Case Report

jfms OPEN REPORTS

Journal of Feline Medicine and Surgery Open Reports
1–6

DOI: 10.1177/20551169231216859
journals.sagepub.com/home/jfmsopenreports

This paper was handled and processed by the American Editorial Office (AAFP) for publication in *JFMS Open Reports*

Sage

Severe polycystic liver disease in a cat

Emily M King[1], Maria Pappano[2], Sarah K Lorbach[2], Eric M Green[2], Valerie J Parker[2] and Megan E Schreeg[1]

Abstract

Case summary Ductal plate malformations (DPMs) are poorly documented in the veterinary literature, particularly those of the polycystic liver disease (PCLD) phenotype. A 13-year-old female spayed cat presented with progressive icterus, abdominal distension, weight loss and elevated liver enzymes. Initial empirical treatment consisting of amoxicillin/clavulanate, ursodiol and later prednisolone was attempted; however, clinical signs progressed. On abdominal ultrasound, numerous large hepatic cystic masses were noted, characterized by an anechoic center with a heterogeneous, hyperechoic wall. A post-mortem examination confirmed numerous hepatic cysts, the larger of which resulted in hemorrhage and subsequent hemoabdomen. Histologically, these cysts were determined to be of biliary origin, and a diagnosis of PCLD was assigned.

Relevance and novel information Herein, we present a detailed report of clinical, gross and histologic findings in a cat clinically affected by PCLD. This case demonstrates that cysts present in this congenital disease can ultimately lead to hepatobiliary malfunction and clinical decline via marked expansion of cysts, compression of the liver and hemoabdomen from cyst rupture. DPMs, specifically PCLD, should be considered in cats presenting with multifocal large hepatic cysts.

Keywords: Biliary cyst; ductal plate malformation; lymphocytic cholangitis; hepatic cysts; hemoabdomen

Accepted: 9 November 2023

Case description

A 13-year-old female spayed domestic shorthair cat was presented to The Ohio State University Veterinary Medical Center for evaluation of increased liver enzymes with icterus. Increased liver enzymes were first noted incidentally 1 year prior (Table 1) during routine bloodwork. On presentation to our service, the cat weighed 3.27 kg and had a body condition score (BCS) of 5/9 with mild muscle atrophy. The cat was eating a complete and balanced adult maintenance diet and was not receiving any other medications or supplements. Physical examination revealed icterus but was otherwise unremarkable. Abdominal ultrasound with bile sampling and liver biopsies were declined. Empirical treatment for presumptive bacterial cholangitis was prescribed, consisting of amoxicillin trihydrate/clavulanate potassium (13.75 mg/kg PO q12h) and ursodiol (15 mg/kg PO q24h). Vomiting was observed 10 days later, prompting the discontinuation of antibiotics and initiation of prednisolone (1 mg/kg PO q24h). One month later (day 33), a physical examination revealed a weight loss of 0.11 kg (3.16% of body weight), a BCS of 4/9, moderate muscle atrophy, dehydration, icterus and a gallop rhythm. A round, firm mass was palpable in the right cranial abdomen. A complete blood count revealed a thrombocytopenia (49 $\times 10^9$/l) with

[1]Department of Veterinary Biosciences, College of Veterinary Medicine, The Ohio State University, Columbus, OH, USA
[2]Department of Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio State University, Columbus, OH, USA

Corresponding author:
Valerie J Parker DVM, DACVIM (SAIM, Nutrition), Department of Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio State University, 601 Vernon Tharp St, Columbus, OH 43210, USA
Email: parker.888@osu.edu

Table 1 Selected serial biochemistry results

Variable	1 year prior	Day 1	Day 33	Reference interval
ALT (IU/l)	342	466	386	24–115
AST (IU/l)	115	161	143	12–45
ALP (IU/l)	122	264	388	10–61
Total bilirubin (mg/dl)	0.9	5.0	7.6	0.00–0.1
Cholesterol (mg/dl)	160	214	237	77–264
Albumin (g/dl)	3.0	3.1	3.0	2.8–4.1
BUN (mg/dl)	15	21	22	18–39
Creatinine (mg/dl)	0.8	1.2	0.8	0.7–2.0

ALP = alkaline phosphatase; ALT = alanine transaminase; AST = aspartate transaminase; BUN = blood urea nitrogen

platelet clumps and a mild monocytosis (1.16 $\times 10^9$/l). Chemistry revealed a mixed hepatopathy with progressive hyperbilirubinemia (Table 1).

