Emergency Caudate Liver Lobectomy and Blood Transfusion in a Pet Rabbit (*Oryctolagus cuniculus*)

Introduction

Liver lobe torsion in pet rabbits (*Oryctolagus cuniculus*) is becoming a more widely recognized disease. This disease is an acute process that has variable and vague clinical signs. Some rabbits will have signs such as anorexia, lethargy, and abdominal pain. These clinical signs can rapidly progress with death being reported in 12 to 72 hours.[1] It not well understood why liver lobe torsion occurs in rabbits, but the caudate lobe is the most commonly affected, although other lobes have also been reported as affected. In a report of sixteen cases there were 10 cases involving the caudate lobe, 5 affecting the right lateral, 2 affecting the left lateral, and 1 affecting the right medial lobe.[2] Most cases affect a single lobe, but there are rare reports of two lobes being affected.[2]

Since the clinical signs are vague it is necessary to perform full diagnostics to determine if there is disease in the liver, urinary tract, gastrointestinal tract, or other location in the body. Gastrointestinal disease, such as gastrointestinal stasis, may occur secondary to liver lobe torsion. Serum chemistry for hepatic disease will often show elevation in liver enzymes including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl transferase (GGT). Liver lobe torsion may cause anemia due to hemorrhage from the congested lobe. Radiographs may show hepatomegaly or no change to the liver. If hepatic disease is suspected then ultrasound of the liver is used for definitive diagnosis of liver lobe torsion and look for other hepatic disease such as coccidiosis, bacterial disease, viral disease,

fatty liver disease, or neoplasia.[1] For liver lobe torsion the ultrasound findings may include enlargement of the affected lobe, rounded lobe margins, mixed hepatic parenchymal echogenicity, and free peritoneal fluid. Using color flow doppler a decrease or lack of blood flow in the affected liver lobe is typical.[3]

Treatment/Management/Prognosis

Liver lobe torsion is a painful condition that can lead to build-up of toxins in the torsed lobe and internal hemorrhage. The treatment of choice is liver lobectomy to remove the torsed lobe. The surgery is performed as a ventral midline incision extending from the caudal end of the xiphoid process to the umbilicus or as far as necessary for good visualization of the liver lobes. A retractor or an assisting surgeon can help with visualization. A double ligation of suture, vascular clips, or automatic stapler are used at the torsion prior to removal of the affected liver lobe. The lobe does not get un-twisted prior to removal as there is risk of endotoxemic shock if accumulated toxins in the lobe are released into the blood stream.[1] Liver lobectomy can have good outcome with 100% survival in one report. In this same paper medical management without surgery was also considered a treatment choice with a survival rate of 43%. This supportive care consisted of subcutaneous fluids, analgesic medication, antimicrobial therapy, supplemental feedings, and prokinetic agents for all of the rabbits.[2]

When anemia is present along with a liver lobe torsion a blood transfusion may be indicated to stabilize the patient. After blood loss of 20-25% of blood volume a patient goes into hypovolemic shock.[1] Donor rabbits should be found based on a normal packed cell volume (PCV), lack of disease, vaccination status, and size compared to the recipient. With any blood donation in mammals there is concern about recipient antibodies reacting with donor red blood

cell antigens. Due to the lack of information about blood groups in rabbits a major cross match should be performed by testing for coagulation when the recipient plasma is mixed with donor whole blood.[3] Close monitoring is still necessary to assess for reaction such as disseminated intravascular coagulation, bronchospasm, vascular collapse, or fever indicative of febrile non-hemolytic reaction. If a reaction occurs then the transfusion should be stopped. For febrile non-hemolytic reaction, the transfusion can be restarted at a slower rate after 15 minutes. For the other reactions corticosteroid, fluids, and bronchodilators may be indicated.[3] If there is no reaction then the transfusion rate can gradually be increased from the initial 1.5mL/kg/hr up to 12mL/kg/hr. A recheck PCV should be assessed one to two hours after the transfusion finishes.[3]

Case History and Presentation

A 22 month old neutered male rabbit presented on the emergency services for refusing to eat his treats that afternoon. On physical examination the rabbit was noted to have reduced gastrointestinal sounds and be about 5% dehydrated with prolonged skin tenting. Otherwise the examination was unremarkable and the patient was bright and interactive.

