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Case Reports

CONGENITAL BILIARY ANOMALY WITH SECONDARY CHOLANGIOHEPATITIS IN A SIAMESE CROSS KITTEN

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SUMMARY

A 5-month-old Siamese cross kitten was presented with jaundice and a palpable abdominal mass at the right cranial quadrant. The extra-hepatic biliary system was markedly distended upon abdominal ultrasonography. Complete bile duct obstruction was ruled out due to the presence of urobilinogen, light brown stool, and consistentlynormal alkaline phosphatase (ALP) levels. Head tremors developed on the second day of hospitalization. Tentative diagnoses of congenital biliary anomaly and hepatic encephalopathy werederived and exploratory laparotomy revealed a severely distended and tortuous bile duct indistinguishable from the gallbladder with negative duodenal filling. Modified cholechoduodenostomy was performed however the kitten did not recover from general anaesthesia. Secondary cholangiohepatitis and hepatic encephalopathy were confirmed upon histopathologic examination.Primary congenital biliary atresia or choledochal cyst with secondary cholangiohepatitis was suspected. Biliary anomalies are rare in cats with only two cases reported in the literature. These conditions are often challenging to diagnose and due to the limited treatment options, have a poor prognosis.

Keywords: Abdominal mass, congenital biliary anomaly, hepatic encephalopathy, jaundice, secondary cholangiohepatitis

INTRODUCTION

The biliary system consists of the gallbladder, intrahepatic and extra-hepatic bile ducts as well as some hepatocytes and they are involved in the production and transportation of bile. When hepatocytes secrete bile, it is collected by the right and left hepatic ducts which drain into the common hepatic duct and gets stored in the gallbladder. After feeding, the gallbladder contracts and releases bile through the cystic duct into the common bile duct which opens into the duodenum. In cats, the terminal portion of the common bile duct merges with the major pancreatic duct before it reaches the duodenum (Williams, 2009).

Biliary atresia is a rare congenital anomaly where there is narrowing or discontinuity of the bile ducts (Hampson *et al*., 1987; Alagille, 1984; Perlmutter and Shepherd, 2002). Choledochal cysts on the other hand are any cystic dilations of the bile duct (Singham *et al.*, 2010). Both these conditions can lead to cholangiohepatitis which is defined as inflammation of the biliary system involving the hepatic parenchyma (Blood *et al.*, 2007).

CASE REPORT

A 5-month-old, intact male, unvaccinated, Siamese cross kitten was presented to the University Veterinary Hospital, Faculty of Veterinary Medicine, Universiti Putra Malaysia with the primary complaint of jaundice.The kitten was adopted four days prior to presentation and two days after adoption was administered an anthelmintic and sprayed with an ectoparasiticide at a veterinary clinic.

During that time, the kitten was already icteric and had bilateral serous ocular discharges.Upon presentation, the kitten was dull and severely emaciated. Physical examination revealed pale and icteric mucous membranes. Moderate ulceration was also observed at the base of the tongue. A smooth, firm, and bouncy mass approximately 5cm in diameter was palpated at the right cranial quadrant of the abdomen. The kitten was well hydrated with normal vital signs and both kidneys were normal upon palpation.

Hematology and serum biochemistry analysis revealed a regenerative anaemia (packed cell volume 20%; reticulocyte index 5%), lymphopenia (0.61×10^9/L; RI 1.5 – 7.0 × 10^9/L), 5-fold elevation in alanine transaminase (ALT)(559.7 U/L; RI 10 – 90 U/L), 1-foldincrease in gamma-glutamyltransferase (GGT) (12 U/L; RI <6.0 U/L), normal alkaline phosphatase (ALP); and hyperglobulinemia (49.6 g/L; RI 25 – 45 g/L). Urinalysis revealed presence of urobilinogen, bilirubinuria and bilirubin crystals. Results for faecal simple floatation and fecal sedimentation were negative and helped to rule out *Platynosomum fastosum* infestation.

Left lateral abdominal radiographs revealed a mass effect at the mid-cranial abdomen which altered the normal stomach axis and displaced theintestines slightly caudally (Figure 1a). There was also loss of serosal details of abdominal organs as the kitten was severely emaciated. On the ventro dorsal view, a large and well demarcated tortuous radiopaque structure was found at the right cranial abdomen (Figure 1b).

Abdominal ultrasonography revealed a large anechoic structure and several smaller similar structures with hypoechoic flecks at the right cranial abdomen, which was believed to be a distended bi-lobed gallbladder with tortuous bile duct (Figure 2).