Diagnostic imaging

On day 33, an abdominal ultrasound examination (Figure 1), performed by a board-certified radiologist, revealed a cystic structure measuring 8 × 4 × 4 cm in the left liver with a well-defined, heterogenous wall, filled with anechoic fluid and multiple free-floating echogenic foci. Several smaller cystic structures were noted throughout all liver lobes, and the intrahepatic bile ducts were dilated up to 5 mm in diameter. The gallbladder wall was mildly thickened with numerous, small cystic structures along the luminal surface. The cystic duct was dilated up to 1 cm, with several small cystic structures along the wall and compressed by the large cystic hepatic mass. There was scant, anechoic, perihepatic effusion that was unable to be sampled. Radiographic conclusions were consistent with fibropolycystic liver disease (ductal plate malformation [DPM]/polycystic liver disease [PCLD]). Bile aspiration and liver biopsy were declined. Of note, an abdominal ultrasound performed 11 months prior, by a board-certified radiologist, revealed an ultrasonographically normal liver and gallbladder. Hepatic cytology at that time revealed presumptive glycogen accumulation and mild hepatocellular hyperplasia.

Case management

A DPM – specifically PCLD – was suspected and the cat was discharged with palliative care (ursodiol and prednisolone). Two months later (day 67), the cat was presented with severe abdominal distension. Physical examination showed progressive, severe cachexia with icterus. The abdomen was tense on palpation and contained numerous presumed cysts of various sizes extending to the caudal abdomen. Therapeutic drainage of the cysts was offered and declined. Recommendations were made to continue medical therapy. Then, 46 days later (day 113), the cat presented with decreased appetite, weakness, ataxia and progressive abdominal distension. The owner elected euthanasia. Before necropsy, a post-mortem abdominal CT was performed, which revealed progressive cyst enlargement (Figure 2).

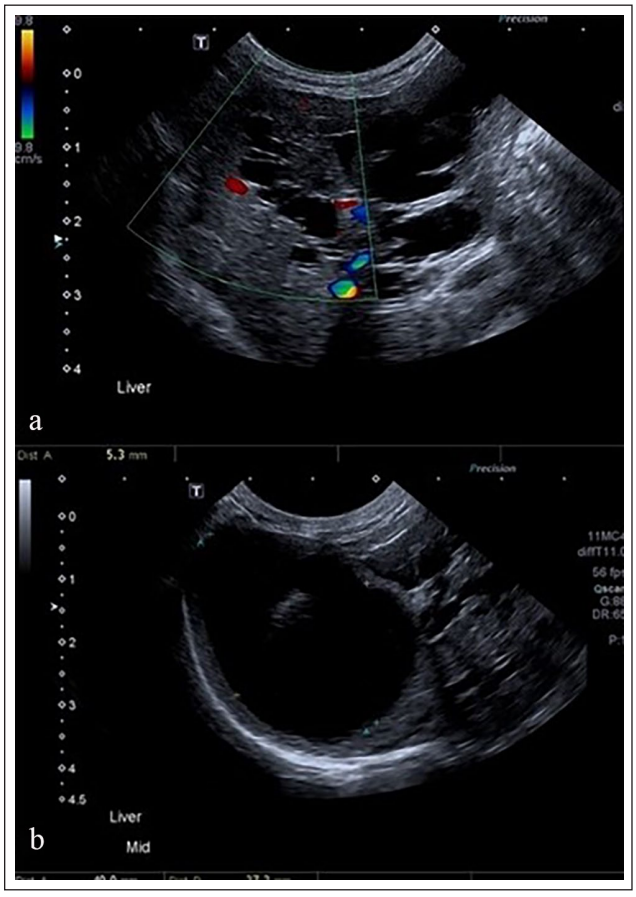

Figure 1 Ultrasonographic images of the liver of the cat: (a) portion of the largest cystic structure and (b) the dilated biliary ducts are seen as anechoic tubular structures lacking Doppler signal

