Cancer: Above the belt, below the diaphragm

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I. Hepatobiliary cancer
- <1.5% of all canine malignancies
- primary tumours are 2.5 times less likely than metastatic tumours in dogs. This is not true with cats!
- hepatobiliary masses are more likely to be malignant in dogs, but more likely to be benign in cats.

A. Four basic categories:
- Hepatocellular carcinoma: this is the most common form seen in canines. There are three main types: massive, nodular and diffuse. The diffuse form is thought to be the final spectrum of the cancer where the lesions are multifocal to coalescing. The massive form comprises around 50-80% of all cases, nodular 16-25% and diffuse 0-19%. The massive form has a low metastatic rate (0-37%) compared to the diffuse and nodular forms where rates of 93-100% have been reported. Sites of spread include lymph nodes, peritoneum and lungs. There does not appear to be any breed or sex predilection, but males and Schnauzers have been reported more often.
- Biliary carcinoma and adenomas: this is the most common hepatobiliary neoplasia in cats, with the adenomas or cystadenomas comprising 50% or more of feline cases. In the malignant group, cholangiocarcinomas are most common in cats. Overall, nodular forms are less common than the massive and diffuse forms. With cats the lesions are more likely to be extrahepatic; whereas with canines, they tend to be intrahepatic. In humans there has been a link with a trematode aetiology, this has not been proven in animals. The malignant forms in this group tend to have an aggressive biological behaviour with metastatic rates up to 88% in dogs and 67-80% in cats. Sites of spread include regional lymph nodes, lungs as well as intraperitoneal involvement (carcinomatosis).
- Carcinoids: these rare tumours are actually of neuroendocrine origin and are usually intrahepatic in presentation. They have an aggressive biological behaviour with 2/3’s of cases have a diffuse presentation within the hepatobiliary system and 1/3 present with nodular lesions. The metastatic rate is ~93%. These tumours have also been reported to occur in the gastrointestinal tract and pancreas, with a guarded prognosis in these locations too.
- Sarcoma: these are also less common liver tumours. Overall 1/3 of patients present with a single massive lesion and 2/3’s present with nodular lesions. The more common forms are haemangiosarcoma, leiomyosarcoma and fibrosarcoma. They tend to all have an aggressive behaviour with metastatic rates between 86-100%. Disseminated histiocytic sarcoma could also fit in this group.

B. Clinical signs and diagnostics: often patients are asymptomatic or present with non-specific clinical signs such as weight loss, inappetance and lethargy. Often the bloodwork is also non-specific such as a leucocytosis, anaemia and thrombocytosis. Increased clotting times or coagulation factor abnormalities have been reported but often they are clinically irrelevant. Liver enzyme elevation can be seen but in dogs there is no correlation between magnitude of elevation and degree of liver involvement (there may be a correlation with cats). Azotaemia is often seen in cats. Patients can have increased globulins and hypoglycaemia, possibly hypoalbuminaemia. Imaging will often identify the tumour, sometimes due to size of mass it is difficult to tell where it is
originating from. Ultrasonic appearance does not correlate with tumour type although there has been more recent work utilising contrast ultrasonography. Aspirates or cutting needle biopsies can be considered although there is a risk that representative tissue may not be collected. Sometimes these patients are taken directly to surgery if there is no documented metastasis; the final diagnosis can be obtained once the entire mass has been resected.

C. Treatment: surgery is mainstay of treatment for massive forms of hepatocellular carcinomas. These can be tricky, with a reported 4.8% intraoperative mortality rate and 29% complication rate. There are various surgical techniques such as finger fracturing, mass ligation for more lateralized masses, mattress sutures, automatic staplers and utilizing a ligasure device. Diffuse and nodular forms are not surgical cases, embolization techniques have been described however there is a steep learning curve with these specialized techniques. Radiotherapy (RT) is unlikely to be an option as the liver cannot tolerate >30Gy. 3D conformal RT has been described in 6 dogs with inoperable hepatocellular carcinoma. The role of drug therapy is unclear but could be considered as a palliative option.

D. Prognosis: good if the mass can be surgically resected. Median survival times of 4yrs or greater have been report for massive hepatocellular carcinomas. Left sided tumours have a better prognosis as these are more amenable to resection and; as expected, patients with completely resected tumours do better. The diffuse and nodular forms of these cancers have a very poor prognosis.

E: What's new! In humans, angiosomal microwave ablation has been developed. There has been a shift to move away from standard chemotherapy. There are now numerous case reports and series using these therapies in veterinary patients. Percutaneous electrochemotherapy for non resectable liver tumours, the H-fire technique, has recently been described by the veterinary oncology group at the Virgina-Maryland University.

