Please Note: This Case Summary was submitted in 2024, when a Discussion section was not required. All 2025 case summary submissions MUST include a Discussion section.

Diagnosis and Treatment of a Hepatocellular Carcinoma in a Children's Python (*Antaresia childreni*)

Introduction

Published literature describes numerous neoplasia types in the Reptilia class and necropsy reports suggest that captive reptiles have a similar incidence to those in mammals[1]. Snakes frequently develop tumors and, as has been repeatedly shown, a very high number of snake neoplasms are malignant[2]. Recent literature evaluating the prevalence of tumors in snakes found that 20.8% of neoplasms were malignant tumors of the liver, gallbladder, and alimentary tract, second only to malignant mesenchymal tumors of the skin and soft tissue (30.2%)[3]. Frequently, the history and presenting clinical signs are non-specific, including anorexia and lethargy. Visible lesions can sometimes be observed, such as cutaneous lesions or coelomic swelling. A complete diagnostic investigation including complete blood cell count (CBC), biochemistry, and imaging should be performed to evaluate the health of the patient and localize a potential lesion[4]. Options for imaging include radiography, ultrasonography, endoscopy, and computed tomography (CT) scan, which is preferred due to its higher sensitivity[4]. A combination of modalities can be useful for enhanced lesion evaluation. If a potential tumor is identified, it can be differentiated from other disease processes—e.g. abscess or granuloma formation—using fine needle aspiration (FNA) or biopsy for cytological and histological analysis, respectively[5]. Both require analgesia, but FNA can be performed under sedation with ultrasound guidance. Biopsies require general anesthesia and can be obtained by coeliotomy or coelioscopy if internal[1]. Histopathology provides more detail than cytopathology by supplying the extent of margin completeness as well as improved tumor identification[5].

Treatment/Management/Prognosis

As with other domestic species, neoplastic treatment options for snakes should be selected case-by-case. Considerations should include tumor type and aggressiveness, body system or location, local or systemic spread, patient's age and overall health, and the owner's financial budget[1].

Surgical intervention for localized tumors is the most effective[1,2,5], with greater survival time than for untreated snakes[3]. As it involves general anesthesia and surgical risks, appropriate stabilization should be performed to improve the chances of a successful outcome. Complete removal is required to be curative[5]. If metastasis is present, systemic treatment, e.g. chemotherapy, should be used[1].

Chemotherapy can be used locally (intratumoral chemotherapy) or systemically, depending on whether the lesion is singular or has metastasized[1]. Caution is needed when using chemotherapy in reptilian patients as their lower metabolic rate can make them more sensitive to it[1]. Furthermore, available literature is poor for chemotherapy medication dosages. Often treatment plans are based on empirical and anecdotal doses, which may increase the failure rate and even the toxicity risk. Significant immunosuppression may also be seen, suggesting CBC monitoring, and the use of prophylactic antibiosis to prevent secondary bacterial infections[1].

Electrochemotherapy provides electrical impulses after intratumoral administration of chemotherapy to improve tissue penetration and prolong the drug's effect[1]. Reports show this doesn't negatively affect surrounding healthy tissue or have significant side effects, however, the electrical impulses can be painful so analgesia—with sedation or general anesthesia—is needed[1].

Radiation therapy can be used in non-resectable tumors or as palliative treatment. Radiation therapy can be effective against localized tumors, but local and systemic side effects—including vasculitis, cellulitis, lethargy, inappetence, secondary infection, and death—are common[1].

Although the options discussed so far are the main tumor treatments, other options are available for localized neoplasia, including laser therapy, photodynamic therapy, and cryotherapy[1]. In addition to treating the tumor, supportive care measures—analgesia, fluid therapy, and nutritional support—should be part of the treatment plan[4].

Many factors will determine the prognosis of neoplastic disease in snakes, the most decisive being local or systemic[1,5]. Localized tumors that can be removed surgically with complete margins carry the best prognosis, whereas those that infiltrate surrounding tissues that are non-resectable or those that have systemic involvement are regarded as having poor prognosis[1,5].

