Oncology Case Report – Haemangiosarcoma

Abstract

This case study style lecture draws upon the previous oncology lectures to provide an in-depth case study report of oncology veterinary nursing in practice. It follows the case of a canine patient with a haemangiosarcoma through from presentation to diagnosis and to treatment and discusses the case in detail, so is an ideal lecture for any VN who has an interest in oncology.

Learning outcomes

- Application of previous oncology knowledge in case study
- In-depth understanding of haemangiosarcoma presentation, diagnosis and treatment

Course Notes

Oncology Nursing Case Report:
Sally, a 14 year old female neutered Bichon Frise, with a Splenic Haemangiosarcoma

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The patient was referred to our hospital following a two week history of intermittent vomiting and anorexia, with concurrent pallor and abdominal distension. These episodes lasted for up to an hour. The owners reported that the abdominal tension resolved and dog was normal between episodes.

There were no other salient problems and the patient was not on any medications, had been vaccinated yearly and had not travelled outside the U.K.

The patient was bright, alert and responsive, but nervous and difficult to handle. Body weight was 9.17kg, with a body condition score of 3.5/5. On physical examination a discreet mobile non-painful mass was palpated in the cranioventral abdomen. No other physical abnormalities were detected. Vital parameters were within normal limits. Mucous membranes were pink and capillary refill time was ~1 second. No cardiac murmurs were audible on auscultation and there were no abnormal lung sounds. Hydration status was adequate.

The patient's problem list was as follows: intermittent episodes of abdominal pain, bloating, vomiting and inappetence; abdominal mass.
**Differential Diagnoses:**

Abdominal mass in cranio-ventral abdomen:

- Splenic hepatic, pancreatic, gastrointestinal, lymph node mass
- Adrenal and renal masses (less likely)

Splenic mass – any neoplasia, including:

- Haematoma
- Haemangioma
- Haemangiosarcoma
- Lymphosarcoma
- Leiomyosarcoma
- Liposarcoma
- Metastatic lesion
- Splenic cyst
- Hyperplastic lymphoid tissue

Hepatic lesions:

- Hepatoma
- Haematoma
- Metastatic spread
- Hepatocellular carcinoma
- Hepatic cyst

**Diagnostics and Results:**

- A blood sample was taken for a complete blood count (CBC), serum biochemistry and coagulation profiles – all were within normal limits.
- Urine specific gravity and dipstick analysis were performed and were unremarkable.
- Orthogonal thoracic radiographs revealed no abnormalities.
- On abdominal ultrasound a 4cm heterogenous mass was seen in the spleen (figure 1). There were also multiple smaller lesions in the surrounding splenic parenchyma. A 5cm cystic lesion was seen in the caudal right liver lobe, as well as three-four “target” lesions in the liver parenchyma.
- Recommended transabdominal Tru-cut® biopsy of the splenic mass was declined by the owner due to the perceived risk. (The owner took the dog home following imaging.)
Two days later the dog was re-admitted for an exploratory celiotomy. The spleen was resected and sent for histopathology, along with tissue biopsies from the hepatic lesions. Fluid was aspirated from a cyst-like lesion in the liver parenchyma and sent for cytological analysis.

Echocardiography was performed to exclude gross evidence of cardiac involvement and ascertain suitability for anthracycline therapy. No abnormalities were found.

Electrocardiography (ECG) showed no rhythm irregularities.

Blood typing for DEA 1.1 antigen was performed in case spontaneous splenic haemorrhage or surgical bleeding occurred and the patient required a blood transfusion. The patient was DEA 1.1 negative (figure 2).

Figure 1: Splenic mass, as seen on ultrasound examination (‘photo: Andrew Denning, Imaging Referrals)

Figure 2: Blood typing was performed in case haemorrhage required transfusion.
**Diagnosis and Prognosis:**

Splenic haemangiosarcoma (HSA).

The owner was given a guarded prognosis. Studies suggest median survival times of one to three months, when patients are treated with surgery alone, with 10% of patients alive at 1 year; survival is three times longer if patients are treated with chemotherapy after surgery (>9 months).

The pathologist reported the hepatic nodules to be benign nodular hyperplasia, with no evidence of metastatic spread to the liver.

**Treatment:**

The first line treatment was palliative splenectomy surgery. This was followed with adjunctive chemotherapy. Six cycles of single-agent doxorubicin at 21 day intervals were planned. However, due to adverse effects, the patient completed only two cycles before being changed to an analogue drug – mitoxantrone, which she tolerated without significant adverse effects.

**Case Discussion:**

Haemangiosarcoma is a vascular endothelial cell malignancy, of unknown aetiology. It is the most common splenic tumour in dogs. Certain large breeds are over-represented, e.g. German Shepherd Dogs and their crosses, Golden Retrievers and Great Danes. 50-70% of splenic masses are diagnosed as HSA on histopathology. Splenic HSAs are highly malignant, with both local infiltration and systemic spread. Most splenic HSAs will have metastised by the time of presentation / diagnosis, even if gross metastasis is not detected on imaging performed prior to surgery. Common metastatic sites include liver, heart, abdominal organs and lungs. A quarter of dogs with splenic HSA have concurrent cardiac involvement. HSA can arise from any anatomic site – the heart, liver and skin being the most common.

