

## **Hemangiosarcoma (HSA) of the Spleen, Part I:**

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The typical scenario goes like this: *He was OK and then he suddenly collapsed. He looked weak and pale and his belly was distended. He had trouble getting up. We rushed him to the vet. Their quick assessment was serious and we had life saving decisions to make. Exploratory surgery was proposed as the best hope to remove the bleeding spleen.*

Occasionally, dogs develop bleeding into the sac around the heart which causes sudden weakness or collapse due to compression on the heart. There should be a third option for families other than surgery or euthanasia. We can provide Pawspice which embraces medical management of the cancer and symptoms or hospice.

There is a 60-80% chance that splenic masses in German shepherds, Golden and Labrador retrievers are cancerous (hemangiosarcoma, HSA). The expected survival for dogs with HSA, if they survive surgery past the first week, is maybe two to four months but after that, life expectancy is extremely poor. Very few dogs make it past one year. Surgery is rarely suggested to remove a mass that has developed on the heart.

The attending veterinarian assesses blood tests and x-rays of the chest and abdomen. A transfusion may be indicated. If possible, an ultrasound of the abdomen and heart is performed and a sample obtained that might diagnose the mass. These additional tests may define and determine the extent of the condition so the attending doctor can make a more clear recommendation and prognosis. The long-term benefit with exploratory surgery is not immediately predictable even with the tests. The decision is not simple.

I gave these grim terms to Mr. Gary Lloyd regarding Marty, his 19 year-old 90 pound Collie, in April 1999. Mr. Lloyd turned the tables on me and said, ***“Doc if you are telling me that Marty might live 4 more months with the surgery either way, and he has a 20% chance to live longer, if it’s not cancer, why wouldn’t I want to try?”*** FYI...Old Marty's splenic mass was not cancer and he survived past his 22<sup>nd</sup> birthday!

The spleen is a large, long, flat organ located in the left side of the abdomen. It stores blood and has the ability to make new blood cells while it serves to filter out old blood cells. The spleen also helps to maintain immunity and resistance to infections. There are several different conditions of the spleen that may affect your dog's health but the most serious one is HSA (2% of all tumors in dogs). Dogs develop most of their splenic problems at an older age as a result of splenic tumors. Some tumors get very large and cause the spleen to bleed or rupture. Removal of the spleen is compatible with a quality life in pets and people. The spleen is part of the immune system, but it is not a vital organ and is not essential to life.

The warning signs of splenic tumors in dogs are very easy to overlook. Pets with enlarged spleens are less active. The lips and tongue may appear pale due to a low red blood cell count (anemia). In advanced stages of splenomegaly (enlarged spleen), the abdomen appears distended or enlarged. Some family members are amused by the distension and tell themselves that their pet looks pregnant. People don't read this as a bad sign because their dog still eats and acts well. Older dogs are more commonly affected with benign splenic tumors (hyperplastic nodules). Big dogs, especially German Shepherds, Golden Retrievers, and Labrador Retrievers are commonly affected with HAS. Schnauzers, a small breed, are also at greater risk. There is no known cause for HSA, but genetic factors are being studied due to the obvious breed prevalence.

The cells that become malignant in HSA are the endothelial (blood vessel) cells. These cells create the circular walls of blood vessels. Genetic mutations presumably result in cancer. The cells multiply uncontrollably and develop into huge, cavernous tumors. Since blood vessels exist in every tissue, HSA can originate as a primary tumor in most tissues, but the heart (right atrium), skin, subcutaneous tissue and muscle are the most common primary sites after the spleen. With the exception of solar induced cutaneous HSA found in Whippets and dogs with sun exposed unpigmented skin, HSA spreads rapidly to lungs, liver and local tissues via direct extension and via the blood stream. It is rare in cats.

HSA, is reason enough (in my opinion) for all German shepherd and retriever owners to get an ultrasound screening for their six year plus senior dogs every six to eight months

## **TREATAMENT FOR HEMANGIOSARCOMA, Part II, Updated November 3, 2010**

Surgery to remove the spleen only “debulks” the mass. Surgery often saves dogs with ruptured spleens from bleeding to death. When pet owners cannot afford the cost of surgery, they are usually encouraged to euthanize their beloved dog. This is the “either or” model of modern medicine. However, I believe that there should always be a third option and that option is for pet hospice. The family has the right to take their pet home for the final farewell. The attending veterinarian should prepare a consent form that acknowledges the severity of the pet’s condition and releases their hospital from liability. The pet should have a belly wrap and be sent home with pain control medications, Yunnan Paio, steroids, palliative care instructions and contacts for home euthanasia.