Case History and Presentation

A 17-year-old entire female Children's python (*Antaresia childreni*) weighing 0.67kg was presented for a 6-month history of inappetence. A small amount of normal feces was passed 2 weeks prior. The home enclosure was a 1.5m(L) x 0.45m(D) x 0.6m(H) glass vivarium with aspen shavings as a substrate. The basking temperature was 30°C with an unknown cool end. This was provided by a thermostatically controlled 100W halogen bulb with a 10-hour light cycle. No UV-B light was provided. A large water bowl was provided allowing water intake and free soaking. There was a hide present along with natural wood to climb. The snake's diet consisted of frozen-thawed weaner rats (45–60g). The snake is kept individually with no other reptiles in the household.

The patient was bright and active with a normal body condition score. The heart rate was 56 beats/minute on auscultation and the respiration rate was 12 breaths/minute. No abnormalities were detected on the physical exam.

Case Management and Outcome

Diagnostic investigations were performed, included a CBC, biochemistry, a CT scan, and fecal parasite testing. A fecal wet preparation and flotation were performed; both were negative for parasites and ova. The blood sample site was aseptically prepared with 5% povidone-iodine[a] and the blood draw was performed consciously from the ventral coccygeal vein using a 0.5ml 29G insulin syringe[b]. The CBC and biochemistry[c] results are displayed in Table 1. References ranges were extrapolated from *Morelia spilota ssp.* due to no published ranges being available for *A. childreni*.

The patient was anesthetized using midazolam[d] at 1mg/kg IM and alfaxalone[e] at 5mg/kg IM. This provided an appropriate plane of anesthesia to allow a pre- and post-contrast CT scan[f]. Contrast was provided with iohexol[g] at 500IU/kg using the ventral coccygeal vein. The images were sent to an external telemedicine service[h] for evaluation. The CT images are displayed in Figures 1, 2, and 3.

The CT showed two mass lesions identified within the liver. Possible differentials included neoplasia, abscess, and granuloma formation. The liver also displayed diffuse fat distribution with a low Hounsfield unit (approximately 2) suggestive of hepatic lipidosis. Further investigation options included ultrasound-guided FNA for cytological analysis and incisional or excisional biopsies. Excisional biopsies of both lesions was chosen.

An ultrasound scan was used to locate the sites of the mass lesions (Figures 4 and 5); these locations were marked on the patient with adhesive tape to aid in surgical identification. Analgesia was provided with morphine[i] at 1.5mg/kg IM. Anesthesia was induced with midazolam at 1mg/kg IM and alfaxalone at 10mg/kg IM. Intubation was performed with a flexible tip from a 16G IV catheter[j] and the anesthesia plane was maintained with 0.5–1% isoflurane[k] in 1L/min oxygen. The patient was stable throughout with a heart rate of 60–84 beats per minute as measured by a non-directional Doppler device[l] over the heart. Intermittent positive pressure ventilation was supplied by mechanical ventilation[m] providing 6 breaths/minute throughout the procedure using an Ayre's T-Piece circuit[n]. A main-stream capnograph[o] was attached to the circuit. The surgical theater was heated to 26°C and the patient was placed on a forced-air warming system[p] to maintain body temperature. This was monitored using a cloacal thermometer[q] and maintained at 29.3–30.5°C throughout the surgery.

Lidocaine[r] at a dose of 3mg/kg was used for an incisional locoregional anesthesia block. The surgical site was aseptically prepared with 5% povidone-iodine and adhesive surgical drapes were applied. A scalloped technique was used to incise between the lateral and ventral scales with a scalpel blade at the level of the pre-identified liver lesions. Sharp dissection through the epaxial musculature was performed using Metzenbaum scissors[s]. A retractor ring[t] was used to provide superior visualization of the internal structures. A combination of blunt and sharp dissection was used through soft tissue to reach the liver and identify both lesions (Figures 6 and 7).

Then, bipolar radiosurgery[u] was used to seal the local blood vessels. Curved haemostat forceps[v] were used to clamp around the mass lesions, obtaining as wide margins as anatomically possible, careful not to include the caudal vena cava (Figure 8). A scalpel blade was used to obtain the biopsy. On release of the forceps, careful inspection of the biopsy site was expressed to confirm

no hemorrhage was present (Figure 9). Both mass lesions were sent for histopathology and cultures after being placed in formalin and sterile culture pots, respectively. The liver and surrounding tissue were moistened with warm sterile saline[w] before routine closure. Muscle layers were closed using 3-0 poliglecaprone 25[x] with a simple continuous pattern. The skin was closed using 3-0 polydioxanone[y] with an interrupted horizontal mattress suture pattern.