Gross pathology

A post-mortem examination revealed marked abdominal distension with generalized icterus (Figure 3a). The peritoneal cavity contained 525 ml of blood. The liver was 28% of the body weight (2–5% of body weight is

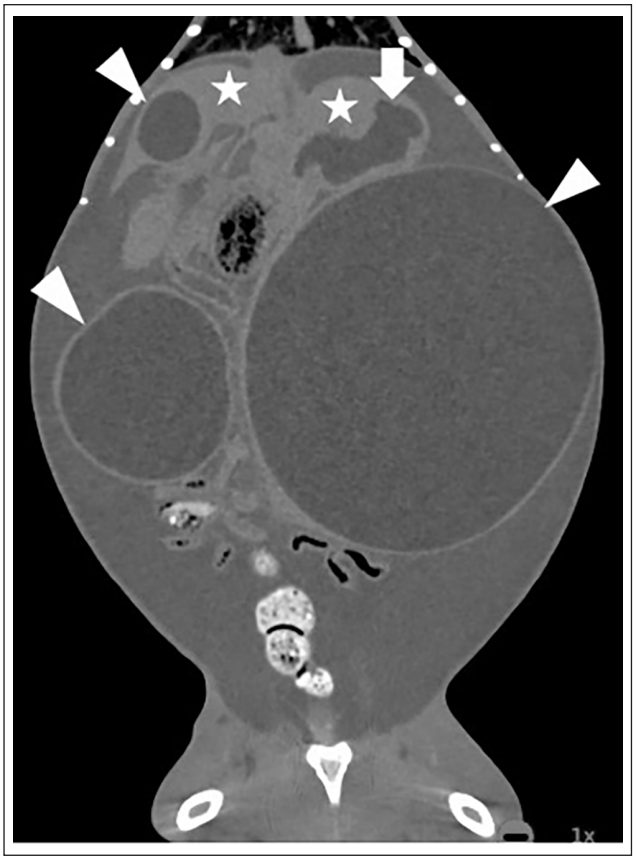

Figure 2 Dorsal plane CT image demonstrating progressive expansion of hepatic cysts (arrowheads) and biliary ducts (arrow) within, and extending from the margin of, the liver (stars)

considered normal). Effacing 60% of the hepatic parenchyma were 30–40 multifocal, well-demarcated, encapsulated, expansile, pale tan cystic masses, with diameters in the range of 3–15 cm, that did not communicate with the intrahepatic biliary tree (Figure 3b,c). The masses contained variable amounts of green-tinged to clear viscous fluid. The largest mass was present in the left lateral lobe and contained approximately 750 ml of fluid. The quadrate lobe of the liver contained a ruptured 5 cm cyst. Overlying and loosely adherent to this ruptured cyst was a 2 cm diameter aggregate of clotted blood. There was a 3 mm diameter blood clot protruding into the lumen of the lobar bile duct where it joined the common bile duct (CBD). The CBD was moderately tortuous but was of normal diameter and patent. Overall, the gross findings supported a presumptive diagnosis of PCLD with cyst dilation, rupture and hemoabdomen.

The remainder of the post-mortem examination identified mild fibrinous peritonitis, moderate hepatic lymphadenomegaly (reactivity), mild left renal cortical atrophy and fibrosis, and bilirubinuria (bright yellow-green urine present in the urinary bladder). Notably, there was no evidence of concurrent renal cysts.