II. Pancreatic cancer
A. Pancreatic adenocarcinoma: there is very little information in the veterinary literature regarding this rare canine cancer. Females and spaniel breeds appear to have a higher incidence. Clinical signs are often vague and non-specific. Alopecia has been described as a paraneoplastic syndrome in feline cases. Interestingly, pancreatic enzyme elevations are inconsistent. This cancer is generally thought to be a biologically aggressive cancer with a high metastatic rate. The liver appears to be a common site of spread. Often there is significant involvement at the time of diagnosis; thus patients are often not surgical candidates. One year survival times have not been reported in dogs although anecdotally I have seen this! A recent report in 34 cats noted metastatic disease in one third of patients and overall median survival was 97 days. Interestingly, 15% of patients were diabetic, raising the query of a possible link between these two diseases.
What new? In humans there is biomedical research looking at a unique topical delivery device which allows local perfusion to the pancreas as well as early detection kits.

B. Insulinoma (Beta cell tumour): these are uncommon tumours where insulin secretion can be partially or completely autonomous and does not respond to falling blood glucose concentrations. When the patient has low blood glucose, the beta cells fail to inhibit insulin secretion. Thus, the hallmark of diagnosis is normal or increased insulin levels in the face of hypoglycaemia. These tumours can also produce other hormones such as glucagon, somatostatin, gastrin, IGF-1, GH and pancreatic polypeptides. Sometimes their expression can be linked to metastasis.
Stage 1: only pancreatic involvement
Stage 2: local lymph node involvement
Stage 3: distant metastasis

The rate of spread is thought to be 50% in dogs, although one study noted that 43% of reported suspected metastatic lesions were actually not! (Tobin ’99). Sites of spread include regional lymph nodes and liver, spread to lungs is thought to be rare. Up to 15% of patients will have more than one nodule in the pancreas, which has ramifications in regards to surgery. Clinical signs are related to the hypoglycaemia (seizures, collapse, ataxia, muscle fasciculation, strange behaviour) and are often worse post exercise or fasted. Paraneoplastic peripheral neuropathies have been reported. Often the tumour (and secondaries) are not visible with ultrasonography and CT has been associated with false positive reports. This was confirmed by a Dutch study where they compared ultrasonography with CT and SPEC. Out of the three, CT was the superior but intraoperative identification was deemed the best! Thus, surgery can be both a diagnostic and therapeutic tool. Both lumpectomies and partial pancreatectomies have been described for insulinomas. It is important to biopsy the regional lymph nodes and liver at the time of surgery. Post-operative complications include pancreatitis, hypoglycaemia and hyperglycemia (beta cell atrophy) can be seen. Sometimes medical management prior should be considered. This includes prednisolone and one study noted a 1.5 year improvement in outcome if prednisolone was commenced upon relapse. Diazoxide has been noted to inhibit insulin secretion, stimulate hepatic gluconeogenesis and glycogenolysis as well as inhibit tissue use of glucose. Response rates of ~70% have been reported. Unfortunately Diazoxide tends to be cost prohibitive in Australia. Streptozocin has also been trialled, older studies reported a risk of nephrotoxicity. More recently streptozocin improved the duration of normalglycemia in 17 dogs. Octreotide (a somatostatin receptor ligand) has been reported to alleviate hypoglycaemia in ~50% of patients. Regarding prognosis, there is a large variation in the literature: surgery in patients with no metastasis 1-3.5 years, with medical management only ~7-9 months.

Ferrets: Insulinomas comprise ~25% of all ferret cancers, more often in middle age to older animals. They often present with signs of pytalism, weakness and lethargy; ~20% of ferrets will have normal insulin levels! Up to 75% of ferrets will have multiple nodules and ~50% will have a concurrent adrenal tumour. The best treatment approach appears to be nodulectomies or a partial pancreatectomies, where median survivals of 14 and 22 months have been reported respectively. Medical management with prednisone and diazoxide can be used as well.