The patient remained in the hospital for 3 days post-operation for monitoring and supportive care. Morphine was continued at 1.5mg/kg IM q24hr; meloxicam[z] was added at 0.2mg/kg IM q48hr and Hartmann's solution[aa] at 15ml/kg ICe q12hr. The day after surgery, the patient was gavage-fed a carnivorous critical care formula[bb] at 20ml/kg. There was no indication for antibiotic therapy.

The submitted biopsy samples were negative for bacterial and fungal involvement. However, the histopathology confirmed both lesions to be hepatic carcinomas (Figure 10) with complete margins along with diffuse hepatic lipidosis (Figure 11). After diagnosis, chemotherapy with tyrosine kinase inhibitors was offered in addition to surgical resection; however, difficulty and owner health risks with safe administration of cytotoxic medication and frequent dosing made this option less desirable. Chemotherapy was declined and ultrasound monitoring of the liver was chosen. After the patient returned to normal food intake, the displayed hepatic lipidosis would be monitored with ultrasound to ensure resolution.

Home care involved the removal of abrasive enclosure furniture and substrate. The patient was kept on puppy incontinence pads, with a hide and a water bowl to drink from but not submerge the body in until the sutures were removed at 6 weeks post-surgery. Meloxicam was continued for at 0.2mg/kg IM q48hr for 10 days. The patient was rechecked 10 days post-surgery and was gavage-fed 30ml/kg of carnivorous critical care formula. 7 days later the patient was fed a hopper rat (30g), which was accepted immediately. A larger next feed item (60g) was offered 7 days after

this, and again accepted. At this time the patient was brighter and more active than before surgery and now eating normally. The snake was reassessed 3 months and 6 months later, with ultrasonography confirming no recurrence of the tumors.

Endnotes

[a] Povidone-Iodine, Orion Laboratories Pty Ltd, WA Australia

[b] 0.5ml 29G Insulin syringe, Terumo, Sydney, NSW, Australia

[c] Abaxis VetScan VS2, Zoetis Australia Pty Ltd, Rhodes, NSW, Australia

[d] Midazolam Siegfried Hameln GmbH Medication, Hameln, Germany.

[e] Alfaxalone (10mg/ml), Jurox Animal Health, Rutherford, NSW, Australia.

[f] CT scanner 128-slice Somatom go.Up, Siemens-Healthineers, VIC, Australia .

[g] Omnipaque, Sanofi Winthrop, Paris, France.

[h] VetCT Thomson Ave, Cambridge, UK.

[i] Morphine (15mg/ml), Siegfried Hameln GmbH Medication, Hameln, Germany.

[j] 16G IV Surflo Catheter Terumo, Sydney, NSW, Australia

[k] Isoflurane, Zoetis Australia Pty Ltd, Rhodes, NSW, Australia

[l] Doppler Ultrasonic Flow Detector 811-B, Parks Medical Electronics, Aloha, OR.

[m] SAV04 Small Animal Ventilator; Vetronic Serviced LTD, Abbotskerswell, UK.

[n] Ayres T-Piece, VetQuip, Erskine Park, NSW, Australia

[o] EtCO2 Sensor – Mainstream, Bionet, Tustin, CA.

[p] Bair Hugger, Arizant Healthcare Inc., Eden Prairie, MN.

[q] Digital Thermometer, Terumo, Sydney, NSW, Australia.

[r] Lignocaine (20mg/ml), Troy Laboratories, Glendenning, NSW, Australia.

[s] Metzenbaum scissors, Knight Benedikt, Seven Hills, NWS, Australia.

[t] Lone Star Retractor® system with Elastic Stays, CooperSurgical, Corporate Drive Trumbull, CT.

[u] Gima Diatermo MB 160 Electrosurgery Unit, Gessate, Italy.

[v] Curved Crile Haemostatic forceps, Knight Benedikt, Seven Hills, NWS, Australia.

[w] Saline solution, Abbott Laboratories, Abbot Park, IL.

[x] Monocryl, Ethicon, Johnson & Johnson Medical Pty Ltd, North Ryde, NSW, Australia.

[y] PDS II, Ethicon, Johnson & Johnson Medical Pty Ltd, North Ryde, NSW, Australia.