Microscopic pathology

A histologic evaluation of the cystic hepatic masses revealed a wall composed of mature spindle cells within a thick collagenous stroma with moderate lymphoplasmacytic inflammation (Figure 4a,b). The lumen of the cysts was lined by a single layer of cuboidal biliary epithelium with varying erosion/ulceration. There was moderate hemorrhage within and adjacent to the cyst walls, and moderate compression and atrophy in parenchyma adjacent to the cysts. In portal tracts away from the cysts, there was moderate proliferation of bile ducts, and bile ducts were cuffed by moderate numbers of lymphocytes and fewer plasma cells accompanied by increased circumferential fibrous stroma and spindle cells (Figure 4c). Centrilobular hepatocytes had mild accumulation of lipid vacuoles. Importantly, cystic masses did not microscopically communicate with the sections of evaluated biliary tree.

Collectively, PCLD was favored as a diagnosis for the liver cysts. Additional diagnoses of moderate chronic lymphocytic cholangitis and mild hepatic lipidosis were also assigned. Caroli's malformation was initially considered as a differential diagnosis; however, Caroli's malformation will be patent with the surrounding biliary tree, which was not identified in this case. Further, there was no gross or histologic evidence of CBD dilation or ascending bacterial infection, two lesions that commonly accompany Caroli's malformation. Biliary neoplasia (eg, biliary cystadenocarcinoma) was considered unlikely given the lack of evidence of invasion or proliferative activity of biliary epithelium lining cysts.

Discussion

This case of feline PCLD resulted in clinical decline due to gradual expansion of the cysts. PCLD is a subtype of biliary malformations known as DPMs, congenital malformations that occur secondary to abnormal development of the ductal plate, the embryologic precursor of intrahepatic bile ducts.[1,2] DPMs can affect different levels of the intrahepatic biliary tree, resulting in a variety of malformations, including biliary hamartomas (von Meyenburg complexes), Caroli's disease, congenital hepatic fibrosis (CHF) and PCLD.[1–3] In this case, the gross and histologic findings are consistent with PCLD.

Concurrent polycystic kidney and liver disease is well documented in cats. While the true incidence of PCLD in cats is not established, one study of 71 feline liver biopsies found that PCLD was present in 5.6% of cats.[4] In another study detailing feline polycystic kidney disease (PKD), 68% of cats had concurrent DPMs, with CHF and PCLD being most common.[5] Other cases of concurrent feline PKD and DPMs have been reported,[6–8] and associated pancreatic cysts may also be present.[5,9,10] Autosomal dominant mutations in *pkd1* have been discovered as the primary mutation associated with PKD in cats.[11] In