Hematology and serum biochemistry analysis were repeated on Day-5 hospitalisation that revealed a normocytic, normochromic, non-regenerative anaemia (packed cell volume 20, reticulocyte index <1%), marked neutrophilia with left shift (segmented neutrophils 28.12 ×

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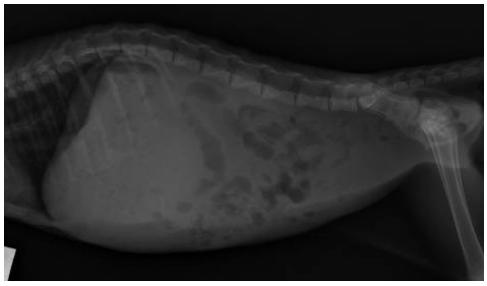
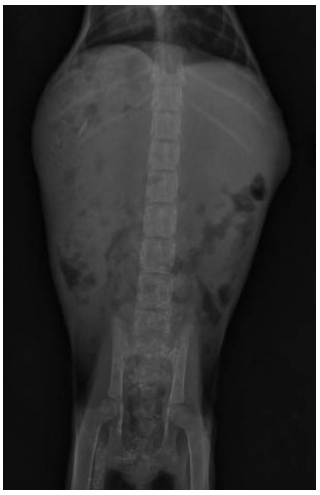


Figure 1a. Mass effect at mid-cranial abdomen altered the stomach's orientation axis and displaced the intestines slightly caudally

Figure 1b. Large, well demarcated, and tortuous radiopaque structure at left cranial abdomen



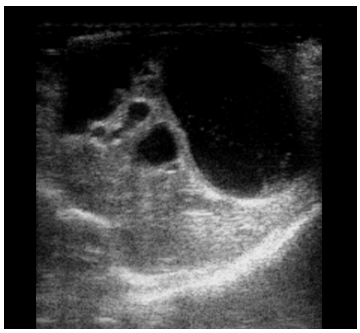


Figure 2. Large and several smaller anechoic structures believed to be a distended bi-lobed gallbladder and tortuous bile duct

10^9/L; RI 2.5 – 12.5 × 10^9/L) (band neutrophils 1.11 × 10^9/L; RI <0.3 × 10^9/L), monocytosis (1.11 × 10^9/L; RI 0.2 – 0.8 × 10^9/L), and eosinophilia (2.22 × 10^9/L; RI 0.1 – 1.5 × 10^9/L) which were not present 4 days ago, indicating an acute infection or inflammation suspected due to peritonitis. There was still marked hyperbilirubinemia (total bilirubin 124.9 µmol/L; RI 1.7 – 17.0 µmol/L) however there was a slight reduction in the ALT (244.7 U/L; RI 10 – 90 U/L). Once again, the alkaline phosphatase was within normal limits but the GGT was elevated further (16 U/L; RI <6.0 U/L).

Treatment initiated included intravenous fluid boluses of 0.9% NaCI and 10% Duphalyte® TID, Ornipural® (1ml, IV, BID), Marboflocaxin (2mg/kg, IV, SID) and Papain (150,000 USP unit, PO, BID).

On the second day of hospitalisation, the kitten displayed head tremors and hepatic encephalopathy was suspected, therefore lactulose (667g/L, 0.5ml/kg, PO, BID) and i/d diet® (Hill's Prescription Diet), 1/8 can, PO, TID were added to the treatment regime.

Tentative diagnoses of congenital biliary anomaly and hepatic encephalopathy were derived and on Day-5 of hospitalisation, an exploratory laparotomy was performed. The extra-hepatic biliary duct was severely tortuous and distended with dark green bile which upon digital compression did not lead to duodenal filling (Figure 3). Therefore, a modified choledochoduodenostomy was attempted whereby an opening was made between the common bile duct and duodenum (Figure 3).

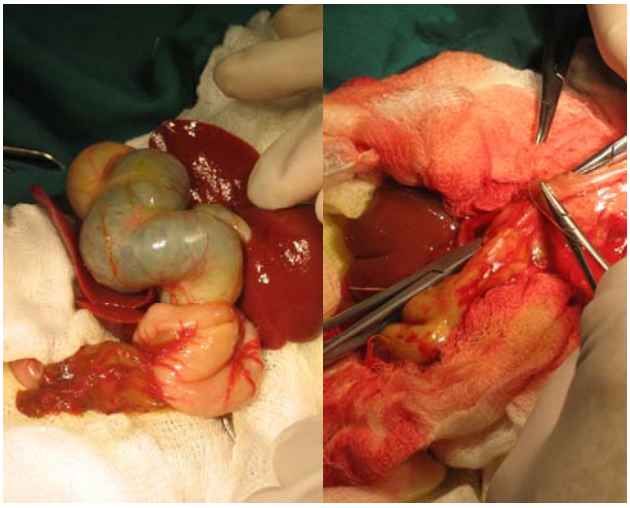


Figure 3. (Left) Exploratory laparotomy revealed severely distended and tortuous biliary system containing dark green bile; (Right) Modified choledochoduodenostomy - an opening was made between the common bile duct and duodenum

