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CASE REPORT

Diagnosis and treatment of a congenital portosystemic shunt in a ferret (*Mustela putorius furo*)

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A 3-year-old female neutered ferret presented with progressive weight loss was diagnosed with portosystemic shunting based on increased fasting bile acids, rectal ammonia tolerance testing and advanced imaging. Ammonia reference values were determined in 16 healthy ferrets. A congenital extrahepatic spleno-caval shunt was visualised with ultrasonography and CT angiography of the abdomen. Complete surgical shunt closure by suture ligation was performed, without clinical improvement after surgery. Euthanasia was elected 4 months postoperatively because the clinical condition deteriorated. This is a case report of advanced diagnostics and surgical treatment of a congenital extrahepatic portosystemic shunt in a ferret, demonstrating rectal ammonia tolerance testing and imaging as feasible techniques for the diagnosis.

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INTRODUCTION

Congenital portosystemic shunts have been described extensively in dogs and less in cats (Winkler *et al.* 2003, Nelson & Nelson 2011, Tivers & Lipscomb 2011, White & Parry 2016, White *et al.* 2017, Valiente *et al.* 2020), but has rarely been described in ferrets (Huynh & Laloi 2013). Portosystemic shunts may be congenital or acquired. Congenital shunts typically consist of a single vessel that connects the portal vein to the systemic circulation (White *et al.* 2017). Surgical or minimally invasive shunt attenuation (Youmans & Hunt 1998, Hunt & Hughes 1999, Murphy *et al.* 2001, Mehl *et al.* 2007, Falls *et al.* 2013) is recommended to promote hepatic function. Acquired shunting results from portal hypertension which can be caused by liver cirrhosis, portal thrombosis or congenital conditions like congenital hepatic fibrosis or arteriovenous fistula.

This case report is the first to describe advanced diagnostics including a pilot study on ammonia metabolism in ferrets, as well as surgical treatment of a congenital portosystemic shunt in a ferret. We show that fasting plasma ammonia and ammonia tolerance testing may aid in diagnosing portosystemic shunting in ferrets, similar to dogs (van Straten *et al.* 2015).

CASE DESCRIPTION

A 3-year-old female surgically neutered ferret of 660 g presented with progressive weight loss despite a good appetite for 2 years. This ferret was kept outdoors in a group. Clinical examination revealed no icterus or other abnormalities. A complete blood count and serum biochemistry were run, abnormalities included increased fasting bile acids (82 µmol/L; reference 0 to 28.9 µmol/L) and hypoalbuminaemia (18 g/L; reference 28.0 to 43.9 g/L) (Hein *et al.* 2012) (Table S1). Abdominal ultrasound (Microconvex transducer; C8-5; Epic 5, Philips Healthcare, the Netherlands) performed using isoflurane mask anaesthesia revealed no abnormalities. Symptomatic treatment was started with omeprazole (Losec; Astrazeneca, 0.7 mg/kg PO q24h), amoxicillin-clavulanic acid (Synulox; Phizer 12.5 mg/kg PO q12hr for 3 weeks), metronidazole (Flagyl; Sanofi, 20 mg/kg PO q12hr for 3 weeks) and supplemental feeding with a highly digestible, high-energy diet (Royal Canin convalescence support™). Although the ferret clinically improved, bile acids remained increased without icterus at 64 to 124 µmol/L.

One year later, clinical signs recurred and fasting bile acids were 98 µmol/L. Ultrasound was repeated using isoflurane mask

anaesthesia and showed a short, left dorsally positioned U-shaped aberrant vessel between the portal vein and caudal vena cava. Triple-phase CT angiography [CT scanning parameters: 180 kV, 180 mAs, 81 mm FOV, 1 second rotation time, matrix 512×512; 1 mm slice thickness with a soft tissue filter (U40), 300WW-60WL; Somatom Definition AS 64 slice, sliding gantry; Siemens Healthcare, the Netherlands] using isoflurane mask anaesthesia and manual contrast medium bolus injection (Xenetix; Guerbet, 350 mg I/mL), identified a 3-mm diameter shunting vessel from the splenic vein to the prehepatic caudal vena cava on the left side and secondary microhepatica (Figs 1 and 2). No right gastric vein dilatation or other shunts were visible. These findings were consistent with a left gastro-caval shunt (White & Parry 2016, White *et al.* 2017).