[z] Meloxicam injection (5mg/ml), Boehringer Ingelheim Ltd, North Ryde, NSW, Australia

[aa] Hartmanns Solution, Abbott Laboratories, Abbot Park, IL.

[bb] Emeraid Carnivore, Lafeber, East Road, Cornell, IL.

References

1) Christman J, Devau M, Wilson-Robles H, et al. Oncology of Reptiles Disease, Diagnosis and Treatment. Vet Clinics: Exotic Animal Practice 2017;20:87-110
2) Dietz J, Heckers KO, Aupperle H, et al. Cutaneous and Subcutaneous Soft Tissue Tumours in Snakes: A Retrospective Study of 33 Cases. Journal of Comparative Pathology 2016;155:76-87
3) Duke EG, Harrison SH, Moresco A, et al. A Multi-Institutional Collaboration to Understand Neoplasia, Treatment and Survival of Snakes. Animals (2022) 12: 258.
4) Mayer J, Moore AS. Oncology. In Mader's Reptile and Amphibian Medicine and Surgery, 3rd Edition, Diver S and Stahl S (eds). Elsevier, 2019; 827-834.
5) Harrisons TM, Kitchell BE. Principles and Applications of Surgical Oncology in Exotic Animals. Vet Clinics: Exotic Animal Practice (2017) 20:235-254

Lab data/imaging

	Result	Unit	Reference Range
Packed Cell Volume	20	%	16-32
White Blood Cell Count	10.0	10^3/μL	2.7-24.8
Aspartate Aminotransferase	32.0	U/L	2-45
Creatine Kinase	560.0	U/L	3-1230
Uric Acid	269.0	mmol/L	0-553
Glucose	3.0	mmol/L	0.2-3.2
Calcium	4.2	mmol/L	2.72-5.11
Phosphorus	1.3	mmol/L	0.26-2.55
Total Protein	82.0	g/L	54-103
Albumin	18.0	g/L	16-29
Globulin	64.0	g/L	37-76
Potassium	6.2	mmol/L	3.0-7.1
Sodium	154.0	mmol/L	140-172

Table 1
In-house blood results on the day of presentation showed normal CBC and biochemistry.

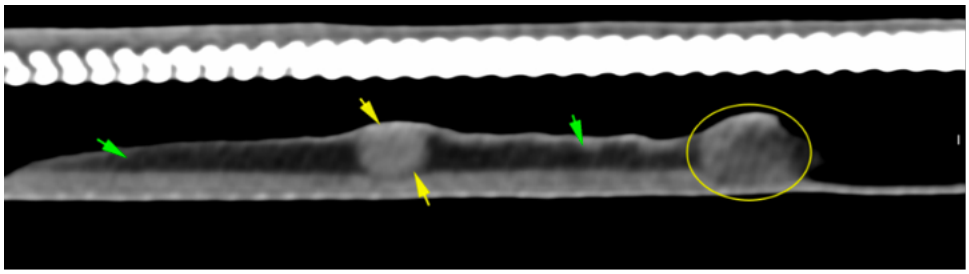

Figure 1
Sagittal plane of the liver showing the cranial-most mass lesion (yellow arrows), caudal-most lesion (yellow circle) and hepatic tissue displaying diffuse fat distribution (green arrows)

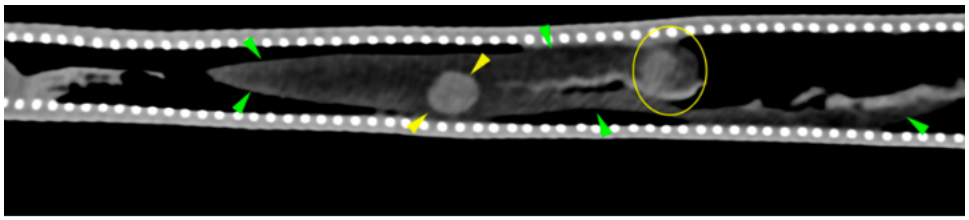

Figure 2
Dorsal plane of the liver showing the cranial-most mass lesion (yellow arrows), caudal-most lesion (yellow circle) and hepatic tissue displaying diffuse fat distribution (green arrows)