Clinical signs vary. In some patients a splenic mass may be an incidental finding in an asymptomatic dog. Others may have vague and transient signs, as this case. This patient’s signs were thought to relate to intracapsular splenic pain and intermittent abdominal haemorrhage due to splenic rupture, with auto-transfusion. Other signs can include general malaise, weight loss, episodic weakness, abdominal dissention, tachycardia, tachypnoea, mucous membrane pallor. Patients may present as acute emergencies with dyspnoea, abdominal effusion or hypovolaemic shock as a result of tumour rupture and haemorrhage. Or sudden death may occur.

Definitive diagnosis is made on histopathology. Excisional biopsy provides tissue specimens and is also therapeutic. For appropriate treatment planning and to allow accurate prognosis, HSAs are staged with a “Tumour, Node, Metastasis” (TNM) protocol (table 1). This system uses size / character of the primary tumour, whether it has spread to regional lymph nodes or metastasised to categorise the disease. Staging in this case consisted of CBC, biochemistry and blood coagulation profiles, urinalysis, three-view thoracic radiographs, echocardiography, ECG and abdominal ultrasound. This patient was clinically staged at T1, N0, M0.

Anaemia and thrombocytopenia are common in HSA. This may be due to immune-mediated processes, sequestration, haemorrhage or disseminated intravascular coagulation (DIC). DIC, may be a paraneoplastic syndrome associated with HSAs, which may cause depletion of coagulation factors and allow spontaneous haemorrhage to occur.
Radiography was performed under general anaesthetic prior to surgery, allowing inflation of the lungs for maximum diagnostic gain. Three-view thoracic radiography can show gross pulmonary metastatic disease. No sign of metastasis was evident in the patient. Thoracic radiographs may also be used to reveal pleural or pericardial effusion due to haemorrhage or associated heart failure or secondary cardiac tumour. Splenomegaly was evident on the patient’s abdominal radiographs.

Abdominal radiography can also be used to demonstrate anomalies consistent with primary or metastatic HSA and may show peritoneal effusion. However, abdominal ultrasonography is more useful to examine abdominal organ parenchyma and demonstrate fluid related to haemorrhage or ascites – neither was seen in this patient. Ultrasonography is valuable to examine the primary neoplasm and check for metastases, with splenic HSA often having a mottled appearance and hepatic HSA appearing hypoechoic.

Diagnostic abdominocentesis can be performed to obtain fluid for cytological analysis. Most effusions due to HSA are hemorrhagic, with a high packed cell volume and cytological examination is often non-specific for HSA. Likewise, fine-needle aspiration cytology of cavitated splenic masses is often unrewarding as there is typically excessive blood contamination, without characteristic neoplastic cells. However, FNA may help to exclude HSA in patients with splenic nodules that have been incidentally found on ultrasound examination.

Cardiac arrhythmias may occur with splenic neoplasms before, during or after surgery. Therefore ECG is recommended prior to anesthesia, with follow-up monitoring during and after splenic surgery.

Early diagnosis and aggressive surgical resection of gross disease with adjuvant chemotherapy offers the longest survival time and best quality of life (QOL). Whilst surgical removal of a bleeding mass relieves clinical signs for a period of time, it alone generally won’t increase predicted survival time because the patient will succumb to distant metastasis within few months.

This patient was splenectomised via a ventral midline coeliotomy. There was no free blood in the abdomen, but the splenic mass began haemorrhaging when handled. Biopsies were submitted from the spleen and liver lesions and fluid aspirated from a large hepatic cyst was analysed. The entire spleen was submitted for gross examination and histopathology of multiple sections.

For monitoring, this patient was kept in our intensive care unit for 24 hours post-surgery, as major vessels had been ligated and the liver biopsied. The patient was maintained on polyionic crystalloids – lactated ringer’s (Hartmann’s) solution, at 4ml/kg/hour to compensate for losses, support circulation and maintain intravenously access. She was given intravenously morphine at 0.35mg/kg every four hours until midnight and then buprenorphine at 0.02mg/kg intravenously for the following 36 hours.

A monitoring plan which included fluid therapy, pain scoring/titrated analgesia and observation for signs of haemorrhage was implemented. The patient’s demeanour, heart rate and rhythm (by ECG), pulse rate and character, respiratory rate and effort, mucous membrane colour and capillary refill time were recorded every 15 minutes for the first hour after surgery, then hourly until midnight, when the patient appeared stable. At this point, there was no abdominal distension and the patient was sleeping, with no vocalisation or signs of discomfort. Observations were therefore reduced to every four hours throughout the night. The following day the patient was bright alert and responsive and did not appear painful when examined. Food was offered but the patient was highly stressed and unkeen to eat. The patient would not settle and the owners reported that the patient was prone to “high anxiety”, therefore a clinical decision was made to administer a light sedation (acepromazine at 0.02mg/kg). Within half an
hour the patient was resting comfortably and willing to accept hand feeding. The sedation was repeated as required during hospitalisation (~12 hourly). The patient was discharged two days after surgery, with no medications.