Case Management and Outcome

For initial treatments buprenorphine[a] 0.03mg/kg and saline 0.9% 100mL/kg were both given subcutaneously. Diagnostics of serum chemistry, complete blood cell count (CBC), and whole body radiographs were recommended and approved by the owner to assess the severity and cause of illness. The radiographs showed that there was a mild distension of the stomach with a large amount of ingesta within. There was no indication of an obstruction of the gastrointestinal tract. The radiologist review also noted that the caudate lobe of the liver appeared prominent on the

ventrodorsal view. The CBC showed an almost equal proportion of heterophils and lymphocytes with no elevation in the absolute counts of cells or changes in morphology. As there is typically a significantly higher proportion of lymphocytes to heterophils in a healthy rabbit, the equal proportion of heterophils and lymphocytes can be seen as a sign of inflammation. There was a mild decrease in the red blood cell count at 4.4 M/uL (4.5-6.9 $x10^6/\mu L$)[b] with a reticulocyte percentage of 3.6% or absolute count of 156,600 per uL. Based on the absolute reticulocyte count this anemia has a mild to moderate regenerative response. The in-hospital bloodwork showed a PCV of 30% (31.3-43.3%)[b] and elevations in liver enzymes on the serum chemistry with ALT of 309 U/L (52-80 U/L)[b] and alkaline phosphatase (ALP) of 91 U/L (6-14 U/L)[b]. Ultrasound of the liver showed a slightly hypoechoic caudate liver lobe with good blood flow of all liver lobes on color flow doppler. A definitive diagnosis of liver lobe torsion could not be made, but was suspected. Hospitalization with supportive care was recommended with a plan to repeat serum chemistry and ultrasound the next day, sooner if the patient declined. The patient was hospitalized overnight with supportive care of intravenous fluids 100mL/kg/day, intravenous enrofloxacin[c] 10mg/kg twice a day, intravenous metronidazole[d] 15mg/kg twice a day, and subcutaneous buprenorphine 0.03mg/kg three times a day. Oral treatments included syringe feedings of a liquid herbivore diet[e] 20mL/kg three times a day, oral meloxicam[f] 1mg/kg daily, oral Laxatone[g] 1mL/kg twice a day, and oral lactulose[h] 1mL/kg twice a day. In the morning a repeat short serum chemistry panel showed an ALT of 371 U/L and ALP of 69 U/L. The PCV had decreased to 27% and the repeat liver ultrasound showed a hypoechoic caudate liver lobe with decreased blood flow on color flow doppler. Based on ultrasound appearance, decreasing PCV, and increasing ALT a caudate liver lobe torsion was suspected and the owner approved emergency liver lobectomy.

For surgical induction the patient was pre-medicated with buprenorphine 0.03mg/kg and midazolam[i] 1mg/kg intravenous and intubated with an endotracheal tube using endoscopic guidance. A midline incision was made on the ventrum just caudal to the xiphoid and extended towards the umbilicus until there was adequate visualization. The upper gastrointestinal tract and liver lobes were retracted until the caudate lobe was visible. About 5mL of free blood was noted in the abdomen. There was a torsion at the base of the caudate lobe with a dense, congested appearance to the lobe. 2-0 absorbable polydioxanone monofilament suture[j] was used to place two encircling ligations at the torsion site before removing the caudate lobe. No hemorrhage was noted. A routine close was performed with 4-0 absorbable polydioxanone monofilament suture in a simple continuous pattern of the body wall then in an intradermal pattern for skin closure.

The skin was sealed with cyanoacrylate tissue adhesive[k]. A reversal of flumazenil[l] 0.05mg/kg was given intramuscularly. The patient recovered unremarkably and stayed in hospital for monitoring overnight. A PCV about 5 hours post-operative was 25%. Due to the declining PCV and level of anemia a blood transfusion was performed. The patient's companion had been staying in hospital in case a transfusion was warranted. The companion was anesthetized for venipuncture from the jugular vein. The donation was difficult to obtain, with multiple attempts made. 13mL of blood was obtained rather than the recommended 10mL/kg. While collecting the blood it was mixed with anticoagulant citrate dextrose solution (ACD)[m] at a ratio of 1 part solution to 7 parts blood.[3] A major crossmatch was performed by placing 2 drops of recipient plasma with 1 drop of donor whole blood on a slide to monitor for coagulation. No coagulation was observed. The recipient received diphenhydramine[o] 2mg/kg intramuscularly to reduce the risk of reaction. The donor blood was given through an 18micro blood filter[n].[3] During the donation heart rate, respiratory rate, attitude, mucous membrane color, and temperature were