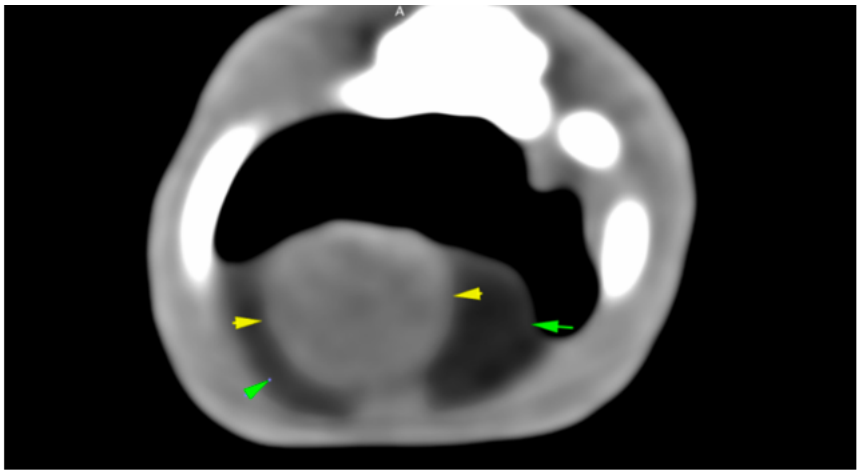

Figure 3
Transverse plane of the liver showing the cranial-most mass lesion (yellow arrows) and hepatic tissue displaying diffuse fat distribution (green arrows)

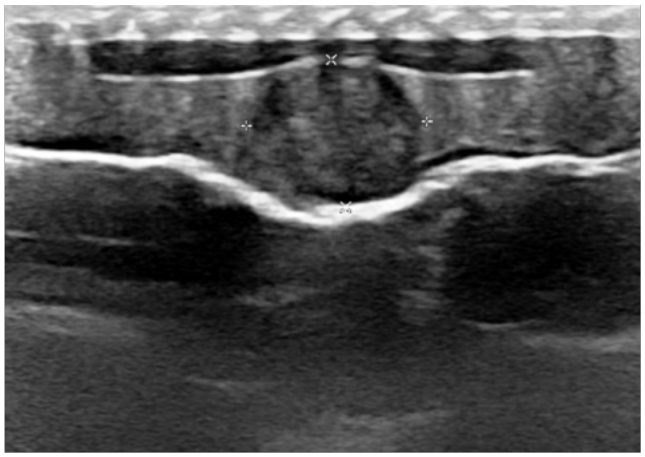

Figure 4
Ultrasonographic image of the cranial liver lesion measuring at 12.4 x 10.2mm.

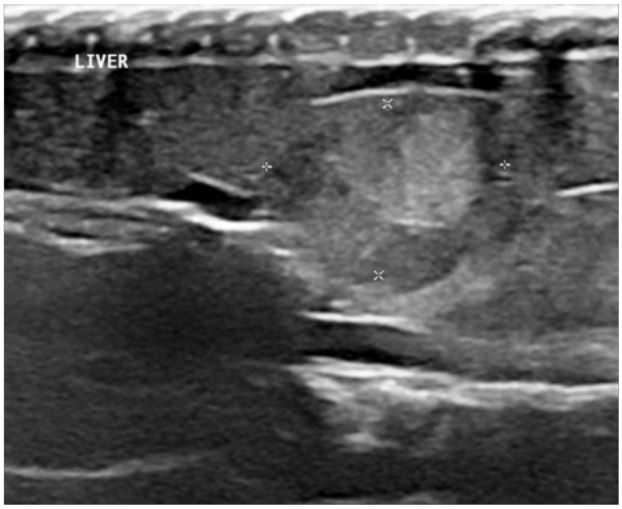

Figure 5
Ultrasonographic image of the caudal liver lesion measuring at 14.1 x 10.1mm.

