

CASE REPORT

Gall bladder rupture associated with cholecystitis in a domestic ferret (*Mustela putorius*)

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A six-year-old neutered female albino ferret was presented with an acute episode of lethargy and anorexia. Clinical examination revealed marked cranial abdominal pain. A severe neutrophilic leukocytosis was present. Abdominal ultrasound was consistent with a diffuse peritonitis and severe bile duct inflammation. Cytology of the abdominal effusion revealed bile peritonitis. An exploratory laparotomy was performed and the gall bladder appeared inflamed with multiple perforations. A cholecystectomy was performed. The ferret recovered without complication. Bacteriological culture of the bile and gall bladder yielded a pure growth of *Pseudomonas aeruginosa*. Histopathological analysis of the gall bladder and liver was consistent with a marked cholecystitis and cholangiohepatitis. On the basis of sensitivity testing, the ferret was treated with marbofloxacin for one month. No complications or recurrence were seen up to 1 year after the diagnosis. To the author's knowledge, this is the first report of bile peritonitis secondary to gall bladder rupture in a ferret.

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INTRODUCTION

Ruptured gall bladder secondary to cholecystitis is a life-threatening condition in small animals (Bromel *et al.* 1998). Several reports of cholestasis and obstructions have been reported in ferrets but none have involved rupture which necessitates rapid diagnosis and surgical treatment (Hall and Ketz-Riley 2011, Hauptman *et al.* 2011). This case report describes the history, clinical signs, clinicopathology and histopathology findings associated with a ruptured gall bladder in a ferret and its successful treatment. On the basis of this report, ruptured gall bladder should be included in the differential diagnosis of acute abdomen in ferrets.

CASE REPORT

A six-year-old neutered female albino ferret weighing 0.8 kg was presented to the Centre Hospitalier Vétérinaire Frégis for

an acute 2-day episode of lethargy and anorexia. No previous medical history was reported. Clinical examination revealed diffuse pain over the cranial aspect of the abdomen. Rectal temperature was within normal limits [39.5°C, reference interval, 37.8 to 40°C (Morrissey 2012)].

A blood sample drawn from the cranial vena cava was submitted for haematological and biochemical analyses. Haematology revealed a marked neutrophilic leukocytosis [30.9×10⁹/L, reference interval, 3 to 16.7×10⁹/L (Hein *et al.* 2012)] associated with thrombocytosis [1510×10⁹/L, reference interval, 264 to 910×10⁹/L (Hein *et al.* 2012)]. Serum biochemistry demonstrated hypoalbuminaemia [19 g/L, reference interval, 28 to 43 g/L (Hein *et al.* 2012)]. The liver enzymes, alanine aminotransferase and alkaline phosphatase and bilirubin were within their respective reference intervals (Table 1).

An intravenous catheter was placed in the cephalic vein and fluid therapy was initiated [0.9% NaCl and 5% glucose solutions (Baxter) at a rate of 3 mL/kg/hour]. Antibiotic therapy was

Table 1. Haematology and biochemistry findings from a ferret with ruptured gall bladder

| | | Hein et al. (2012) | Case at time of admission |
|------------------------|--------------------|-----------------------|------------------------------|
| Red blood cell count | $\times 10^{12}/L$ | 7.4 to 13 | 8.8 |
| Haemoglobin | mmol/L | 8.6 to 13.6 | 8.9 |
| Haematocrit | L/L | 0.4 to 0.7 | 0.47 |
| White blood cell count | $\times 10^9/L$ | 3.0 to 16.7 | 30.9 |
| Neutrophils | $\% \times 10^9/L$ | 17.2 to 81.9 | 80 |
| Absolute | $\times 10^9/L$ | 0.9 to 7.4 | 24.7 |
| Eosinophils | $\% \times 10^9/L$ | 0.0 to 5.7 | 1 |
| Absolute | $\times 10^9/L$ | 0 to 0.7 | 0.3 |
| Basophils | $\% \times 10^9/L$ | 0.0 to 1.4 | 0 |
| Absolute | $\times 10^9/L$ | 0.0 to 0.2 | 0 |
| Lymphocyte | $\% \times 10^9/L$ | 12.6 to 80.6 | 15 |
| Absolute | $\times 10^9/L$ | 0.6 to 10.5 | 4.6 |
| Monocyte | $\% \times 10^9/L$ | 0.0 to 6.5 | 4 |
| Absolute | $\times 10^9/L$ | 0.0 to 0.5 | 1.2 |
| Thrombocytes | $\times 10^9/L$ | 171.7 to 1280.6 | 1510 |
| ALT | IU/L | 49 to 242.8 | 88 |
| ALKP | IU/L | 13.3 to 141.6 | 27 |
| Total bilirubin | umol/L | 0.0 to 3.3 | 7 |
| Urea | mmol/L | 4.8 to 16.9 | 0.5 |
| Creatinine | umol/L | 23.0 to 76.7 | 2 |
| Total protein | g/L | 54.7 to 77.9 | 51 |
| Albumin | g/L | 28.0 to 43.9 | 19 |
| Glucose | mmol/L | 3 to 8.5 | 5.8 |