monitored. The transfusion was initially given at a rate of 1.5mL/kg/hr intravenous and increased to 13mL/kg/hr since the patient had no indication of reaction to the donation. Two hours after the blood transfusion ended the PCV was 28% which was maintained the next morning on another PCV check. In the morning the ALT on repeat serum chemistry remained elevated at 340 U/L and the ALP was normal. The patient was comfortable and improving clinically, so they were discharged the next day. The patient continued on the meloxicam, Laxatone, lactulose, enrofloxacin, metronidazole, and syringe feedings orally. The patient was also started on oral famotidine[p] 0.5mg/kg daily, oral gabapentin[q] twice a day, and a liver supplement 0.25mL/kg twice a day. The liver supplement is to help promote the health and healing of hepatocytes through the silymarin in milk thistle and other ingredients. The supplement consists of Hepasil[r], milk thistle extract[s], lactulose, and S-adenosyl-L-methionine[t]. Unfortunately, the patient missed an appointment to recheck PCV 5 to 7 days after discharge. At the recheck examination 17 days after discharge the patient had recovered well. The PCV was 37% and the ALT was normal at 44 U/L. Treatments were discontinued as prescribed.

Endnotes

a. Buprenorphine hydrochloride, Par Pharmaceuticals, Chestnut Ridge, NY
b. Carpenter, James W. Exotic Animal Formulary. 6th. St. Louis: Elsevier, 2022.
c. Enrofloxacin 22.7%, Dechra Veterinary Products, Overland Park, KS
d. Metronidazole, Hospira Inc., Lake Forest, IL
e. Herbivore Critical Care, Oxbow Animal Health, Omaha, NE
f. Meloxicam, “Meloxidyl”, Covetrus North America, Dublin, OH
g. “Laxatone”, Vetoquinol USA, Inc., Fort Worth, TX

h. Lactulose, Hi-Tech Pharmacal Co, Inc., Amityville, NY

i. Midazolam, Akorn Inc., Lake Forest, IL

j. Suture, “Webmax”, Aspen Veterinary Resources, LTD., Liberty, MO

k. Cyanoacrylate tissue adhesive, “VetBond”, 3M Deutschland GmbH, Neuss, Germany

l. Flumazenil, West-Ward, Eatontown, NJ

m. Anti-Coagulant Citrate Dextrose Solution (ACD) Solution A, Terumo BCT, Inc., Lake Wood, CO

n. "Hemo-nate filter" 18micro blood filter, Utah Medical Products, Inc., Midvale, UT

o. Diphenhydramine, Hikma, Berkeley Heights, NJ

p. Famotidine, Mylan Institutional LLC, Rockford, IL

q. Gabapentin, Amneal Pharmaceuticals LLC, Bridgewater, NJ

r. “Hepasil”, USANA Health Sciences, Inc. - Salt Lake City, UT

s. Milt thistle - Nature's Answer, Hauppauge, NY

t. S-adenosylmethionine, “Denamarin”, Nutramax Laboratories, Veterinary Sciences, Inc., Lancaster, SC

u. Zoetis Reference Laboratories, Louisville, KY

v. Comprehensive Diagnostic Profile, VetScan VS2, Zoetis United States, Parsipanny, NJ

w. Prep Profile II, VetScan VS2, Zoetis United States, Parsipanny, NJ

References

1. Varga Smith, Molly. Textbook of Rabbit Medicine. 3rd. London: Elsevier, 2022. January 2023.

2. Graham, Jennifer E, Orcutt, Connie J, Sue A, et al. *"Liver Lobe Torsion in Rabbits: 16 Cases (2007 to 2012)."* Journal of Exotic Pet Medicine 23.3 (2014): 258-265. January 2023.

3. Graham, Jennifer E, Grayson A Doss and Hugues Beaufrère. Exotic Animal Emergency and Critical Care Medicine. Hoboken: Wiley, 2021. January 2023.

