ESSENTIAL TIPS FOR SPLENIC MASSES
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KEY POINTS
- Dogs with splenomegaly and splenic masses generally follow the “double two-thirds rule”: 2/3 have splenic neoplasia, and 2/3 of those have hemangiosarcoma. So 1/3 do not have cancer! Hemangiosarcoma is not the only differential for a dog with a splenic mass.
- Hemangiosarcoma (HSA) is the most common primary canine splenic cancer in dogs, and it is locally aggressive and highly metastatic.
- The likelihood of splenic tumor increases with anemia, nucleated RBC, abnormal RBC morphology, or splenic rupture.
- Prognosis for splenic masses cannot be determined without histology which usually requires surgery. A common clinical error is to assume HSA based on the presence of a splenic mass. Large masses are not necessarily malignant. Several splenic lesions have similar ultrasound and gross appearances.
- Except for lymphoma, splenectomy is the treatment of choice for splenic tumors when there is no evidence of metastasis based on staging tests. Even at surgery, it is often impossible to distinguish various diseases based on gross appearance of the spleen or liver.
- Dogs with HSA treated with local therapy and chemotherapy live longer than dogs without treatment and with local therapy only but 1-year survival rates are still low (10%). Chemotherapy is generally well tolerated in most dogs, and only a minority develops significant toxicity.

WHO, WHAT, WHERE, WHY
Splenic neoplasia can arise from any of the normal splenic tissues including blood vessels, lymphoid tissue, smooth muscle and connective tissues. Common splenic tumors include HSA, mast cell tumor, lymphoma and various sarcomas. Hematomas are the most common benign splenic masses. Splenic tumors usually occur in large breed dogs. Breeds most at risk are German shepherd dog, golden Retrievers, and Labradors. German shepherds also have a high prevalence of hyperplastic nodules and hematoma.

Clinical signs are typically vague, non-specific and include enlarged abdomen, anorexia, lethargy, depression, vomiting, and diarrhea. Clinical signs also vary with how advanced disease is, so dogs may have acute and often dramatic acute signs including collapse and hypovolemic shock. In one study 80% of dogs with acute abdomen and no history of trauma had malignant cancer and 88% were HSA. Splenomegaly is readily detectable through abdominal palpation, radiography and ultrasonography.

Differentials Diagnoses: Hemangiosarcoma is not the only differential for a dog with a splenic mass. A common clinical error is to assume HSA based on the presence of a splenic mass. Large masses are not necessarily malignant. Several splenic lesions including HSA, hemangioma and hematoma have similar ultrasound and gross appearances.

Lymphoma (LSA): LSA that involves the spleen is most commonly part of multicentric LSA and typically is a diffusely infiltrative disorder. Some lymphomas may occur as solitary splenic nodules, especially marginal zone lymphoma and mantle subtypes of the indolent form. Similarly acute and chronic leukemias can also diffusely infiltrate the spleen.

Malignant Histiocytosis (MH): MH is an uncommon cancer of atypical histiocytes and has progressive, multicentric involvement of multiple organs, including the spleen, liver, lymph nodes, and bone marrow. The Bernese mountain dog has a familial predilection.

Mast Cell tumors (MCT): Tumors of primary visceral organs including the spleen are rare in dogs. Visceral mastocytosis is typically preceded by a poorly differentiated cutaneous MCT.

Splenic sarcoma: Splenic sarcomas are non-angiomaticous, non-lymphoid tumors of connective tissues and include fibrosarcoma, leiomyosarcoma, extraskeletal osteosarcoma, and undifferentiated sarcomas.
A high mitotic index (MI) of >9 is a negative prognostic factor for survival. Splenic sarcomas tend to be fatal within 1 year. Splenic leiomyosarcoma have a high metastatic rate but dogs that survive the initial post-surgical period have a MST of 8 months.

**Hemangioma:** Hemangiomas are benign tumors of blood vessels. Surgery is curative.

**Non-neoplastic:** hematoma, abscess, nodular hyperplasia, granuloma

**HEMANGIOSARCOMA (HSA)**

HSA is an aggressive malignant cancer of transformed vascular endothelial cells. It causes local infiltration and rapid systemic metastasis. German shepherds and golden Retrievers are at greatest risk. Gross metastasis is present at diagnosis in more than 50% of cases. Excluding cutaneous cancers, it accounts for about 5% of primary cancers in the dog.