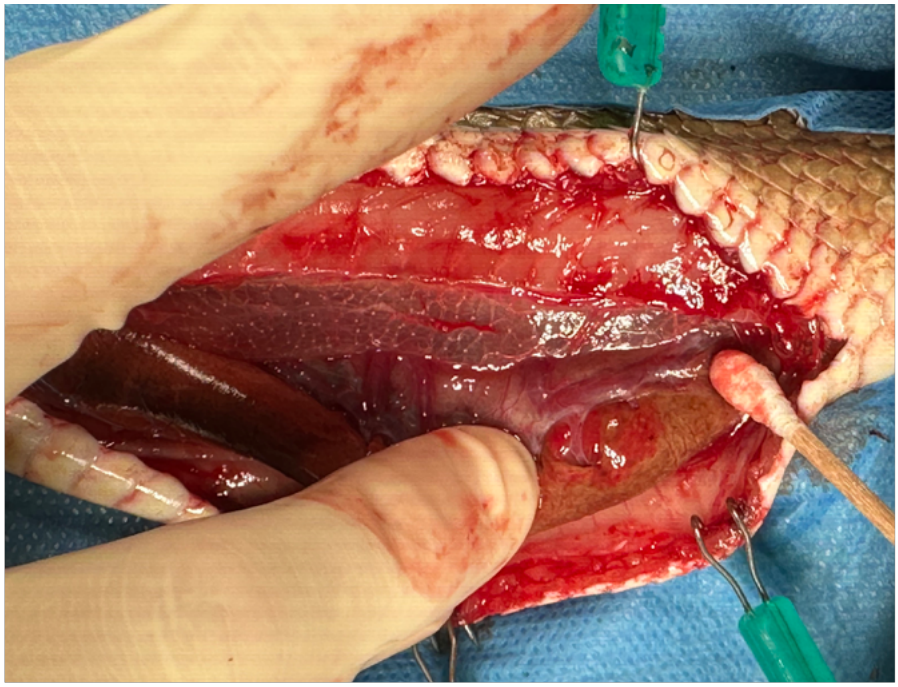

Figure 6
Surgical image of the coeliotomy displaying the cranial liver mass lesion

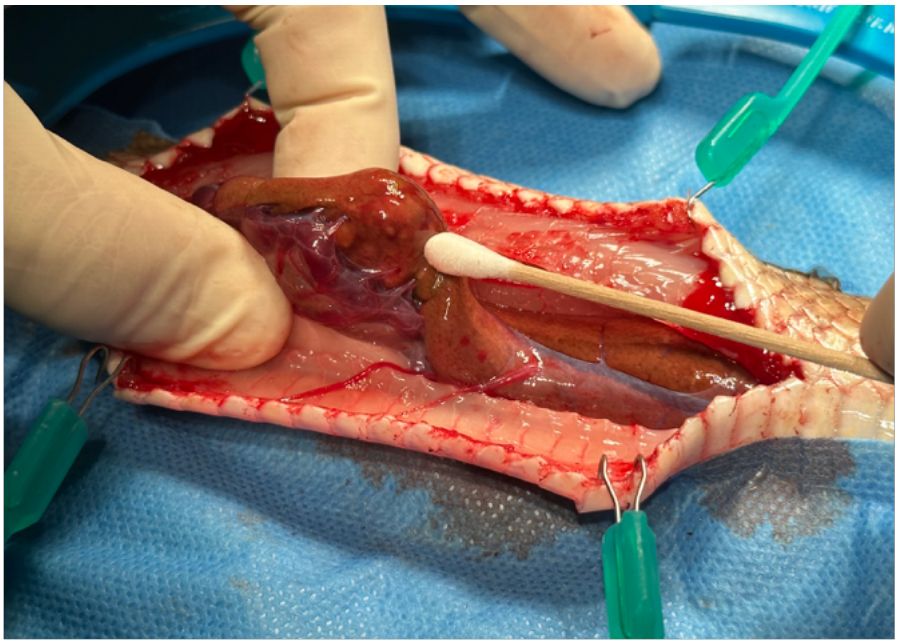

Figure 7
Surgical image of the coeliotomy displaying the caudal liver mass lesion