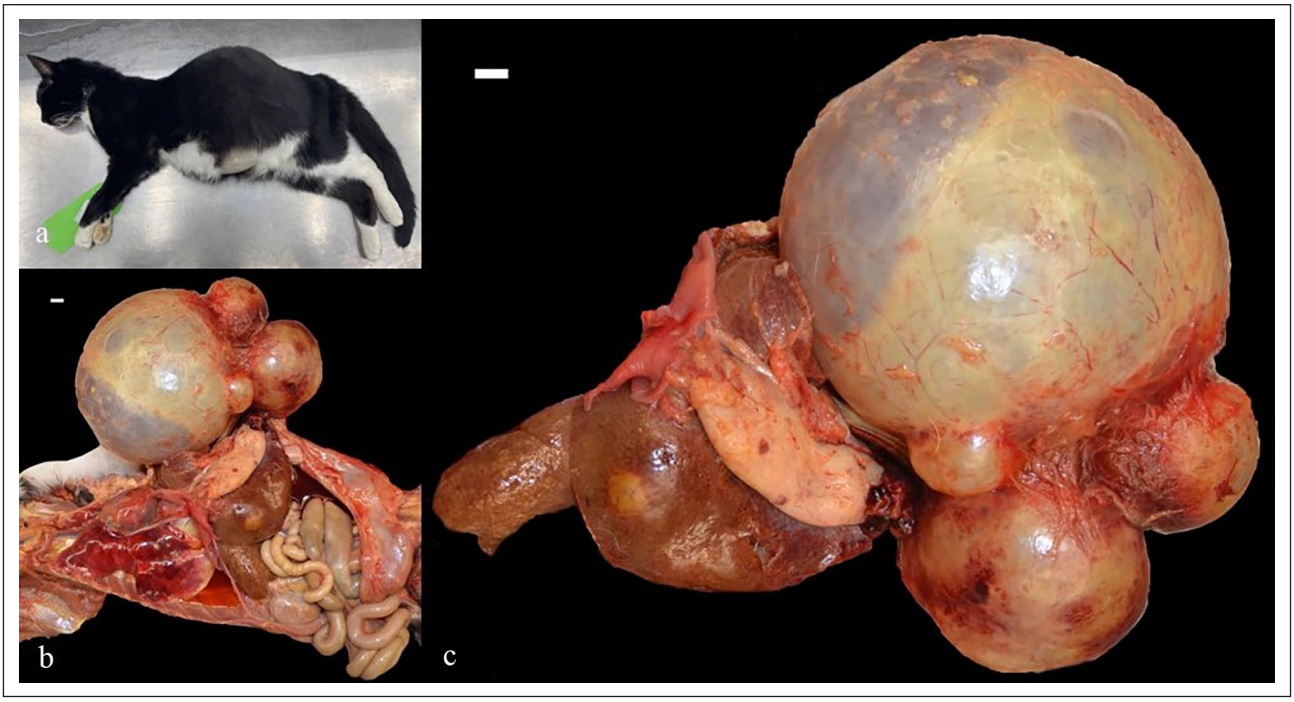

Figure 3 Gross features of polycystic liver disease in a cat: (a) marked abdominal distension was noted on external examination; (b) abdominal distension was attributed to a regionally extensive mass arising from the liver; and (c) the mass was composed of multiple thin-walled, hemorrhaging cystic dilations arising from the left lateral liver lobe. (b,c) Scale bars = 1 cm

this case, lack of appropriate sample collection for DNA testing precluded assessing for *pkd1* mutation, and concurrent kidney cysts were not identified.

In humans, PCLD can occur in the context of either PKD (ADPKD) or isolated PCLD, both of which are considered DPMs.[12] Sole involvement of the liver is considered autosomal dominant, while simultaneous involvement of the kidney can be autosomal dominant or recessive.[13] ADPKD is more common, associated with mutations in *pkd1* and *pkd2*, and is primarily characterized by renal cysts, with concurrent liver cysts in 83–94% of patients.[11,14,15] In contrast, isolated PCLD, in which only liver cysts are present, is rare, and a genetic cause remains undiscovered in cats.[1,4,6–8] PCLD has also been reported in hamsters,[16] llamas,[17] alpacas[18] and chamois.[19] PCLD is well characterized in hamsters; it may be associated with concurrent cysts in the epididymis, seminal vesicles, pancreas and endometrium, and in some reports has been shown to affect >75% of a population.[15,20–22] In many of these reports, liver cysts were incidental findings, but some animals demonstrated anorexia, colic and weight loss. Similarly, in humans, PCLD is often asymptomatic until cyst enlargement results in a clinical impact, including pressure atrophy of adjacent hepatocytes,[12] obstructive cholestasis, pain, abdominal distension and compression of other organs resulting in decreased appetite, portal hypertension, and/or obstructive shock.[12] In this case, we suspect that the exacerbation of hepatocellular and cholestatic clinicopathologic parameters was due to compression from the cysts. Further, cyst rupture led to hemoabdomen and clinical decline; to our knowledge, this is the first time this observation has been made in cats with PCLD, although intracystic hemorrhage has been reported in humans.[23]

This cat had concurrent lymphocytic cholangitis, which may have been a separate contributor to the hepatocellular clinical signs in this patient. In one author's experience (MES), concurrent portal lymphoplasmacytic inflammation adjacent to DPMs is common, but it is unclear whether this represents the disease entity of feline lymphocytic cholangitis or reflects a reactive change. Neutrophilic cholangitis has been associated with other biliary malformations in cats (eg, choledochal cyst, Caroli's malformation) in a recent study, but this is presumably related to these malformations affecting the extrahepatic biliary tree and increasing susceptibility to ascending bacterial infection.[24] Associations between cholangitis syndromes and other DPMs in cats, including PCLD, have not been demonstrated; therefore, the relationship between historic hepatobiliary signs, lymphocytic cholangitis and the presence/progression of PCLD in this cat remains unknown.

