

## What is hemangiosarcoma?

Hemangiosarcoma is one of the most malignant forms of cancer in dogs. It is a cancer of the cells that line the blood vessels (endothelial cells) and therefore can be found in any part of the body. This cancer is typically encountered in older, large breed dogs with potential predispositions noted in males and in certain breeds (German Shepherds, Golden Retrievers and Labrador Retrievers). The most common primary site for hemangiosarcoma is the spleen, accounting for ¼ to ½ of the splenic tumors that arise in dogs. Hemangiosarcoma can also occur in less typical locations of the body including the liver, heart, kidney, bone and in the central nervous system.

This tumor type generally exhibits a highly aggressive tumor behavior locally as well as distantly. Metastatic rates associated with most hemangiosarcomas are >50% at the time of diagnosis. Therapy options and most anticipated response rates to therapy are comparable across the different presentations and bleeding at any site can be life threatening. Survival times are often dependent on location as well as ability to surgically excise the mass.

## How is it diagnosed?

Hemangiosarcoma affecting internal organs (ie spleen, liver, kidney, heart) is dangerous because there are very few signs of the cancer until an emergent bleeding event occurs, resulting in an acute onset of collapse, pale mucous membranes, cardiovascular effects and blood in the abdomen/pericardium. At this point, emergent intervention (ie surgery, pericardiocentesis) is indicated to control the bleeding, address the associated clinical signs related to blood loss, remove infiltrated masses or organs, and to obtain a definitive diagnosis. Occasionally, this cancer may be detected incidentally on radiographs, ultrasound or echocardiogram; however, on review of recent history, signs of transient lethargy and weakness are frequently noted. Meanwhile, presentations involving the skin/subcutaneous/intramuscular tissues typically manifest as progressive masses that are appreciated externally. Those affecting the bone exhibit signs of bone pain associated with radiographic bone lesions. In most cases, tissue biopsy is needed to definitively diagnose hemangiosarcoma, as other benign and malignant causes can cause similar abnormalities.

Staging tests recommended to define extent of disease include blood work, urinalysis, coagulation profil, thoracic/abdominal imaging and echocardiogram. Echocardiogram can interrogate the right atrium/auricle for signs of heart base masses as well as evaluate for pericardial effusion and evidence of ventricular disease that may be related to systemic disease. This may affect treatment options including surgery and chemotherapy.

Staging for hemangiosarcoma is based on the Tumor, Node, Metastasis (TNM) system.

\*Stage I (T0-1N0M0): No evidence of neoplasia (typically achieved post operatively) or associated with a tumor <5 cm, confined to the primary site with no regional/distant metastasis.

\*Stage II (T1-2N0-1M0): Tumor <5 cm or greater than or equal to 5 cm in diameter, that is either confined to the primary site, ruptured (hemoabdomen/pericardial effusion), or invading subcutaneous tissue with evidence of regional lymph node involvement, with evidence of distant disease spread.

## How is hemangiosarcoma treated?

- **Surgery:** Surgery is the primary treatment to address intra-abdominal masses, right auricular appendage masses, subcutaneous/intramuscular masses, and bone lesions. This is preferably done before the mass or masses rupture, when the patient is stable. Unfortunately, with those presentations associated with liver and splenic disease, surgery often has to be done on an emergent basis when the patient is in a critical state.
- **Radiation Therapy:** Radiation therapy is reserved for palliative therapy for tumors involving the subcutaneous/intramuscular tissues and to help address bone pain with hemangiosarcomas of the bone. It is otherwise not used for intra-thoracic/intra-abdominal hemangiosarcoma presentations.
- **Chemotherapy:** The primary chemotherapy medication used to treat hemangiosarcoma is doxorubicin (Adriamycin). Some protocols combine this agent with cyclophosphamide; however, no significant added benefit has been noted with the combination.
- **Immunotherapy:** Immunotherapy, involving liposomal-encapsulated muramyl tripeptidephosphatidylethanolamine (L-MTP-PE), can be considered in addition to conventional chemotherapy approaches in hopes of stimulating the immune system response. This option is only offered as an investigational option and has not been approved in the US.
- **Metronomic Chemotherapy:** This involves two medications (piroxicam and cyclophosphamide) that are administered daily and have been found to increase remission periods in patients with splenic hemangiosarcoma that are free of measurable disease post splenectomy. Metronomic chemotherapy is generally recommended either during the latter portion of conventional chemotherapy or more often after chemotherapy has been completed. Metronomic chemotherapy can also be considered as a less aggressive, more cost-effective alternative to conventional chemotherapy with doxorubicin.
- **Investigational/Clinical Trial Opportunities:** Investigational options and/or clinical trials may also be considered if available, and if patients are eligible for inclusion.

## What is the prognosis for hemangiosarcoma?

The prognosis associated with almost all presentations of hemangiosarcoma, with the exception of primary cutaneous hemangiosarcoma, is considered poor. Stage, whether or not tumor rupture has occurred, and potentially the use of adjuvant chemotherapy +/- immunotherapy are considered prognostically significant.

Prognosis for the most common form – Splenic Hemangiosarcoma, if surgery alone is pursued, irrespective of stage at time of diagnosis, the anticipated median survival time is approximately ~2-4 months. The addition of chemotherapy as adjuvant to surgery when only microscopic disease is present is associated with a more favorable outcome. The use of adjuvant doxorubicin therapy in the setting of microscopic disease increases the median survival time to approximately 6-8 months, with the longest survival times reported in those dogs with Stage I presentations. It has been our experience that 50% of dogs with splenic hemangiosarcoma will have disease recurrence within 1 month of surgery and therefore account for a significant portion of the anticipated non-responsive patient population (unpublished finding). With respect to immunotherapy, the potential benefit for L-MTP-PE in addition to chemotherapy is still not clear. However, initial studies on this compound potentially suggest anti-tumor activity that will need to be further evaluated before this therapy becomes a mainstay in treatment options.