III. Gastrointestinal cancer
A. Gastric: cancer in the stomach seems to have a mild female predilection and Chow Chow’s have a 10-20% increased risk. Collies and Belgium Shepherds are also over-represented. Adenocarcinomas (ACA) are most common and they tend to affect the pylorus and lesser curvature. Metastatic rates for ACA’s in this location can reach 95%, they have a worse prognosis compared to the intestinal counterparts. Leiomyosarcomas (LMSA) tend to involve the cardia and overall have a lower metastatic rate of ~30% (although in another study it was 100%). Paraneoplastic hypoglycaemia can be seen with LMSA. Gastric cancers generally spread to lymph nodes, liver, lung and peritoneum. Interestingly there was also a case report of cutaneous spread; as well as, metastasis to the testicle in 3 cases! Various diagnostics can be considered; regarding biopsies, large gauge are better as there is a concern of achieving false negatives with gastroscopic sampling as only the mucosal surface is viewed and serosal extension can’t be seen. Surgery is often challenging due to location that is affected (lesser curvature, antrum and pylorus) and extent of involvement. Often there is microscopic infiltration of the
tumour well beyond what is palpable or visual intra-operatively. Although, LMSA’s at
the cardia may be able to be ‘shelled out’. Sometimes a palliative resection can
improve (possibly double) survival time. A total gastrectomy has also been described in
a dog which then lived 8months, although this is not my advocated approach. The role
of drug therapy is unclear, although limited success has been reported with some
agents. In general cancer in this location has a poor prognosis, the Holt study from
2002 reported a median survival time of 2months with surgery, long-term prognosis
was deemed poor due to widespread disease.

B: Intestinal: Overall lymphoma (LSA) and ACA’s are the most common canine
intestinal tumours, followed by LMSA. In cats, LSA is the most common, followed by
adenocarcinomas and then MCT’s. In general cancer in this location affected older
animals with Boxer’s, Sharpei’s and Siamese breeds being overrepresented. Clinical
signs include diarrhoea, weight loss, vomiting, anorexia, haematochezia and tenesmus.

The latter two are more often seen with large bowel forms and the vomiting and weight
loss is seen more with small bowel forms.

i. Small Bowel: LSA is most common, followed by carcinomas. Regarding LSA in this
location; 25% or of dogs and 80% of cats will have concurrent other organ involvement.
There appears to be a slight predilection for jejunal over ilial sites and T-cell variants
are more common. Whilst response rates are fair (~56%), overall median survival times
are poor (13-77days), however it is important to note that there were some patient
outliers which lived up to 700days. ACA’s and LMSA’s in the small intestine have
metastatic rates of up to 70% and 30-50% respectively. Reported survival time are
variable for ACA’s, with metastasis is ~3mo and up to 15mo without spread. In cats,
survival times are between 4-15months, however if they survival the 2 week post op
period, they were more likely to reach the 15mo figure. Additionally, cats that had follow
up chemotherapy (doxorubicin) did better. For LMSA’s, results are similar, ~3months
for patients with spread and ~1year without metastasis. For cats, if they survived the
post period, 1-3 year survival times have been reported, possible even cures.

ii. Large Bowel: the rectum is more commonly involved than the colon, in particular for
ACA’s and polyps. GIST’s and LMSA’s tend to be located at the cecum. Regarding
carcinomas, they can grossly appear pedunculated (these are usually in the distal
rectum), cobblestone (more in the mid rectum) and annular (more in mid rectum).
Whilst not statistically examined, the prognosis for these subtypes are 32, 12 and 2
months, respectively. Malignant transformation has been described for colorectal
polyps, two older studies reported this to occur at rates of 18 and 50%. Lymphoma in
this location has a better prognosis. A recent study of 31 dogs noted a median survival
time of ~5years, with younger dogs doing better. Most cases were high grade, B-cell
and sub-stage ‘b’. Leiomyma’s also tend to have a good prognosis in this location.
For cats with colo-rectal tumours, improvements were noted in patients that had
subtotal colectomies, no metastasis and if they have adjunctive chemotherapy.

C: Gastrointestinal stromal tumours (GIST): these are more commonly seen at the
cecum, but have been noted in the stomach and intestines. Histologically they are
highly cellular mesenchymal tumours and are thought to arise from multipotent stem
cells, similar to the interstitial cells of Cajal. They can be driven by mutations in Kit (a
tyrosine kinase inhibitor). In older literature they were misclassified as LMSA’s. With
the advent of immunohistochemical staining, one study reported that over half of the
previously diagnosed LMSA’s were actually GIST’s! This work also confirmed that
GIST’s are more common in the cecum and large bowel and LMSA’s are seen more in
the small intestine, but can be seen in the cecum too. Overall GIST’s appear to have a
similar prognosis to LMSA’s, ~3yrs if they survive the post op period, otherwise an
overall 80% 1yr survival time is reported.

A jejunal located GIST has been reported in a 12 year old cat.
References