To further assess liver function and ammonia metabolism, fasting plasma ammonia was measured and ammonia tolerance testing was performed. To determine a reference range for ferrets, fasting plasma ammonia and ammonia tolerance testing were performed in 15 clinically healthy female ferrets (approved by the Animal Welfare Body under AVD1080020184847) according to a modified standardised procedure described by Rothuizen & van den Ingh (1982) (Data S1). Mean (±sd) fasting plasma ammonia concentrations ranged from 40 ±6 µmol/L at T=0, to 38 ±11 µmol/L at T=30 minutes (Tables S2 and S3). Reference ranges were established at 34 to 46 µmol/L for fasting plasma ammonia, and 27 to 49 µmol/L for T=30 following ammonia tolerance testing, which correspond to those determined in dogs (24 to 45 µmol/L). In the ferret suspected of having a portosystemic shunt, fasting plasma ammonia was mildly increased (53 µmol/L) but rose significantly at T=30 (>286 µmol/L; Table S2).

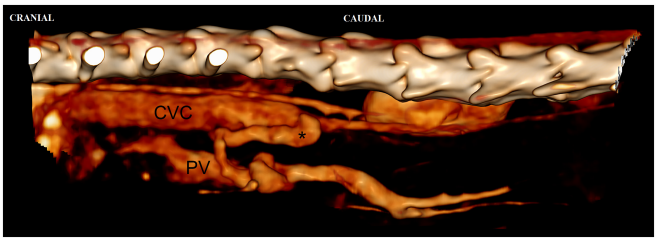

FIG 1. 3D volume CT angiography re-constructed image of the vasculature, left-lateral view. The U-shaped aberrant vessel (*) can be seen curving from the ventrally positioned portal vein towards the caudal vena cava. PV Portal vein, CVC Caudal vena cava

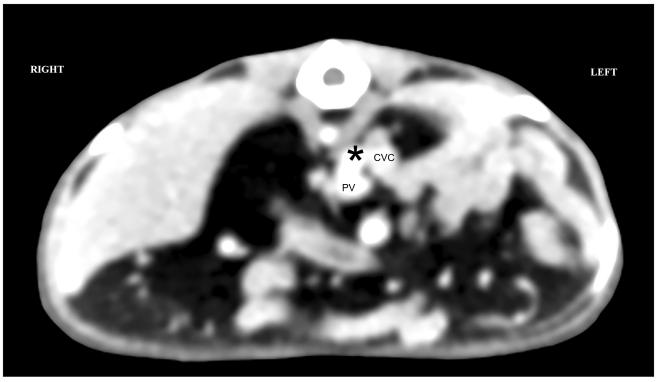

FIG 2. Transverse CT image of the abdomen at the level of the shunting vessel (*) entering the caudal vena cava (soft tissue setting, venous phase postcontrast). The portal vein is noted right lateroventral to this vessel

Before surgical treatment, a moderate content high-quality protein (EmerAid Intensive Care Carnivore combined with Hills L/D) was fed for 6 weeks. No other symptomatic treatment was initiated. The ferret was fasted for 4 hours before surgery and then premedicated with methadone (Comfortan; Dechra, 10 mg/mL; 0.1 mg/kg IM). An IV catheter was placed in the left cephalic vein and the animal was induced using propofol IV to effect (Propo 10 mg/mL, total of 5 mg given), and maintained by isoflurane after endotracheal intubation. Perioperative analgesia consisted of continuous rate infusion with remifentanil hydrochloride (Ultiva; GSK 2 mg/5 mL; 0.2 to 0.4 µg/kg/minute intravenous). A standard ventral midline approach was performed and a 5-mm wide shunt was identified entering the left prehepatic CVC at the level of the epiploic foramen, as was seen on preoperative CT imaging. Following isolation (Fig 3) and temporarily occlusion to monitor for portal hypertension, the shunt was ligated with monofilament, nonabsorbable polypropylene suture (Prolene 4/0; Ethicon). A guillotine biopsy was taken from the right lateral liver lobe using monofilament, absorbable suture (PDS 3/0; Ethicon) for histologic examination. The ferret recovered well following surgery, showing no signs of portal hypertension or postattenuation seizures. Postoperative analgesia consisted of buprenorphine (Buprecare; AST Farma, 10 µg/kg SC q6-8 hours) for 5 days. Liver histology described discrete portal veins in some portal tracts and an increased number of arterioles, indicative of portal hypoperfusion (Fig 4A). Rubeanic staining for copper deposition yielded negative results.