Following exploratory surgery and splenectomy, the standard treatment recommended was the VAC chemotherapy protocol. However, the published survival times are very disappointing. Many families elect to put their dog into palliative care or Pawspice which focuses on treating symptoms while using kinder gentler standard cancer care such as the protocol described below. The goal is to maintain a good quality of life for the post operative pet since the quantity of life is likely to be short.

The VAC protocol uses IV Vincristine, Adriamycin™ and Cyclophosphamide (Cytoxan™). Most oncologists use doxorubicin (Adriamycin™) as a single agent or as a base drug with vincristine and cyclophosphamide. Standard doses for soft tissue sarcoma are used for each cycle of three weeks for six cycles. Vincristine is used at 0.7mg/m<sup>2</sup> for two weeks on day 8 and 15 after Adriamycin which is used at 30 mg/m<sup>2</sup> IV starting on day 1 and every 21 days. Cytoxan is used at 50 mg/m<sup>2</sup> orally every other day or at 50-75 mg/m<sup>2</sup> daily dose on days 3-6 of every 3-week cycle or at 100 mg/m<sup>2</sup> IV on day 1 with Adriamycin and at the start of every 3-week cycle. If the dog is anemic, obese or has pre existing heart disease, precautions and substitutions must be made with the VAC protocol due to adverse events: cardio toxicity, bone marrow suppression, nausea, vomiting, etc.

In search of a kinder gentler approach, I have treated my anemic, older and inoperable heart lesion cases with carboplatin at 300 mg/M<sup>2</sup> every 21 to 30 days, piroxicam, metronomic chemotherapy (mCTx) and nutraceuticals (Yunnan Paio, Angiostop, Astragalus, Agaricus Bio, IP6, Vitality, Onco Support and Platinum Performance). This supplementation to the diet is known as “Immunonutrition.” I find that dogs treated with carboplatin/mCTx have a great quality of life and have few if any side effects (adverse

events). Our Pawspice patients' quality of life and survival times are generally better than dogs treated with the standard VAC protocol because they have no life threatening issues resulting from therapy. Since my Pawspice philosophy encourages kinder and gentler chemotherapy, the program described above would be how I would treat my own dog and this protocol would be my first choice.

## WHAT'S NEW FOR HEMANGIOSARCOMA?

HSA is the most extreme example of the body's poor regulation (dysregulation) of angiogenesis. Many growth factors are involved in signaling endothelial cells to grow and survive. Billions of research dollars help scientists study the mechanisms of how the body signals these growth factors and stimulates their specific cell surface receptors.

New information from the Veterinary Cancer Society's annual meeting in 2014 showed that Metformin, an anti diabetes Rx, can help reduce resistance to chemotherapy. It also has anti cancer benefits on its own as people on this Rx have 30% less cancer. So don't be surprised if your dog will be given doxycycline and metformin for cancer!

A HSA review article appeared in the Journal of the ACVIM September/October 2000. This article discussed ways of treating HSA with inhalation and intravenous liposomes (tiny lipid bubbles containing drugs) and intra-abdominal chemotherapy treatments that may stop metastases to the lungs and liver. These methods remain experimental. The article also discussed the use of immune system modulators and angiogenesis inhibitors such as thalidomide and matrix inhibitors such as minocycline (an antibiotic related to doxycycline) and it also discussed using omega-3 fatty acids. Researchers hope to identify antibodies that will target integrins on the surface of endothelial cells and they hope to develop a natural inhibitor known as canine recombinant endostatin to arrest HSA. The review article stressed the importance of using a combination of multiple types of treatment. Sadly, as I am updating this article in 2014, the survival for the great majority of dogs with HSA has not improved significantly. We need more research and more clinical trials to help the millions of dogs that will die from HSA every year.

In October of 2010, we were asked to conduct a clinical trial using T-Cyte, which is a thymus derived growth factor for T-cell numbers and function. T-Cyte stimulates the immune system's T-helper cells and T-killer cells and increases interleukin 2 and 12. Theoretically these T-cells and the interleukins are able to clear the body of cancer. Terry Beardsley, Ph.D., the researcher immunologist who developed T-Cyte, felt that T-Cyte has the potential to help dogs with HSA. When T-Cyte became available for cats with Feline Leukemia and Feline Immunodeficiency Virus, 2 veterinarians reported amazing success in 3 dogs that survived HSA. After our clinical trial, we feel that there is a modest but individual significant beneficial effect using T-Cyte as 4 of our patients in the clinical study outlived the typically poor prognosis of HSA's fatal agenda. Currently, we offer T-cyte as an immunotherapy agent to help increase the body's ability to fight cancer cells and prolong quality of life.