ALT Alanine aminotransferase, ALKP Alkaline phosphatase

initiated with 5 mg/kg marbofloxacin (Marbocyl; Vetoquinol) twice a day and 20 mg/kg metronidazole (Metronidazole; Baxter) intravenously (iv) twice a day as the leukocytosis suggested an infectious process. A dose of 4 mg/kg ranitidine (Azantac; GlaxoSmithKline) was administered iv three times a day (because of the predisposition of ferrets for gastric ulceration) together with 0.1 mg/kg morphine (Morphine Sulphate; Lavoisier) subcutaneously every 6 hours for pain management.

A conscious abdominal ultrasound examination was carried out and revealed diffuse hyperechogenicity of the abdominal fat and the peritoneum as well as mild peritoneal effusion. There was a generalised thickening and hyperechogenicity of the biliary tree. Some gas bubbles were observed in the lumen of the gall bladder (Fig 1). A fine needle aspirate of the peritoneal fluid was performed. Approximately 1 mL of yellow to green turbid liquid was collected. Cytology of the fluid showed numerous polynuclear neutrophils and activated macrophages, some containing bile pigment inclusions. These findings were considered consistent with bile peritonitis.

A median laparotomy was performed. Anaesthetic induction was achieved with 0.2 mg/kg diazepam (Valium; Roche) and 4 mg/kg propofol (Propofol Fresenius; Fresenius Kabi) iv. The ferret was intubated with a 2.5 mm uncuffed tracheal tube and maintained with isoflurane (Aeranne; Baxter) at 2.5% mixed with oxygen. The abdominal cavity and the omental fat were stained by yellow fluid (Fig 2). The gall bladder and the common bile duct were severely inflamed. Several perforations were observed in the gall bladder. The gall bladder was smoothly dissected from the surrounding hepatic tissue. Haemostasis was achieved with bipolar cautery. A 4-0 monofilament absorbable



FIG 1. Ultrasonographic view of the gall bladder. The arrows delineate the gas bubble seen in the lumen of the gall bladder

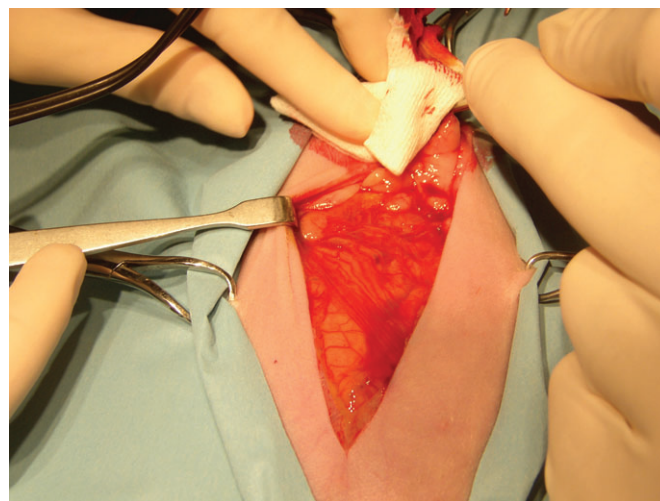


FIG 2. Intraoperative view. Note the generalised yellow staining in the abdominal cavity

