Clinical signs depend on organs involved and can include dyspnea, seizures, and lameness[4]

Genetic Alterations:
- Abnormalities have been described in tumor suppressors *CDKN2A/B*, *RB1*, and *PTEN*[4]

Histiocytic Sarcoma in the lung and eye of a Bernese Mountain Dog

Photos courtesy of Amanda Koehne, DVM

Astrocytoma: Boxer

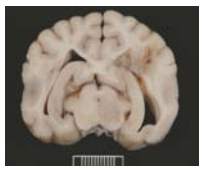
General Information:
- Boxers and brachycephalic breeds are predisposed
- Older dogs are primarily affected
- Represent 17% to 28% of all canine primary CNS tumors[5]

Clinical Manifestation:
- Mentation changes, seizures, vestibular disturbances, and vision loss[5]

Treatment:
- Chemotherapy, generally alkylating agents, either alone or in combination with radiotherapy or surgery
- It is unknown whether therapeutic intervention enhances chances of survival beyond supportive measures[5]

Genetic Alterations:
- Gene modifications associated with brachycephalic skull types or related phenotypes may be connected to the increased prevalence of glial neoplasms and brachycephalic dog breeds[6]
- MRI has dramatically helped to detect and characterize astrocytic tumors in people, and it will likely provide similar benefits for dogs[5]
- Similarly to astrocytomas in humans, canine astrocytomas have also exhibited overexpression of the genes encoding p53 and the epidermal growth factor receptor (EGFR)[2]

Astrocytoma in a Soft Coated Wheaten Terrier



Courtesy of Molly Church, DVM

Osteosarcoma: large breeds

General Information:
- Most common primary bone tumor in dogs
- The mean age is 7 years[7]
- It occurs in large and giant breed dogs: Doberman, German Shepherd, Golden Retriever, Great Dane, Irish Setter, Rottweiler and Saint Bernard[8]

Clinical Manifestation:
- Occurs in the metaphysis of long bones, similar to disease in humans
- Most common in proximal humerus, distal femur, and proximal tibia
- Metastasis usually to lungs and other bones
- Most dogs exhibit lameness, as well as irritability, aggression, and anorexia
- Elevated serum alkaline phosphatase is associated with poor survival[7]

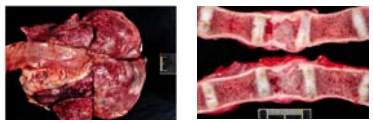
Treatment:
- Palliative radiation
- Amputation or limb spare procedures
- Chemotherapy for metastasis[7]

Genetic Alterations:
- Aberrations in p53 tumor suppressor gene
- In some cases irregular karyotypes and aneuploidy[7]

Osteosarcoma of the proximal humerus in a Rottweiler

Photos courtesy of Amanda Koehne, DVM

Pulmonary and vertebral osteosarcoma metastasis in a Labrador Retriever

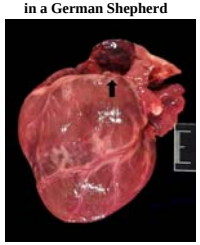


Hemangiosarcoma: German Shepherd

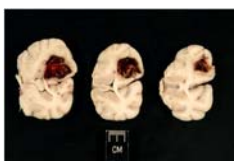
General Information:
- Most common in the spleen, right auricle of the heart, and liver
- Primarily affects older dogs
- German Shepherd Dogs are predisposed[1]

Clinical Manifestation:
- Clinical signs vary greatly depending on the tumor's location
- Can cause sudden death due to tumor rupture and/or dramatic blood loss[1]

Right auricular hemangiosarcoma in a German Shepherd



Metastatic hemangiosarcoma in the brain of a Beagle



Photos courtesy of Amanda Koehne, DVM

Treatment:
- Surgery: most common approach
- Chemotherapy, and occasionally radiation
- Average survival time < 1 year[9]

Genetic Alterations:
- Mutations in the tumor suppressor gene *TP53* have been reported[8]
- VEGF may play a role in canine disease[10]

Lymphoma: Golden Retriever

General Information:
- Most common tumor of the hematopoietic system in dogs
- Classification of canine lymphomas follows a similar classification scheme to that used for humans[13]
- Golden Retrievers are predisposed
- Higher incidence in middle-aged dogs (6-7 years)[14]

Clinical Manifestation:
- Clinical signs are highly variable and reflect the organs involved
- Lymphadenopathy, anorexia, and lethargy are common
- Typically, by the time it is diagnosed, lymphoma involves multiple lymph nodes and organs in the body[15]
- Clinical staging: I-V [13]

Treatment:
- Average survival is 12 months with chemotherapy
- CHOP protocol is often used for treatment: cyclophosphamide, doxorubicine, vincristine, and prednisone[16]

Genetic Alterations:
- Chromosomal gains and losses segregate specifically with B-cell tumors and T-cell tumors[17]
- A deletion of chromosome 14 has been seen exclusively in B-cell lymphoma and occurs in Golden Retriever with a higher incidence than in other species[8]

Lymphoma of the stomach (arrows) and gastric lymph node (*) in a Springer Spaniel

Photo courtesy of Amanda Koehne, DVM

Canine Comparative Oncology and Genomics Consortium

In 2004, a collaboration of veterinary and medical oncologists, pathologists, surgeons, geneticists, and molecular and cellular biologists joined to form the Canine Comparative Oncology and Genomics Consortium (CCOCG) through the NIH National Cancer Institute. Its goal is to "provide a forum for discussion and sharing of resources and reagents, and to guide the development of novel technologies that would allow the study and use of appropriate canine cancers in the global study of cancer biology and therapy."[11] The CCOCG maintains a repository for canine tumor specimens with the goal to collect 3000 canine tumor samples, particularly tumors that occur in both dogs and humans, over a three year period.[12] The CCOCG is currently accepting applications for tissue release.

Conclusions

Studying cancer in dogs is important, not just for the well being of our pets, but also for gaining insight into tumorigenesis and response to treatment across species. It is well understood that many traits are shared between human and canine cancers. By studying similarities and differences in tumors across species, we are able to enrich our understanding of these complex diseases. Never before has it been more important for human and veterinary medical professionals to collaborate. Programs such as the Canine Comparative Oncology and Genomics Consortium will aid in these collaborative efforts by providing shared resources for the cancer research community.

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