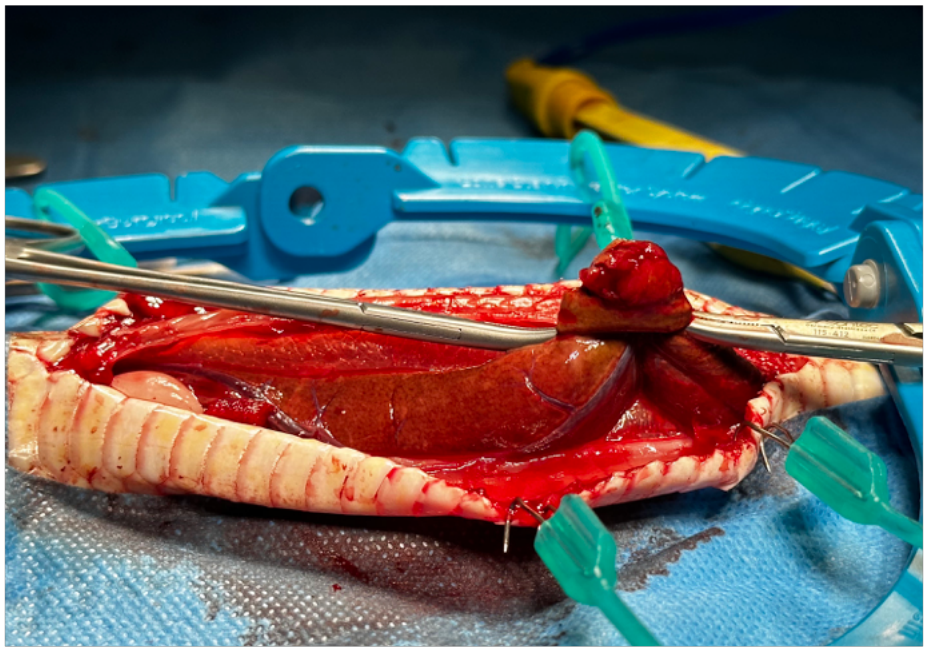

Figure 8
Surgical image of the coeliotomy displaying the cranial liver mass lesion after homeostatic forceps applied to liver tissue immediately prior to excisional biopsy

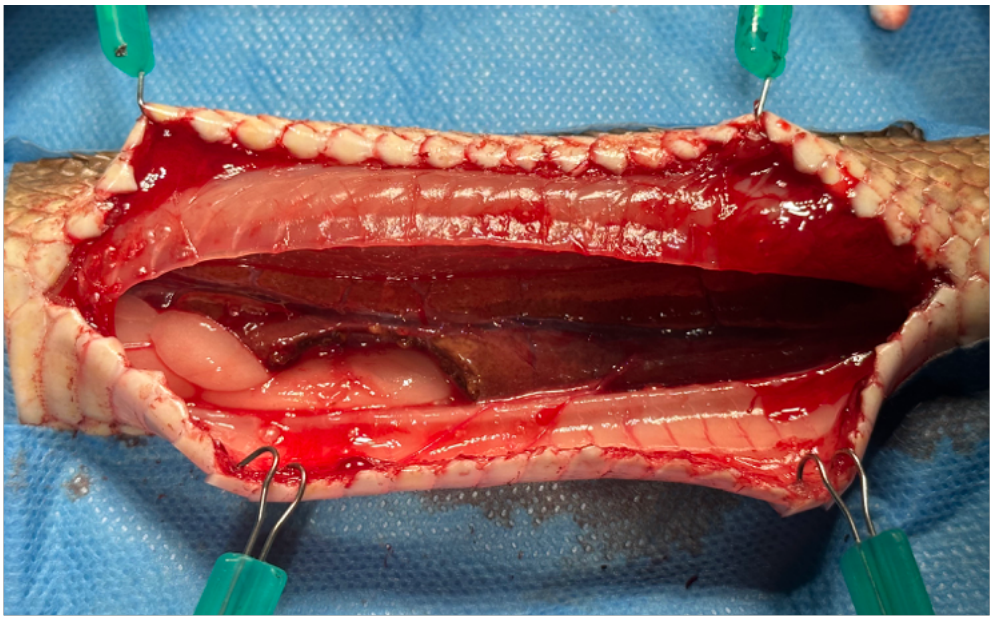

Figure 9
Surgical image of the coeliotomy displaying the caudal liver mass lesion site after the excisional biopsy was performed