After the procedure, tramadol (4mg/kg, IV, TID), metronidazole (10mg/kg, IV, TID) and ranitidine (2mg/kg, IV, TID) were administered. The kitten was placed in the intensive care unit however, it did not recover from general anaesthesia and died the next morning.

Post mortem examination revealed a severely distended and thickened bile duct indistinguishable from the gallbladder. Histopathologic examination (Figure 4) of the liver revealed severe loss of hepatic architecture, marked periductal fibrosis, bile duct proliferation, mixed inflammatory infiltrate and severe hepatic parenchymal fibrosis. Meanwhile, histopathology results of the common bile duct and gallbladder revealed lymphocytic cholangitis and extensive fibrosis. All these findings confirmed the presence of chronic cholangiohepatitis .

Gross examination of the brain revealed loss of vermiform structures of the cerebellum and histopathologic examination demonstrated a loss of Purkinje cells in the cerebellum suggestive of thiamine deficiency (Figure 5). Furthermore spongiosis andgliosis in the cerebrum confirmed the diagnosis of hepatic encephalopathy.

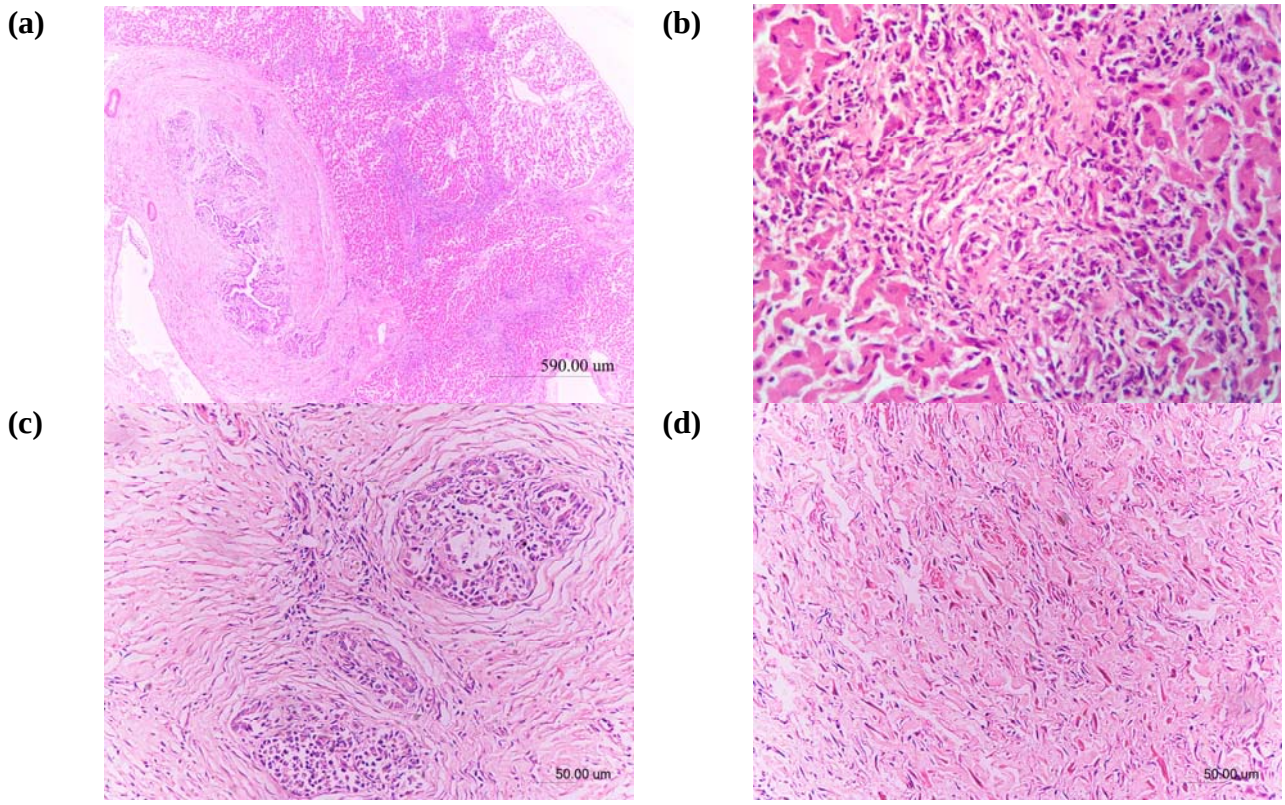


Figure 4. Chronic cholangiohepatitis: (a) Severe loss of normal hepatic architecture with marked periductal fibrosis and bile duct proliferation. (b) Mixed inflammatory infiltrate and severe hepatic parenchymal fibrosis. (c, d) Lymphocytic cholangitis and extensive fibrosis