Laboratory Data & Imaging

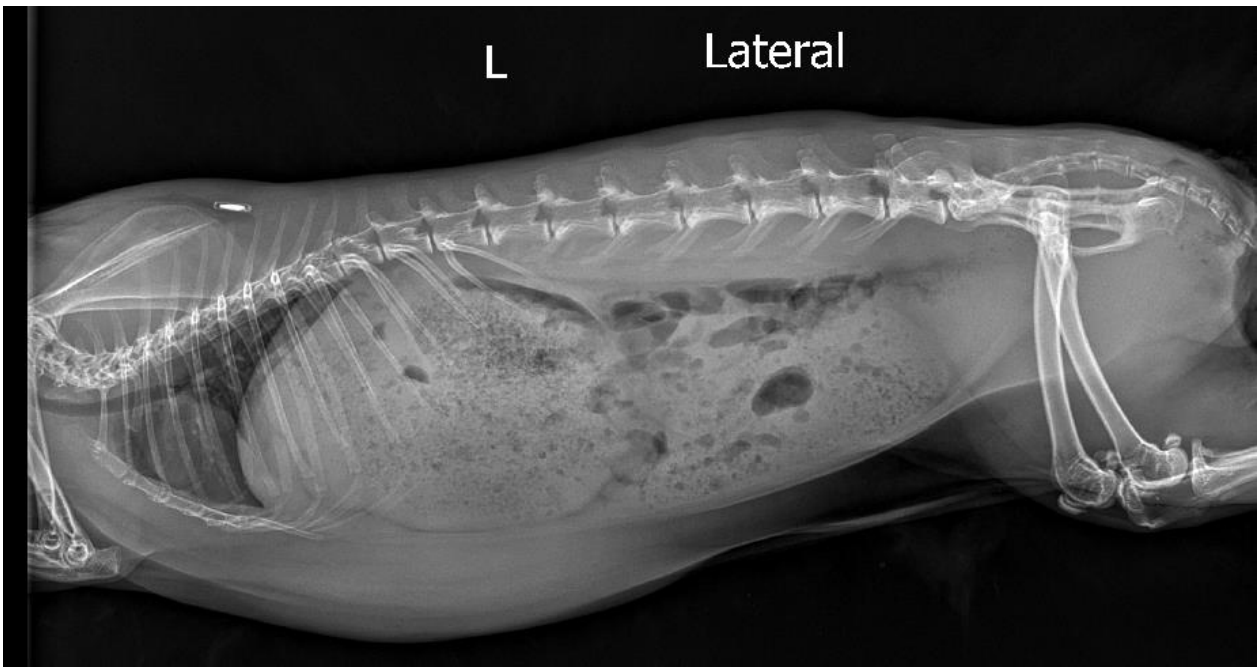

Image 1 – A 22 month old rabbit with caudate liver lobe torsion. Left lateral radiograph taken on presentation demonstrates an ingesta filled stomach with mild distension.