suture (Biosyn; Covidien) was circumferentially placed around the cystic artery and the cystic canal. The gall bladder was then resected and submitted for histopathology and bacteriology (Fig 3). Hepatic biopsy was also performed. Patency of the common bile duct was evaluated and the bile content was easily emptied in the duodenum by gentle pressure. The abdominal cavity was flushed with sterile warm saline repeatedly. The muscular layer and the subcutaneous layer were closed routinely. Recovery from anaesthesia was uneventful. A dose of 0.2 mg/kg Meloxicam (Metacam; Boehringer Ingelheim) was given postoperatively once a day. The following day, the ferret was clinically improved and started to eat spontaneously. The medications (antibiotic and non-steroidal anti-inflammatory

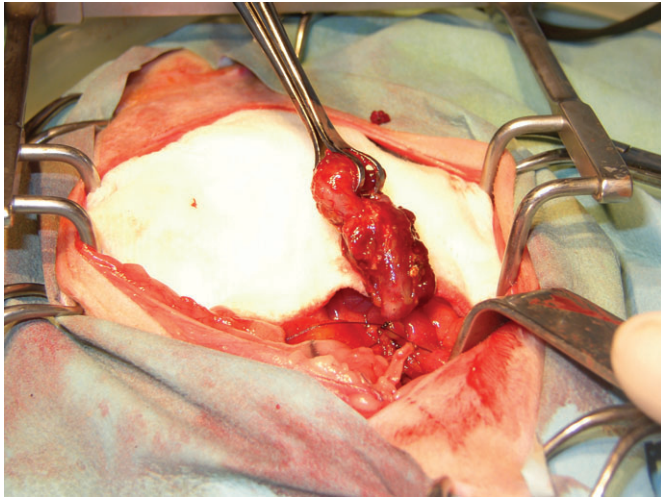


FIG 3. Intraoperative view. The gall bladder is severely inflamed and has multiple breaches

drugs) were continued. The ferret was discharged 3 days after admission.

Bacteriological culture of the bile and the gall bladder yielded a pure growth of *Pseudomonas aeruginosa* with intermediate susceptibility for marbofloxacin.

Histopathological examination revealed a severe lymphocytic and granulomatous cholecystitis associated with cystic glandular hyperplasia of the gall bladder mucosa. The liver parenchyma was consistent with a marked lymphocytic cholangiohepatitis.

The ferret was re-evaluated 1 and 3 weeks later. The leukocyte count was gradually decreasing (from $18.6 \times 10^9/L$ to $8.9 \times 10^9/L$), the thrombocyte count had normalised ($332 \times 10^9/L$) and the albumin concentration had increased (22 g/L) 3 weeks postoperatively. Anti-inflammatory treatment was discontinued a week after the surgery and the antibiotic treatment was discontinued 4 weeks postoperatively. A year after the surgery, the ferret was still doing well.

DISCUSSION

Bile peritonitis is a life-threatening condition known in humans, dogs and cats (Ludwig *et al.* 1997, Gabriele *et al.* 2010). In domestic species, gall bladder perforations have been commonly associated with cholecystitis (Parchman and Flanders 1990, Ludwig *et al.* 1997, Bromel *et al.* 1998, Mayhew *et al.* 2002). Ascending tract infections are involved in the pathogenesis of cholecystitis in cats and dogs (O'Neill *et al.* 2006, Brain *et al.* 2006). *Escherichia coli* is the most common bacteria isolated in cases of cholecystitis in cats and dogs (O'Neill *et al.* 2006, Wagner *et al.* 2007, Brain *et al.* 2006, Huynh and Laloï 2013). In ferrets, some findings suggest that the same pathogenesis can be extrapolated. *Helicobacter cholecystus* was isolated in three ferrets which were part of a colony with signs of hepatobiliary lesions (Garcia *et al.* 2002). The presented case showed direct ultrasonographic visualisation of a gas bubble which was consistent with a gas forming bacteria such as *P. aeruginosa* which was later isolated.