Spleen is the most common primary site, but other common sites include right atrium, liver, skin and subcutis. HSA may be solitary, multifocal in an organ, or widely disseminated. Metastasis is typically hematogenously or via transabdominal transplantation. Metastasis is most commonly to the liver and lungs. Less common sites of metastasis include the omentum, mesentery, brain, muscle and bone. HSA is considered the most common metastatic tumor to the brain.

**DIAGNOSTIC WORK UP FOR HSA**

**CBC and chemistry panel:** The likelihood of splenic tumor increases with anemia, nucleated RBC, abnormal RBC morphology, or splenic rupture. The anemia may be regenerative with splenic rupture depending on the duration. Neutrophilic leukocytosis may also be present. Other abnormalities include Howell-Jolly bodies, poikilocytosis, acanthocytosis, schistocytosis and/or thrombocytopenia. Thrombocytopenia is common in 75-97% cases and ranges from mild to severe. A coagulation panel should be run if HSA is suspected.

**Imaging:** Three-view chest radiographs are mandatory to rule out pulmonary metastasis and pleural fluid. Three-views significantly decreases the false-negative rate. Abdominal ultrasound confirms the mass and allows detection of abdominal effusion, defines splenic architecture, and provides detailed evaluation of the abdominal organs and is less affected by abdominal effusion than radiographs.

**FNA and cytology:** Ultrasound-guided FNA is relatively simple, cost-effective and typically a safe procedure. It is most helpful for cases where the diagnosis eliminates the need for surgery, such as lymphoma. For diffuse splenomegaly, the spleen is accessible for cytology. But even with ultrasound-guidance, if non-representative tissues are sampled, you may get a false negative of benign or reactive. In one study, only 61% of cases did cytology match histologic diagnoses. FNA is not recommended for mixed echogenicity masses suspicious of HSA as the masses are often extremely friable so there is an increased risk of hemorrhage in addition to the low diagnostic yield due to hemodilution. HSA effusions are serosanguinous or frank blood and usually do not clot. Unfortunately cytology is typically non-diagnostic.

**Cardiac evaluation:** Since 25 to 45% of dogs with splenic HSA have concurrent right atrial HSA, an echocardiogram is recommended. In my experience this is lower at presentation. Arrhythmias can occur with benign and malignant lesions.

**TREATMENT MODALITIES FOR HSA**

**Treatment pearls:** Treatment for HSA is ideally both local and systemic. Chemotherapy improves the MST, but HSA is still a frustrating cancer for owners and veterinarians with shorter survival times than many malignant cancers in dogs. The majority of dogs tolerates chemotherapy quite well and will maintain a good to excellent quality of life even during chemotherapy.

**Treatment:** Surgery Except for lymphoma, splenectomy is the treatment of choice for splenic tumors when there is no evidence of metastasis based on staging tests. Even at surgery, it is often impossible to distinguish various diseases based on gross appearance of the spleen or liver – including hematoma,
nodular hyperplasia, hemangioma and HSA. Ideally the entire spleen should be submitted fresh on cold packs or in formalin. Biopsy of normal liver is controversial and may not be useful. The abdomen should be thoroughly explored and any suspicious lesions removed or biopsied. About 25% of dogs develop arrhythmias post-op. An ECG should be monitored during and after surgery, and they usually resolve within 24-48 hours.

**Treatment: Chemotherapy** The goal of chemotherapy is to achieve is to delay the metastatic disease that develops quickly after splenectomy. Since chemotherapy improves the MST, it is considered part of the standard of care. Single agent doxorubicin and combination protocols are most common.

Recently low dose oral chemotherapy (metronomic) was comparable to conventional doxorubicin. This protocol included low dose cyclophosphamide, piroxicam and etoposide. Current studies are evaluating whether conventional chemotherapy followed by maintenance metronomic chemotherapy for VEGF-receptor kinase inhibitors such as tocerinib will improve outcome.

**PROGNOSIS FOR HSA:** Overall the prognosis with surgery alone is poor and reported MST in dogs treated with surgery alone ranges from 1 to 3 months, and less than 10% survives 1 year. Adjunctive chemotherapy improves the MST to 4 to 6 months, and doxorubicin-based protocols are the mainstay. Stage I, non-ruptured tumors may have an improved prognosis when chemotherapy is administered after surgery. Low grade tumors may also have a better prognosis.

**Additional Resources**