A re-visit appointment was made for ten days. At this point the surgical incision was checked and the sutures removed. The option of adjunctive chemotherapy was discussed with the owner.

Doxorubicin chemotherapy has proven to be the most effective cytotoxic drug against canine HSA. Various studies have evaluated the benefit of combination chemotherapy protocols over single-agent doxorubicin, but have showed no advantage in survival times, but an increase in adverse effects. Our current standard of care used single-agent doxorubicin at 30mg/m² every 21 days. The owners were keen to proceed with chemotherapy.

**Administration of Chemotherapy:** The patient's body surface area was calculated from body weight in kilograms. She was then prepared for chemotherapy and the dose calculated. In patients under 10kg, the dose is reduced due to an increase in toxicity in smaller patient body surface areas. The calculated dose was 1mg/kg. To reduce the risk of nausea, the patient was premedicated with 1mg/kg of maropitant, given by subcutaneous injection.

Doxorubicin must be given intravenously – leakage into perivascular tissue, causes severe tissue damage with pain, necrosis and skin sloughing that may require surgical debridement and, in severe cases, amputation. In common with many cytotoxic drugs, doxorubicin may induce gastrointestinal side effects (mild → severe) and myelosuppression. Transient cardiac arrhythmias and cumulative heart muscle are also side effects – this is why there is a maximum dose which can be given in a patient’s lifetime. Patients are screened and monitored throughout their treatment. This patient's heart scan showed no obvious abnormalities.

Twenty-four hours after doxorubicin administration, the patient was re-admitted for vomiting, haemorrhagic diarrhoea, inappetence and abdominal discomfort. She was managed symptomatically with intravenously fluid therapy (lactated ringer’s solution), ondansetron (a centrally acting anti-emetic chosen for chemotherapy-related nausea) and Promax® (a probiotic-containing nutraceutical, aimed at restoring natural gut flora). Food was withheld for 12 hours, then offered, little and often. The following day, the patient had improved and was discharged. The patient was seen one week later and was well, with an unremarkable nadir CBC.

Two weeks later the patient re-presented for the next chemotherapy. For this, and for all subsequent treatments, the patient was sedated on admission (acepromazine – 0.02mg/kg and butorphanol – 0.2mg/kg subcutaneously) – which made her calmer and more manageable. Prior to chemotherapy administration, the patient was premedicated with ondansetron, intravenously at 0.2mg/kg. Ondansetron was dispensed for at-home administration – 0.5mg/kg orally every 12 hours for four days. Despite these precautionary measures, 24 hours later the patient needed re-hospitalisation for symptomatic management.

The doxorubicin regime was therefore stopped. However, the owner was still keen to pursue therapy, so mitoxantrone was chosen for the next round. This is an anthracycline anti-tumour antibiotic, similar to doxorubicin, with similar indications (figure 3). Gastrointestinal side effects are less profound, but myelosuppression is greater. It was given at a dose of 5mg/kg intravenously every 21 days for four doses.

The patient experienced no adverse effects following the first mitoxantrone treatment, but the CBC one week later revealed significant myelosuppression. Total white blood cell count was 1.88 x 10⁹/l (6-15) and neutrophil count was 0.42 x 10⁹/l (3.6-12). The patient was prescribed antibiotics (amoxicillin/clavulanate – 12.5mg/kg [combined] and metronidazole – 10mg/kg, both orally every 12 hours. Next time, the mitoxantrone dose was reduced to 4mg/kg – the patient had no further problems.
At the end of the chemotherapy protocol the patient’s abdomen was re-imaged to check for recurrence/progression and no significant changes were seen. The patient was checked monthly and remained well, with a good QOL.

Thirteen months after initial presentation, the owner reported the patient was unwell – she was anorexic, lethargic and quiet, appearing to be intermittently nauseous. A physical examination was performed, followed by blood and urine samples, none of which showed any significant abnormalities. Abdominal ultrasound revealed progression of the initial hepatic changes, multiple heterogeneous cavitated lesions and an overall altered hepatic echogenicity. The owner declined any further investigations or treatment, electing for immediate euthanasia. Post-mortem was not performed, but the ultrasonographic changes were presumed to be related to haemangiosarcoma.

**Bibliography/Further Reading:**


**Table 1:**

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<th>Tumour, node, metastasis (TNM) staging – used for many tumour types:</th>
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- **T (0-4):** refers to the size or direct extent of the primary tumour, e.g. 0 is “in situ” tumour,

One is localised to a single area and four have metastasised
**N (0-3):** refers to the degree of spread to regional lymph nodes, e.g.

- **N0:** tumour cells absent from regional lymph nodes
- **N1:** tumour cells spread to closest or small number of regional lymph nodes
- **N2:** tumour cells spread to an extent between N1 and N3.
- **N3:** tumour cells spread to most distant or numerous regional lymph nodes

**M (0/1):** refers to the presence of metastasis, e.g.

- **M0:** no distant metastasis
- **M1:** metastasis to distant organs (beyond regional lymph nodes)

Use of an "X" instead of a number or other suffix means that the parameter was not assessed.