Hepatocellular Carcinoma in the Canine Patient

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Introduction

Although canine hepatocellular carcinomas (HCC) only account for <1% of all canine tumors, this is still an important tumor to be aware of as it is the most common primary liver tumor. [1,2] Primary tumors are less common in the liver than metastatic tumors.[3] The liver can be a common location for metastasis as it acts as a filter between systemic circulation and abdominal organs. [3] Other hepatocellular tumors include hepatocellular adenoma and hepatoblastoma. Hepatoblastoma is a rare tumor, which has only been reported in one dog. [4] Hepatocellular adenoma are seen more frequently in cats whereas hepatocellular carcinoma are see more commonly in dogs. [4] In most studies of hepatocellular carcinoma there is no breed or sex predisposition, but in few studies, male canines that were >10 years of age showed predominance to females by 1.7:1. [3,5] In some studies, there were higher representations of Schnauzers. [4]

History and Presentation

Nikki is a 10-year-old female spayed Miniature Schnauzer, who presented to Mississippi State University College of Veterinary Medicine Small Animal Emergency on August 6, 2017 for a one and a half day history of inappetence, vomiting/ regurgitation, and shivering/restlessness. The owners described that they thought she was in pain because of her restlessness and shivering. Historically, Nikki has been diagnosed with Cushing's disease, hypertension, and protein-losing nephropathy. She had been treated with Trilostane and benazepril. The trilostane was discontinued on July 21, 2017 due to concern of iatrogenic

hypoadrenocorticism and she was initiated on a tapering dose of prednisolone . Her previous blood work revealed an elevated BUN and creatinine, elevated ALT and ALP, and a mildly elevated calcium. Abdominal ultrasound revealed hyper- and hypoechoic nodules throughout the right liver, and the liver appeared enlarged. . Due to these findings, a fine needle aspirate of the liver was obtained to submit for cytology. Cytology of the liver revealed no cytological evidence of disease.

Upon presentation, Nikki was nervous, alert, and responsive. She weighed 17.16lbs with a body condition score 5/9. Her vitals were within normal limits, but blood pressures were mildly elevated. Lung auscultation was normal, however, a grade I/IV left systolic heart murmur was auscultated. Abdominal palpation revealed a tense abdomen but no pain could be elicited. Fast abdominal SCAN revealed fluid in the abdomen, enlarged liver and gallbladder, and a thickened wall of the bladder..

Pathophysiology

Carcinomas are a type of neoplasia that arise from epithelial cells. [6] Gross morphology of HCC can be described in three ways: massive, nodular, or diffuse. The most common form is the massive lesion usually involving a single lobe as the case was with Nikki. [5] The left lateral lobe is the most common lobe affected by HCC, this has also been observed in cattle. [5] Most HCCs are solitary and have a relatively low rate of metastasis. [7] In one study, only 2 out 48 dogs (<5%) had metastasis occur at the time of diagnosis. [8] In dogs with nodular and diffuse HCC, metastasize to the regional lymph nodes, peritoneum, and lungs is considered more likely. [4]

Diagnostic Approach/Considerations

After Nikki was transferred to the Internal Medicine Service on August 7, 2017, her blood work revealed marked elevation in her liver values, moderate azotemia, and a mild anemia, and mild hypercalcemia. A coagulation profile and ammonium tolerance test were performed to assess liver function and the results were within normal limits. An ACTH stimulation test was performed, and revealed adequate adrenal function. An abdominal ultrasound revealed the liver was enlarged while being hyperechoic and hypoechoic along midline. In addition, a moderate amount of gas was present in the liver along the lateral aspect along with multiple nodules that were coalescing. Interestingly, the liver mass appeared to be growing at a fast rate, as it did not appear on the abdominal ultrasound two weeks prior. The gas filled liver lobe was presumptively thought to be a hepatic abscess. There was mild peritoneal effusion, which was aspirated and submitted for fluid analysis. The results revealed an exudate with 90% non-degenerate, mostly hypersegmented neutrophils and 10% macrophages. A liver aspirate was taken from the gas-containing liver lesion and cytology revealed mesenchymal cell proliferation. A contrast-enhanced abdominal computed tomography scan was performed and most notably revealed a large lobulated liver mass with evidence of both fluid and gas within. This mass was causing a caudodorsal rightward displacement of the stomach and caudal displacement of the small intestines and colon. Surgical removal of the liver mass was recommended.

Treatment and Management

The treatment of choice for most primary and solitary hepatic masses is surgical removal. [6,7,9] If the tumor is localized to a single lobe most often surgical resection may be curative. [3] About 2/3 of the massive hepatocellular carcinomas cases occur in left sided liver lobes, which are easier to resect than the right sided lobes. [7]

Nikki was placed under general anesthesia for a liver lobectomy. The left lateral liver lobe was enlarged and was bluntly dissected. Aspiration was attempted at this time, with no fluid found. A TA30 vascular stapler was used to clamp off the hilus. The lobe was submitted for histopathology along with a biopsy of the right medial liver lobe. A stomach tube and jugular catheter with placed. She was slightly painful on recovery and placed on a Fentanyl constant rate of infusion.

Case Outcome

Histopathology of the left lateral liver lobe disclosed a nodular, bulging, unencapsulated, expansile well demarcated neoplasm. About 50% of the tissue exhibited swelling and necrosis, which may have been the result of outgrowing its blood supply. The final diagnosis was hepatocellular carcinoma. As the cytology of the liver was noted to be meschymal cell proliferation, this highlights the importance of submitting the tissue for histopathology when able, otherwise there would have been improper diagnosis of the hepatic mass. Also, the wedge section of right medial liver revealed changes consistent with portal hypertension and extramedullary hematopoiesis. Hepatocellular carcinomas are relatively common

liver tumor in dogs that generally do not metastasize. Prognosis is generally good if only one liver lobe is involved. Prognosis is less favorable when more than one liver lobe is affected, the tumor is unresectable or metastasis is noted. This is because these tumors are chemoresistant due to their slow growth rate. Additionally, radiation can be complicated but for tumors involving large lesions or right- sided lobes, one can consider radiotherapy. [10] One study showed the development of the three-dimensional conformal radiation therapy has allowed a high-dose radiation therapy to be directed at the tumor, while sparing the neighboring unaffected liver. [10] Since surgery, Nikki has been doing great at home.

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