Canine Cutaneous Melanoma

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Abstract

A 7 year old female spayed Hovawart dog presented to the Cornell University Hospital for Animal’s Oncology service for further treatment options of a previously excised cutaneous malignant melanoma. Four months prior to presentation, the owners noted a small, black raised mass over the dog’s left lumbar region. The mass appeared to double in size over the next 3 weeks, and was surgical excised by the referring veterinarian. The margins of the excision at this time were found to be approximately 1-2 mm and the biopsy revealed malignant melanoma with approximately 40 mitosis per 10 high-powered fields (HPF). A scar revision surgery was performed by Cornell University Hospital for Animal’s Soft tissue surgery service on without complications.

Although melanoma of the haired skin is often benign, this dog's tumor had several criteria of malignancy, which often corresponds with a high metastatic rate. Due to the risk of metastasis, the Oncology service offered systemic therapy and the owner decided on the melanoma vaccine. Diagnosis, treatment options, and prognosis of cutaneous melanoma, along with the use of the melanoma vaccine to prolong survival for malignant melanoma will be discussed below.

Case history

A 7 year old female spayed Hovawart dog presented to the Cornell University Hospital for Animal’s Oncology service for further treatment options of a previously excised cutaneous malignant melanoma. The owner’s noted a black, raised mass over the dogs left lumbar region four months prior to presentation. An aspirate was performed at this time at the referring veterinarian; however the cytology results were inconclusive.
The dog had no clinical signs other than the mass, and no previous medical history. The dog competed in agility and was used as a therapy dog at libraries and hospitals.

The owners monitored the mass and one month prior to presentation to Cornell, it appeared to double in size over a period of 3 weeks. The mass was surgically excised by the referring veterinarian. At this time, a small cutaneous mass was also removed from the right side of the dog’s chest. The subcutaneous mass on the right side of the chest was found to be cystic in nature, however this was not submitted for histopathology. The excised mass over the left lumbar region was submitted for histopathology and the margins of the excision at this time were found to be approximately 1-2 mm and the biopsy revealed malignant melanoma, with approximately 40 mitosis per 10 HPF.

**Physical Exam**

On presentation to Cornell University’s Hospital for Animal’s Oncology service the dog presented for additional treatment options. Physical examination revealed, the dog was bright, alert, and responsive and her vital parameters were within normal limits (T = 102.2 F, P = 140 bpm, RR = 42 brpm). There was a small area that was clipped over the dorsal left flank where the mass excision occurred 2 weeks ago. The incision was approximately 4 cm in length and the epidermis was well apposed, non-absorbable sutures were intact, and no heat, mucopurulent discharge, or inflammation was present. Another area was clipped over the right side of the dog’s chest, where a cyst had been removed. The incision was small, contained no sutures, the epidermis was apposed, and no inflammation, discharge, or heat was present at the site. The remainder of the physical exam was within normal limits.
**Diagnostic Tests**

The initial work-up for the dog included a complete blood count, chemistry, urinalysis, abdominal ultrasound, and three-view thoracic radiographs. The complete blood count, chemistry, and urinalysis were performed to obtain a baseline health status on the dog, and the results were within normal limits. Thoracic radiographs and abdominal ultrasound were performed to search for evidence of metastasis. The three-view radiographs were clinically normal and negative for metastasis. The abdominal ultrasound revealed a diffusely, mildly enlarged spleen with normal echogenicity. Based on these findings, there was no strong evidence of metastasis and overall the dog appeared to be in good health.

**Problem List/Differential Diagnosis**

The problems identified based on history, physical examination, and diagnostic testing include a previous malignant cutaneous melanoma and diffuse, mild splenomegaly. The differential diagnosis for a pigmented cutaneous mass include; benign melanocytoma, melanocytic hyperplasia, hemangioma, hemangiosarcoma, basal cell tumor, or histiocytic sarcoma (Smith, 2002).

The differential diagnosis for diffuse, mild splenomegaly includes; normal breed variation, effects of sedation, mild congestion, or diffuse infiltration (due to inflammation or neoplasia such as lymphoma). Since this dog was sedated for imaging to be performed, it was likely the effects of sedation causing diffuse splenomegaly.
**Procedures and Treatment**

A consult with the Cornell University Hospital for Animal’s Soft tissue surgery service was performed. The soft tissue service decided that a scar revision surgery would be possible over the dog’s left lumbar region. This surgery would ensure adequate margins and excision of any remaining neoplastic cells. A scar revision surgery was performed by Cornell University Hospital for Animal’s Soft tissue surgery service the following week. A 9 x 5 cm elliptical skin incision around the pre-existing scar was made over the left lateral lumbar region using a #15 blade. The incision was extended down to include the dorsal edge of the external abdominal oblique superficial fascia by blunt dissection. The tissue removed was submitted for histopathology. The results of the histopathology performed by Cornell University Anatomic Pathology laboratory revealed no evidence of neoplastic cells, and only scar tissue and inflammation was present. This implies complete excision was achieved.

The slides from the original mass excision performed by the referring veterinarian, were submitted to the Cornell University Anatomic Pathology laboratory for review. The slide review found a highly cellular tissue with cells arranged in bundles and streams, similar to mesenchymal tissue. Some cells had pigment present and there were approximately 40 mitosis per 10 HPF. Immunohistochemistry using both Melan A and S100, revealed diffusely neoplastic cells with moderate to strong positive granular cytoplasmic staining.