Notably, an abdominal ultrasound performed 11 months prior revealed no liver abnormalities. We postulate that the cysts may have been initially microscopic

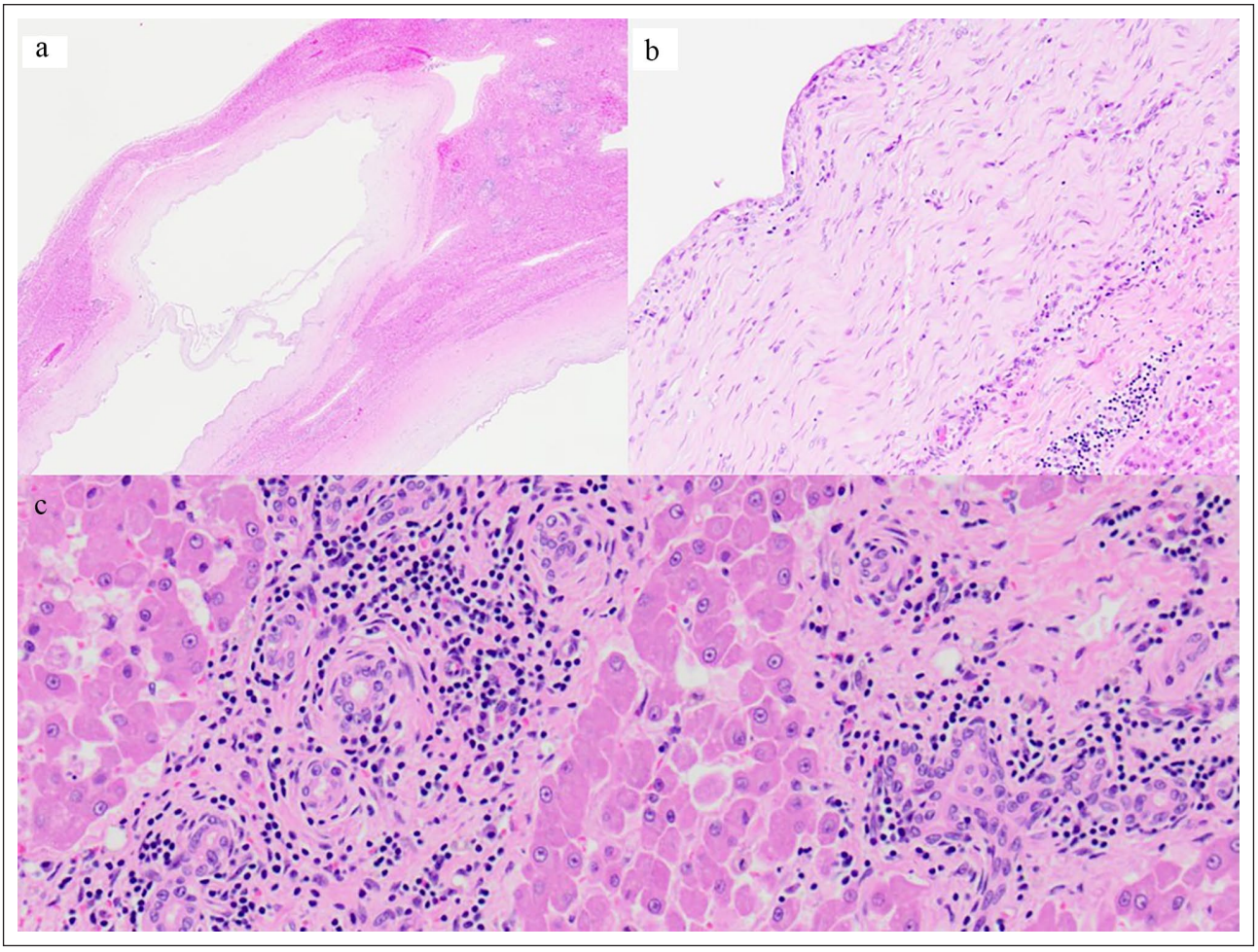

Figure 4 Histologic features of polycystic liver disease in a cat: (a) hepatic parenchyma is microscopically expanded by cavitated structures; (b) the wall of the cystic structures is composed of fibrous connective tissue and lined by cuboidal epithelium (consistent with biliary epithelium); and (c) portal triads adjacent to the cysts exhibit biliary proliferation (ductular reaction) and associated lymphoplasmacytic portal hepatitis

and therefore undetectable, and that over time, the cysts filled with fluid for an undetermined reason. An alternative explanation could be that these cysts represented so-called biliary cystadenomas. In this case, the gross and histologic findings (multifocal expansile biliary cysts throughout the liver) are most consistent with PCLD. The emerging consensus among veterinary pathologists is that the majority of so-called feline biliary cystadenomas actually represent DPMs.[1,2]

In humans, the main goal of treatment of PCLD is to reduce symptoms through reduction of liver volume.[23] Surgical options include cyst aspiration, injection of a sclerosing agent (ethanol) to destroy the epithelial lining and inhibit fluid production, fenestration and segmental resection or liver transplant.[23] Liver transplantation is rarely considered for patients with diffuse small cystic disease when fenestration and aspiration may not be possible.[25] Aspiration and sclerosis have shown moderate success in relieving clinical signs.[23] Drainage of the larger cysts was declined by the cat's owner; however, this would have been palliative at best.

Conclusions