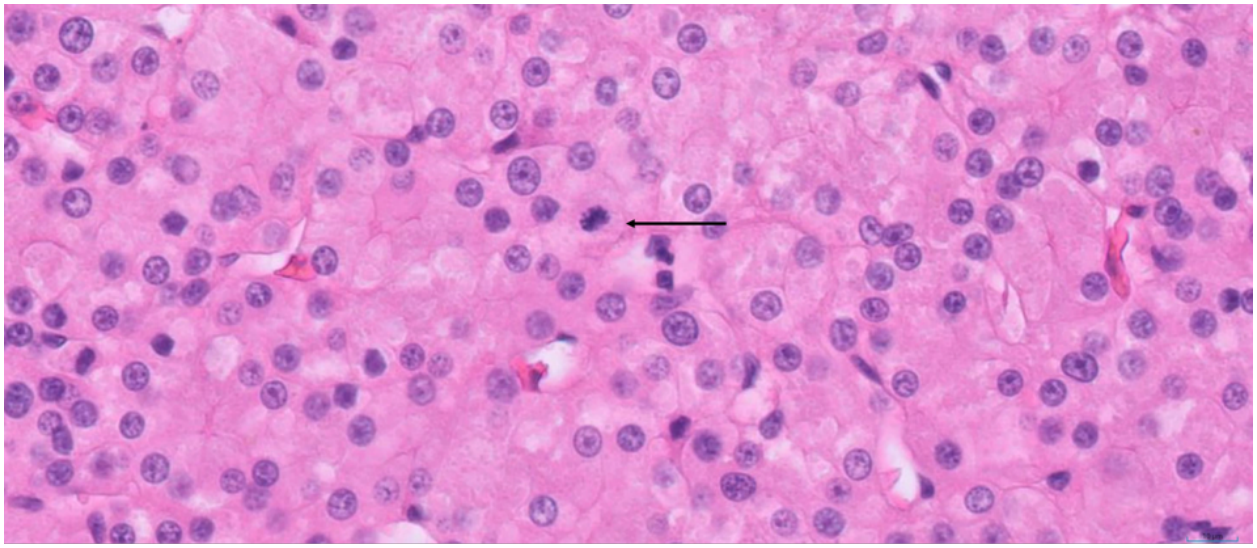

Figure 10
Diagnosis of a hepatic carcinoma
Sheets of neoplastic cells
Well differentiated hepatocytes which display moderate anisokaryosis with increased mitotic figures (arrow) (100x magnification).

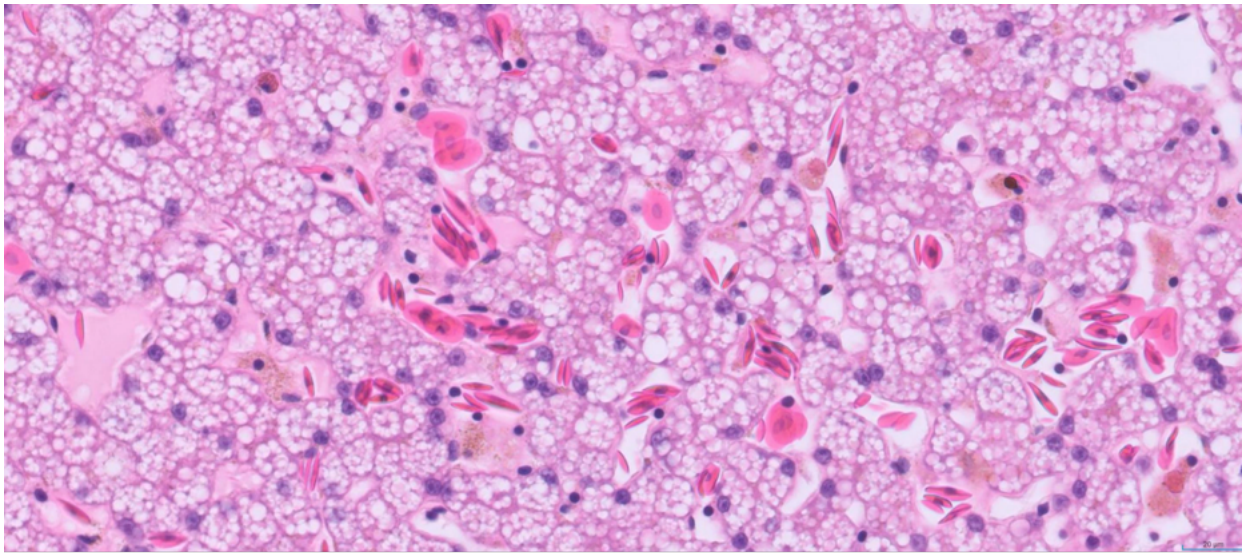

Figure 11
Cytoplasmic lipidosis of the adjacent hepatocytes (60x magnification).