Two months postoperatively, CT angiography confirmed complete shunt closure and an increased liver size. Despite supplementary coaxed feeding with a highly digestible diet with balanced proteins (EmerAid Intensive Care Carnivore), weight remained static. Three months postsurgery, bile acids were 43 µmol/L, whereas ammonia tolerance testing revealed ammonia concentrations of 68 µmol/L at T=0 and 169 µmol/L at

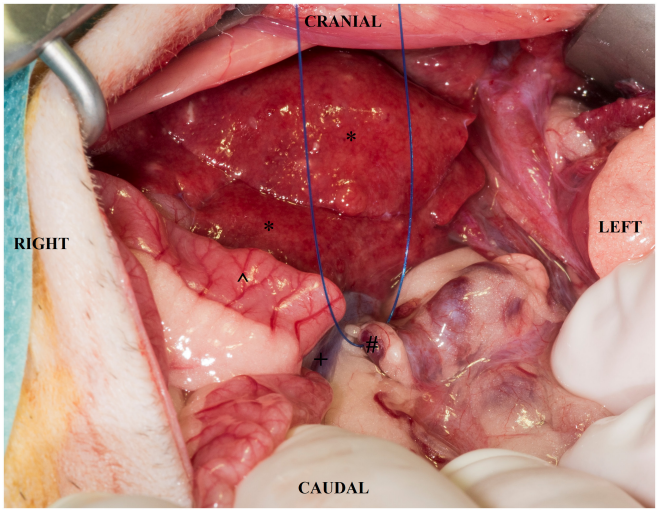

FIG 3. Intraoperative isolation of the shunting vessel with a Prolene 4-0 suture. * Liver, ^ Small intestine, + Caudal vena cava, # Shunt

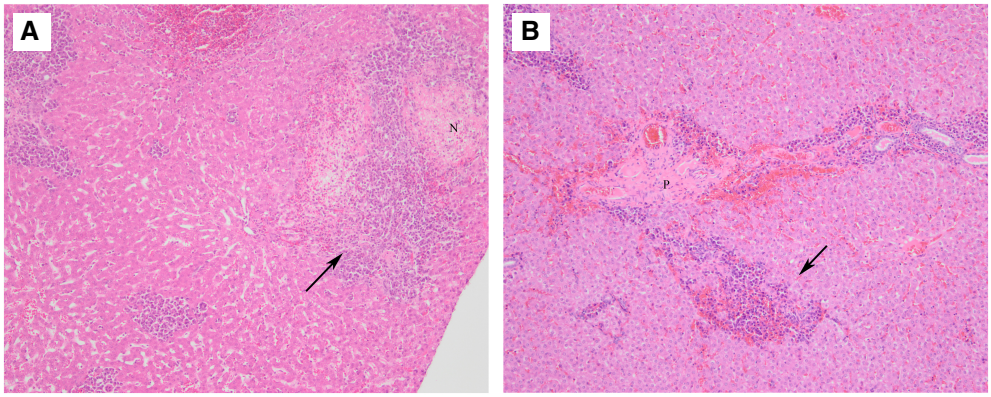

FIG 4. Liver histology (original magnification ×10). Tissue samples were fixed in 4% buffered formalin, embedded in paraffin, cut at 4 µm, and stained with haematoxylin and eosin. (A) Intraoperative liver biopsy showing necrosis (N) and haemorrhage and predominantly plasmacytic infiltrates (arrow). (B) *Post-mortem* liver biopsy. Portal area (P) with predominantly plasmacytic infiltrates (arrow)

T=30, indicating persistent portosystemic shunting. As the body condition score, hyporexia and bile acids (148 µmol/L) worsened, euthanasia was elected 4 months postsurgery. *Post-mortem* examination revealed complete closure of the shunting vessel without macroscopic evidence of acquired portosystemic shunting. Hepatic histology showed more prominent portal veins in multiple portal tracts with subjectively fewer arterioles present, indicating improved intrahepatic portal perfusion. In both intraoperative and *post-mortem* liver samples, plasmacytic portal infiltrates and multifocal acute necrosis were present (Fig 4A, B).

DISCUSSION

This is a case report of a ferret diagnosed and treated surgically for an extrahepatic congenital portosystemic shunt. A single shunt with this morphology is also frequently found in dogs and cats (White & Parry 2016, White *et al.* 2017), therefore a congenital origin is considered likely. Due to the limited experience regarding congenital portosystemic shunts in ferrets, the shunt may have been missed on the initial ultrasound. The morphology differed from an extrahepatic shunt in a ferret described in 2019, which drained *via* the left renal vein and had more collateral vessels, suggestive of an acquired rather than congenital origin (Garcia *et al.* 2019).

Multiple medical treatment options have been reported in dogs and cats that can be done before surgical treatment. In this ferret, a protein-adapted diet was initiated 6 weeks before surgical treatment, but no other medical treatment was given such as lactulose or antibiotics. It is unclear whether this has contributed to the outcome.