We describe the clinical presentation, clinical complications, and gross and histologic findings in a cat with severe PCLD. The major clinical complication was expansion of liver cysts, resulting in liver compression, abdominal distension, and ultimately cyst rupture and hemoabdomen leading to euthanasia. The possibilities of these complications should be considered in management of cats with PCLD and other DPMs. Given the large size, high number and widespread distribution of the hepatic cysts, therapeutic options were limited in this case. Many therapeutic options have been described in humans; these warrant further investigation in veterinary species.

Acknowledgements The authors gratefully acknowledge Drs Ashley Potts, Dan Lantz, Liza Guess and Heather Biggs for their involvement in the described case.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding The authors received no financial support for the research, authorship, and/or publication of this article.

Ethical approval The work described in this manuscript involved the use of non-experimental (owned or unowned) animals. Established internationally recognized high standards ('best practice') of veterinary clinical care for the individual patient were always followed and/or this work involved the use of cadavers. Ethical approval from a committee was therefore not specifically required for publication in *JFMS Open Reports*. Although not required, where ethical approval was still obtained, it is stated in the manuscript.

Informed consent Informed consent (verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (experimental or non-experimental animals, including cadavers) for all procedure(s) undertaken (prospective or retrospective studies). No animals or people are identifiable within this publication, and therefore additional informed consent for publication was not required.