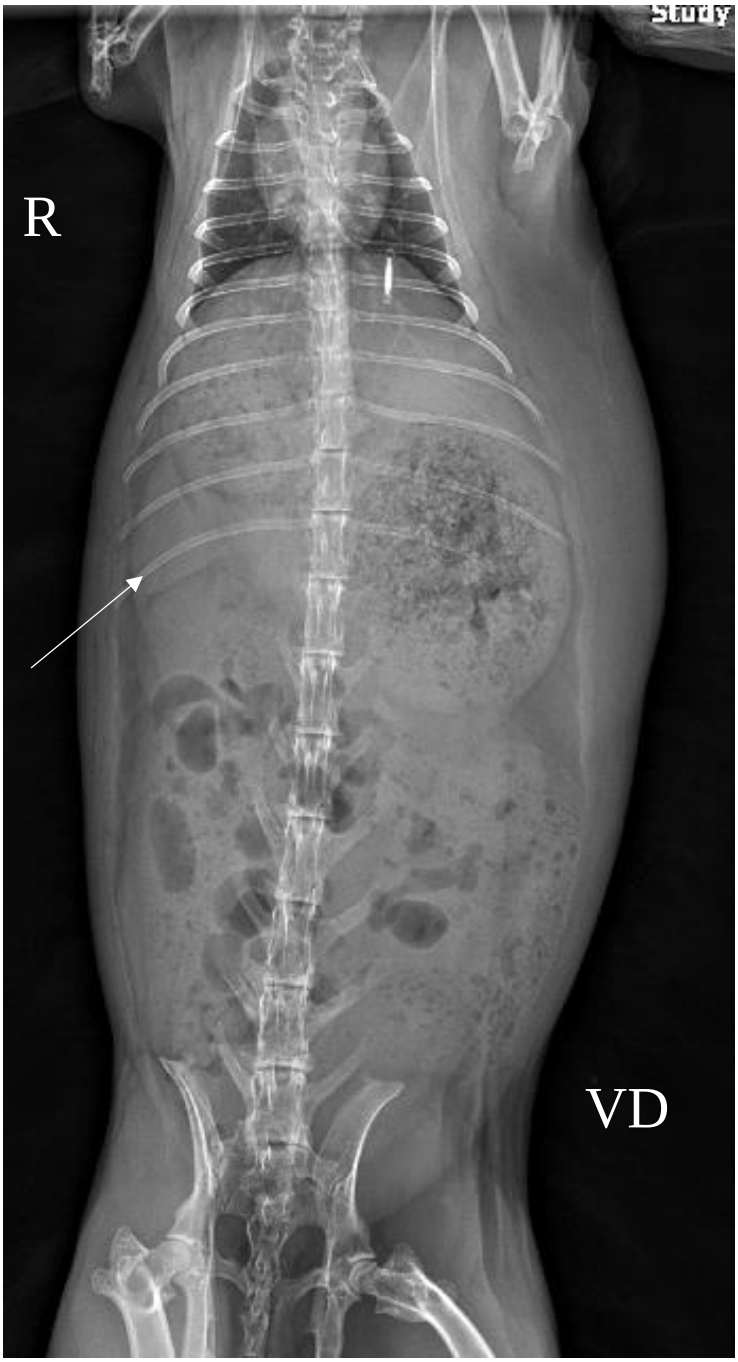

Image 2 – A 22 month old rabbit with caudate liver lobe torsion. Ventrodorsal projection taken on presentation with arrow pointing to the area of a prominent caudate lobe.

	Results	Reference Range
In-House PCV	30	31.3-43.3 %
RBC	4.4	4.5-6.9 $x10^6/\mu L$
Hematocrit	28	31.3-43.3 %
Hemoglobin	10	11.0-14.4 g/dL
MCV	64	59.0-70.1 μm^3
MCHC	35	32.3-34.5 g/dL
WBC	8.3	2.4-12.8 $x10^3/\mu L$
% Heterophils	47	21-73 %
% Lymphocytes	49	9-64 %
% Monocytes	3	1-32 %
% Eosinophils	1	0-0.7 %
% Basophils	0	0-7 %
Heterophils	3910	1.1-7.4 $x10^3/\mu L$
Lymphocytes	4077	0.5-6.5 $x10^3/\mu L$
Monocytes	250	0-3.7 $x10^3/\mu L$
Eosinophils	83	0-0.03 $x10^3/\mu L$
Basophils	83	0-0.4 $x10^3/\mu L$
Platelets	410	192-662 $x10^3/\mu L$
% Reticulocyte	3.6	%
Reticulocyte	156600	/uL

Table 1 – Hematology[u] on presentation. Reference Range[b]

	Results	Reference Range
Albumin	2.8	2.8-4.0 g/dL
ALP	91	6.0-14 U/L
ALT	309	52-80 U/L
Amylase	97	82-343 IU/L
Total Bilirubin	0.3	- mg/dL
BUN	21	9.0-29 mg/dL
Calcium	12.6	7.6-12.2 mg/dL
Phosphate	3.8	3.0-6.2 mg/dL
Creatinine	1.1	1.0-2.2 mg/dL
Glucose	99	109-161 mg/dL
Sodium	149	138-148 mmol/L
Potassium	4.7	3.4-5.1 mmol/L
Total Protein	6.9	6.1-7.7 g/dL
Globulin	4.1	2.1-3.7 g/dL

Table 2 – Serum chemistry 1[v] on presentation. Reference Range[b]

	Results	Reference Range
ALP	69	6.0-14 U/L
ALT	371	52-80 U/L
BUN	12	9.0-29 mg/dL
Creatinine	1.0	1.0-2.2 mg/dL
Glucose	104	109-161 mg/dL
Total Protein	5.7	6.1-7.7 g/dL

Table 3 – Short panel serum chemistry[w] the day after presentation. Reference Range[b]

	Results	Reference Range
ALP	57	6.0-14 U/L
ALT	340	52-80 U/L
BUN	10	9.0-29 mg/dL
Creatinine	0.8	1.0-2.2 mg/dL
Glucose	113	109-161 mg/dL
Total Protein	6.4	6.1-7.7 g/dL

Table 4 – Short panel serum chemistry[w] prior to discharge. Reference Range[b]

	Results	Reference Range
ALP	71	6.0-14 U/L
ALT	44	52-80 U/L
BUN	19	9.0-29 mg/dL
Creatinine	1.2	1.0-2.2 mg/dL
Glucose	125	109-161 mg/dL
Total Protein	6.6	6.1-7.7 g/dL

Table 5 – Short panel serum chemistry[w] 17 days after discharge.
Reference Range[b]