Surgical shunt attenuation is recommended over medical treatment in both dogs and cats (Tivers & Lipscomb 2011, Valiente *et al.* 2020), but did not yield satisfactory results in this ferret. Surgical attenuation can be performed by ligation, thin film banding, ameroid constrictor placement or coil embolization (Youmans & Hunt 1998, Hunt & Hughes 1999, Murphy *et al.* 2001, Mehl *et al.* 2007, Falls *et al.* 2013). Ameroid constrictor and coil embolization were not considered due to the size of this animal. With all techniques, the aim is to achieve complete closure. Complete ligation with a nonabsorbable suture is therefore the preferred technique when no portal hypertension occurs, like in this ferret. It is not known if outcome would have been different after gradual closure.

Liver volume and portal perfusion improved after surgery, but liver function tests remained abnormal. Postoperative CT angiography and *post-mortem* examination failed to identify residual flow through the shunt or acquired shunting, but it is not uncommon for liver function tests to remain abnormal after complete shunt closure (Lawrence *et al.* 1992, Hunt & Hughes 1999, Bristow *et al.* 2017). Primary portal hypoplasia and small extrahepatic or intrahepatic collateral circulation may have affected postsurgical outcome (Tams 2003) and can be missed on gross macroscopic examination.

The outcome in this ferret may have been affected by a delayed diagnosis and treatment (Hottinger *et al.* 1995, Winkler *et al.* 2003, van den Bossche *et al.* 2018). This may be due to this animal kept in group housing, making it more likely that subtle signs of hepatic encephalopathy were missed.

Both intraoperative and *post-mortem* histopathology of the liver showed plasmacytic portal infiltrates and multifocal acute necrosis which may have contributed to an unfavourable outcome in this ferret. The cause of these parenchymal changes was unknown and unlikely to be related to the shunt.

We were able to determine reference values for fasting plasma ammonia and ammonia tolerance tests in clinically healthy ferrets, which may be used for diagnosing congenital portosystemic shunts in ferrets in the future.

Ammonia is a more sensitive and specific indicator for portosystemic shunting than bile acids, as cholestasis and gall bladder contraction do not alter results. Increased ammonia is consistent with portosystemic shunting in most cases. A limitation of our approach was that we omitted to measure bile acids and liver enzymes in the control group to exclude subclinical liver disease. Because clinical signs are often mild and aspecific, elevated bile acids in a ferret without jaundice may be a first indication of a congenital portosystemic shunt. Because fasting plasma ammonia may be normal or only mildly increased, ammonia tolerance

testing has a clear added value in the diagnosis of either congenital or acquired portosystemic shunting.

In conclusion, this report demonstrates that congenital portosystemic shunts should be considered in ferrets displaying weight loss, anorexia, or decreased activity. Ammonia tolerance testing served as a reliable tool to aid in diagnosing abnormal ammonia metabolism. Although postoperative outcome in this case was unsatisfactory, surgical ligation of portosystemic shunt is technically feasible in ferrets. Early diagnosis and recognition may help in a better management of this condition in ferrets.

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Author contributions

Judith Visser: Conceptualization (lead); data curation (lead); investigation (equal); methodology (equal); project administration (lead); writing – original draft (lead); writing – review and editing (lead). **Nico Schoemaker:** Conceptualization (equal); data curation (supporting); methodology (supporting); resources (equal); supervision (equal); writing – review and editing (equal). **Yvonne R.A. van Zeeland:** Data curation (supporting); formal analysis (supporting); methodology (supporting); writing – original draft (supporting); writing – review and editing (equal). **Stefanie Veraa:** Formal analysis (equal); methodology (supporting); writing – original draft (supporting); writing – review and editing (equal). **Marja J. L. Kik:** Formal analysis (equal); investigation (equal); methodology (supporting); writing – original draft (supporting). **Hille Fieten:** Methodology (equal); supervision (equal); writing – original draft (equal); writing – review and editing (equal). **Anne Kummeling:** Conceptualization (supporting); investigation (equal); methodology (equal); supervision (equal); writing – original draft (equal); writing – review and editing (equal).