Complete excision of the scar was achieved with no evidence of neoplastic cells. This likely implies that clean margins were obtained around the dog’s malignant melanoma, however there is always the possibility for error when evaluating margins.
The original findings on histopathology imply that the mass was a highly malignant melanoma with an aggressive mitotic rate of 40 mitosis per 10 HPF. Treatment of malignant melanomas involves both local control (with surgery) and systemic therapy to address the potential metastatic disease. Due to the high chance of metastasis, additional systemic therapy was offered for this dog and the owner elected to treat with the melanoma vaccine.

Discussion

The most common locations for melanoma to occur include the oral cavity, digit, and haired skin. Cutaneous melanoma is one of the most common skin tumors in dogs, consisting of approximately 5-7% of skin tumors and is most commonly benign (Withrow, 2007). Cutaneous melanoma occurs more commonly in dogs with heavily pigmented skin. Predisposed breeds include Boston terriers, Boxers, Chow chow, Cocker spaniels, Dobermans, Golden Retrievers, Scottish terriers (Morrison, 1998). The exact etiology of cutaneous melanoma is unknown, however ionizing sunlight does not appear to be a causative factor like it is in humans (Withrow, 2007).

Location is a very important prognostic indicator for melanoma. Approximately 80% of tumors of the haired skin are benign and 20% are malignant. As demonstrated in the case described above, location should not be the only factor used to determine behavior. A combination of clinical findings and morphologic features such as nuclear atypia and mitotic index should be used to predict behavior (Smedley, 2011). Benign melanomas tend to be well defined, less than 2 centimeters, deeply pigmented, firm but mobile over underlying tissues, and have a mitotic index of less than 3 per 10 HPF.
Malignant melanomas tend to grow rapidly, extend into underlying tissues, be greater than 2 centimeters, ulcerated, and have a mitotic index greater than 3 per 10 HPF.

Prognosis for malignant melanomas is guarded because 30-75% metastasize. The most common locations for metastasis include regional lymph nodes, lungs, and rarely the brain, heart, or spleen. Unfortunately, most dogs with malignant disease will eventually succumb to metastatic disease (Withrow, 2007).

The treatment of choice for malignant melanoma is surgical excision with wide margins. Radiation therapy, chemotherapy, and the melanoma vaccine have also been used as adjunctive therapy. Radiation therapy is not successful in areas of bulky disease and therefore is generally used for incomplete tumor excision or lymph node metastasis. Unfortunately, even when used on small tumors or lymph nodes, radiation therapy tends to have short-lived effects and complete response rates are relatively low ranging from 53% -69%. Chemotherapy has also been shown to have short-lived effects and low response rates. One study found Carboplatin to have about a 28% response rate, while Cisplatin and Piroxicam have been shown to have an 18% response rate (Bergman, 2008).

The melanoma vaccine is a xenogeneic tyrosinase DNA vaccine that was FDA approved in December 2009. Tyrosinase is the rate-limiting enzyme in the production of melanin. There is only a 9% difference between human and canine tyrosinase DNA. The immune response generated against the human DNA is similar enough to attack self-tumor cells (Bergman, 2003). An immune response begins approximately 6 weeks after initial vaccination and reaches its highest levels around eleven months (Liao, 2007). Approximately 8,000 dogs have received this vaccine to date and minimal side effects
have been seen. Side effects include mild local reactions such as pain, erythema, or short-term lameness. Autoimmune depigmentation has also been observed in localized regions such as the pinna or foot pad, however this is a rare side effect (Bergman, 2008).

The true efficacy of the vaccine is not well known. There are no studies involving cutaneous malignant melanoma and treatment with the melanoma vaccine. Studies do support that there is some improvement in survival with the vaccine when compared to surgery alone for oral and digit melanoma. One study involving dogs diagnosed with oral melanoma show a median survival time with conventional therapy to be approximately 30-150 days versus 389 days for treatment with the melanoma vaccine (Bergman, 2003). A study involving melanoma of the digit showed amputation alone had a median survival time of 365 days versus treatment with amputation and the melanoma vaccine to be 467 days (Manley, 2011).

Outcome

In this case, the dog was treated with the FDA approved human tyrosinase DNA vaccine (Bergman, 2003). The dog received four initial immunizations two weeks apart followed by boosters every 6 months. Three-view thoracic radiographs were performed prior to each 6 month booster to check for evidence of metastatic disease. At the last recheck appointment (her second booster), she had no clinical signs or regrowth of the mass, and her three view thoracic radiographs were negative for metastasis.

Conclusion
This case of cutaneous malignant melanoma in the dog, demonstrates that although location is a critical factor in predicting behavior of melanomas, many other features should be examined. Surgical excision with wide margins is the treatment of choice for malignant melanomas, however systemic therapy should also be considered due to the high rate of metastatic disease (Withrow, 2007).

Enhancing immunosurveillance against tumor cells by vaccination is a useful and safe therapy. The success of the melanoma DNA vaccine can be used as a model for other cancers such as Lymphoma, Canine Osteosarcoma, and Feline Mammary Adenocarcinoma (Bergman, 2008). Advancements in research may find that xenogeneic DNA vaccines can play an important role in systemic cancer therapy.
References