Other causes of biliary rupture in small mammals include trauma, cholelithiasis, tumours and parasitic infection (Ludwig *et al.* 1997, Bromel *et al.* 1998, Willard & Fossum 2005). Traumatic gall bladder ruptures in ferrets have not been documented to the authors' knowledge. Cholelithiasis and extrahepatic obstruction have been described but in the absence of rupture (Hall & Ketz-Riley 2011, Hauptman *et al.* 2011). Neoplasia of the biliary tract such as biliary cystadenomas are common in ferrets (Fox *et al.* 1996). No sign of neoplasia was evident on histopathological examination of the submitted samples from the current case. Biliary infection by *Eimeria* species has been described in a ferret but did not cause any damage to the biliary tree (Williams *et al.* 1996).

Blood analyses are useful tools to screen for subclinical liver disease in ferrets (Huynh & Laloï 2013). However, some cases of hepatitis do not trigger elevation of alanine aminotransferase, alkaline phosphatase or bilirubin as observed in this ferret (Burgess 2007). These laboratory finding differs significantly from previous cases reported with bile duct disorders (Hauptman *et al.* 2011, Hall and Ketz-Riley 2011). The finding of neutrophilic leukocytosis in cases of liver disease is variable, however, an association with concurrent peritonitis, as in this case, is common (Sista *et al.* 2013).

Thrombocytosis can be related to counting artifact, stress, trauma, secondary to inflammation or neoplasia (Bourdreaux 2010). The observed hypoalbuminaemia could be caused by liver disease or the concurrent peritonitis.

Extra hepatic bile duct obstructions have been successfully diagnosed by ultrasonography in ferrets (Hauptman *et al.* 2011, Hall and Ketz-Riley 2011). The common bile duct was enlarged and convoluted with signs of cholestasis but no effusion and no rupture were observed in the reported cases. No sign of obstruction was seen in this case but an intense hyperechogenicity of the biliary tree consistent with a cholecystitis was observed and peritoneal effusion was demonstrated. In a review of 10 dogs affected with bile peritonitis, abdominal ultrasound detected effusion in eight dogs (Amsellem *et al.* 2006). Ultrasound guided fine needle aspirate of the peritoneal fluid is a useful tool to diagnose biliary peritonitis. Cytological examination may reveal yellow to green biliary pigment as seen in this case or a characteristic basophilic acellular matrix (Connally 2003, Owens *et al.* 2003). Abdominal effusion and peritonitis in ferrets are reported in cases of systemic coronavirus infection as seen in feline infectious peritonitis (Garner *et al.* 2008). In such cases, a yellow viscous effusion is seen but bile pigment is absent.

Cholecystectomy is the recommended treatment for gall bladder rupture (Bromel *et al.* 1998, Mehler *et al.* 2004, Willard and Fossum 2005, Corfield *et al.* 2007). The anatomy of the biliary tree in ferret is similar to other mammals as is the cholecystectomy technique (Poddar 1977, Blass and Seim 1985). The overall prognosis of biliary tract surgery in dogs ranges from 28 to 66% survival rate (Martin *et al.* 1986, Fahie and Martin 1995, Ludwig *et al.* 1997, Mehler 2011, Amsellem *et al.* 2006). In these cases, bile peritonitis is not always a risk factor but if the peritonitis becomes septic, it is associated with increased mortality (Ludwig *et al.* 1997, Mehler *et al.* 2004). In a retrospective study of

26 cases, the prognosis of bile peritonitis in dogs was 31% survival rate (Mehler *et al.* 2004). Haematological prognostic factors include a leukocytosis greater than $35.7 \times 10^9/L$. Preoperative neutrophil counts are greater in cases of biliary rupture (Ludwig *et al.* 1997, Amsellem *et al.* 2006, Uno *et al.* 2009). There is controversy as to whether hypoalbuminaemia is a risk factor. Mehler (2001) reported that it was not, whereas Amsellem *et al.* (2006) reported that it was. The leukocytosis and the hypoalbuminaemia found in this case reinforce the need for rapid management of such cases so that a positive prognosis is optimised.

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.

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