Conflict of interest

None of the authors of this article has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

References

Bristow, P., Tivers, M., Packer, R., *et al*. (2017) Long-term serum bile acid concentrations in 51 dogs after complete extrahepatic congenital portosystemic shunt ligation. *Journal of Small Animal Practice* **58**, 454-460

Falls, E. L., Milovancev, M., Hunt, G. B., *et al*. (2013) Long-term outcome after surgical ameroid ring constrictor placement for treatment of single extrahepatic portosystemic shunts in dogs. *Veterinary Surgery* **42**, 951-957

Garcia, M. A., Montesinos, B. A., Bonvehi, N. C., *et al*. (2019) Extrahepatic portosystemic shunt in a domestic ferret. Proceedings of the International Conference on Avian Herpatological and Exotic Mammal Medicine. London, UK, April 28–May 2

Hein, J., Spreyer, F., Sauter-Louis, C., *et al*. (2012) Reference ranges for laboratory parameters in ferrets. *Veterinary Record* **171**, 218

Hottinger, H. A., Walshaw, R. & Hauptman, J. G. (1995) Long-term results of complete and partial ligation of congenital portosystemic shunts in dogs. *Veterinary Surgery* **24**, 331-336

Hunt, G. & Hughes, J. (1999) Outcomes after extrahepatic portosystemic shunt ligation in 49 dogs. *Australian Veterinary Journal* **77**, 303-307

Huynh, M. & Laloi, F. (2013) Diagnosis of liver disease in domestic ferrets. *The Veterinary Clinics of North America. Exotic Animal Practice* **16**, 121-144

Lawrence, D., Bellah, J. R. & Diaz, R. (1992) Results of surgical management of portosystemic shunts in dogs: 20 cases (1985-1990). *Journal of the American Veterinary Medical Association* **201**, 1750-1753

Mehl, E. H. L., Kyles, A. E., Case, A. S. E., *et al*. (2007) Surgical management of left-divisional intrahepatic portosystemic shunts: outcome after partial ligation of, or ameroid ring constrictor placement on, the left hepatic vein in twenty-eight dogs (1995–2005). *Veterinary Surgery* **36**, 21-30

Murphy, S. T., Ellison, G. W., Long, M., *et al*. (2001) A comparison of the ameroid constrictor versus ligation in the surgical management of single extrahepatic portosystemic shunts. *Journal of the American Animal Hospital Association* **37**, 390-396

Nelson, N. C. & Nelson, L. L. (2011) Anatomy of extrahepatic portosystemic shunts in dogs as determined by computed tomography angiography. *Veterinary Radiology & Ultrasound* **52**, 498-506

Rothuizen, J. & van den Ingh, T. S. (1982) Rectal ammonia tolerance test in the evaluation of portal circulation in dogs with liver disease. *Research in Veterinary Science* **33**, 22-25

Tams, T. R. (2003) Diseases of the liver and hepatobiliary system. In: Handbook of Small Animal Gastroenterology. 2nd edn. Ed T. R. Tams. W.B. Saunders, St. Louis, MO, USA. p 330

Tivers, M. & Lipscomb, V. (2011) Congenital portosystemic shunts in cats: surgical management and prognosis. *Journal of Feline Medicine and Surgery* **13**, 185-194

Valiente, P., Trehy, M., White, R., *et al*. (2020) Complications and outcome of cats with congenital extrahepatic portosystemic shunts treated with thin film: thirty-four cases (2008-2017). *Journal of Veterinary Internal Medicine* **34**, 117-124

van den Bossche, L., Steenbeek van, F. G., Weber, M., *et al*. (2018) Genome-wide based model predicting recovery from portosystemic shunting after liver shunt attenuation in dogs. *Journal of Veterinary Internal Medicine* **32**, 1343-1352

van Straten, M., Straten, van, G., Spee, B., *et al*. (2015) Diagnostic value of the rectal ammonia tolerance test, fasting plasma ammonia and fasting plasma bile acids for canine portosystemic shunting. *The Veterinary Journal* **20**, 282-286

White, R. N. & Parry, A. T. (2016) Morphology of splenocaval congenital portosystemic shunts in dogs and cats. *Journal of Small Animal Practice* **57**, 28-32

White, R. N., Shales, C. & Parry, A. T. (2017) New perspectives on the development of extrahepatic portosystemic shunts. *Journal of Small Animal Practice* **58**, 669-677

Winkler, J. T., Bohling, M. W., Tillson, D. M., *et al*. (2003) Portosystemic shunts: diagnosis, prognosis, and treatment of 64 cases (1993–2001). *Journal of the American Animal Hospital Assocociation* **39**, 169-185

Youmans, K. R. & Hunt, G. B. (1998) Cellophane banding for the gradual attenuation of single extrahepatic portosystemic shunts in eleven dogs. *Australian Veterinary Journal* **76**, 531-537

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Overview of laboratory values of ferret with cPSS

Table S2. Pilot study – Ammonia tolerance testing in 16 asymptomatic ferrets

Table S3. Boxplot of FA and ATT

Data S1. Animals and methods of pilot study