ORCID iD Valerie J Parker https://orcid.org/0000-0001-6505-8068

References

1 Cullen JM and Stalker MJ. **Liver and biliary system.** In: Maxie G (ed). Jubb, Kennedy & Palmer's Pathology of Domestic Animals. Vol. 2. St. Louis, MO: Elsevier, 2016, pp 258–352.
2 Rothuizen J. WSAVA standards for clinical and histological diagnosis of canine and feline liver disease. Amsterdam: Elsevier Health Sciences, 2006.
3 Venkatanarasimha N, Thomas R, Armstrong E, et al. **Imaging features of ductal plate malformations in adults.** *Clin Radiol* 2011; 66: 1086–1093.
4 Hirose N, Uchida K, Kanemoto H, et al. **A retrospective histopathological survey on canine and feline liver diseases at the University of Tokyo between 2006 and 2012.** *J Vet Med Sci* 2014; 76: 1015–1020.
5 Bosje J, Van den Ingh T and Van der Linde-Sipman J. **Polycystic kidney and liver disease in cats.** *Vet Q* 1998; 20: 136–139.
6 Zandvliet MM, Szatmári V, van den Ingh T, et al. **Acquired portosystemic shunting in 2 cats secondary to congenital hepatic fibrosis.** *J Vet Intern Med* 2005; 19: 765–767.
7 Hirose T, Igami T, Ebata T, et al. **Surgical and radiological studies on the length of the hepatic ducts.** *World J Surg* 2015; 39: 2983–2989.
8 Guerra JM, Daniel AGT, Cardoso NC, et al. **Congenital hepatic fibrosis and polycystic kidney disease not linked to C> A mutation in exon 29 of PKD1 in a Persian cat.** *JFMS Open Rep* 2015; 1. DOI: 10.1177/2055116915619191.
9 Cnossen WR and Drenth JP. **Polycystic liver disease: an overview of pathogenesis, clinical manifestations and management.** *Orphanet J Rare Dis* 2014; 9: 69. DOI: 10.1186/1750-1172-9-69.
10 Dhar DAN, Suchi T, Garg S, et al. **A rare isolated polycystic pancreatic disease. Radiation free diagnostic protocol in selected cases.** *Indian J Endocrinol Metab* 2012; 16: 1054–1056.
11 Lyons LA, Biller DS, Erdman CA, et al. **Feline polycystic kidney disease mutation identified in PKD1.** *J Am Soc Nephrol* 2004; 15: 2548–2555.
12 Mirza H, Besse W, Somlo S, et al. **An update on ductal plate malformations and fibropolycystic diseases of the liver.** *Hum Pathol* 2023; 132: 102–113.
13 Wills ES, Roepman R and Drenth JP. **Polycystic liver disease: ductal plate malformation and the primary cilium.** *Trends Mol Med* 2014; 20: 261–270.
14 Bae KT, Zhu F, Chapman AB, et al. **Magnetic resonance imaging evaluation of hepatic cysts in early autosomal-dominant polycystic kidney disease: the Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease cohort.** *Clin J Am Soc Nephrol* 2006; 1: 64–69.
15 Pirson Y. **Extrarenal manifestations of autosomal dominant polycystic kidney disease.** *Adv Chronic Kidney Dis* 2010; 17: 173–180.
16 Somvanshi R, Iyer P, Biswas J, et al. **Polycystic liver disease in golden hamsters.** *J Comp Pathol* 1987; 97: 615–618.
17 Watanabe TTN, Chaigneau FRC, Adaska JM, et al. **Polycystic liver in two adult llamas.** *J Vet Diagn Invest* 2019; 31: 280–283.
18 Foster A, Duff P, Boufana B, et al. **Adult polycystic liver disease in alpacas.** *Vet Rec* 2013; 172: 666–667.
19 Glawischnig W and Bagó Z. **Polycystic liver disease in senile chamois *(Rupicaprae rupicaprae)*.** *J Wildl Dis* 2010; 46: 669–672.
20 Kaup F-J, Konstýř I and Drommer W. **Characteristic of spontaneous intraperitoneal cysts in golden hamsters and European hamsters.** *Exp Pathol* 1990; 40: 205–212.
21 Gleiser C, Van Hoosier G and Sheldon W. **A polycystic disease of hamsters in a closed colony.** *Lab Anim Care* 1970; 20: 923–929.
22 Percy DH and Barthold SW. Pathology of laboratory rodents and rabbits. Hoboken, NJ: John Wiley & Sons, 2016.
23 Drenth J, Chrispijn M, Nagorney DM, et al. **Medical and surgical treatment options for polycystic liver disease.** *Hepatology* 2010; 52: 2223–2230.
24 Center SA, Randolph JF, Warner KL, et al. **Bacterial culture and immunohistochemical detection of bacteria and endotoxin in cats with suppurative cholangitis-cholangiohepatitis syndrome.** *J Am Vet Med Assoc* 2022; 260: 194–211.
25 Russell RT and Pinson CW. **Surgical management of polycystic liver disease.** *World J Gastroenterol* 2007; 13. DOI: 10.3748/wjg.v13.i38.5052.