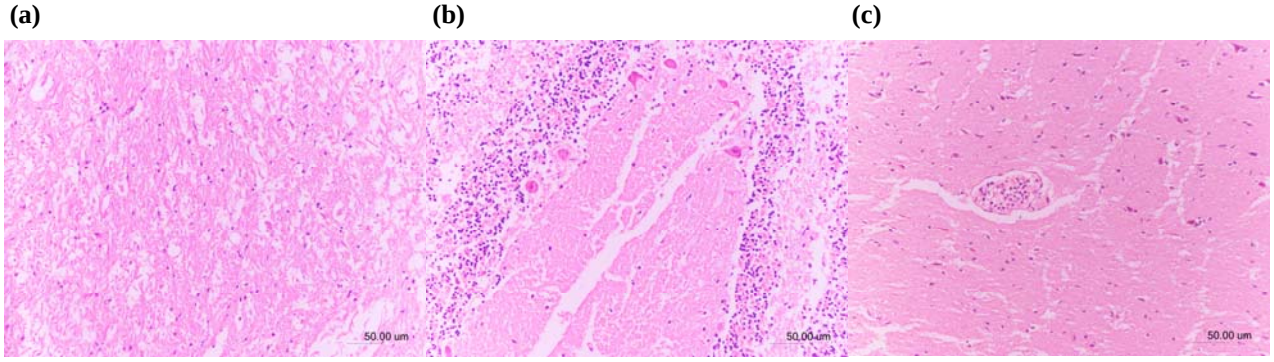


Figure 5. (a) Spongiosis and gliosis in the cerebrum confirming hepatic encephalopathy. (b) Loss of purkinje cells in the cerebellum suggestive of thiamine deficiency. (c) Inflammatory cells within the cerebral vessels.

DISCUSSION

Biliary atresia is a rare congenital anomaly defined bystenosis (Hampson *et al*., 1987), partial (Alagille, 1984)or complete obliterationof the hepatic or common bile ductsat any point from the portahepatis to the duodenum (Perlmutter and Shepherd, 2002). When untreated, the condition results in severe cholestasis, leading to biliary cirrhosis and death (Wildhaber, 2012). Choledochal cysts on the other hand are any cystic dilations of the bile duct (Singham *et al*., 2009) that usually contain bilious fluid and are rich in pancreatic enzymes (Best *et al*., 2010).

Biliary atresia is the most frequent congenital anomaly causing cholestasis in children. In contrast, it is extremely rare in animals with scarce reports documented in a six-month-old cat (Hampson et al., 1987), several calves and lambs (Lofstedt*et al.*, 1988; Harper *et al*., 1990), a four-month-old Border Collie dog (Schulze *et al*., 2000), a rhesus monkey (Rosenberg *et al*., 1983), and a foal (van der Luer and Kroneman, 1982).

As for choledochal cyst, it is a rare pediatricmedical condition and even rarer in animals and to the author's knowledge there is only 1 report of suspected choledochal cyst in a domestic short hair cat (Best *et al.*, 2010).

The reported clinical features of biliary atresia and choledochal cyst are generally non-specific, indistinguishable from each other, and are very similar in both paediatric and veterinary patients. The common clinical features include jaundice; acholic stools; failure to

thrive; hepatomegaly, splenomegaly, and ascites as a result of portal hypertension; abdominal mass; typical cholestatic biochemical liver function tests (Wildhaber, 2012; Hartley *et al*., 2009; Williams, 2009), and sometimes associated complications of ascending cholangitis and pancreatitis.

In this case, the kitten was icteric and severely emaciated with a palpable abdominal mass. However, it did not have acholic stool, the alkaline phosphatase level was normal on both blood results, and there was 3+ urobilinogen in the urine. A logical explanation would be that this kitten did not have a complete bile duct obstruction. The opening at the major duodenum papilla may have been patent but very small such that it seemed as though there was no duodenal filling upon digital compression of the distended bile duct during surgery. Portal hypertension was most likely not severe in this case as the kitten did not develop hepatomegaly, splenomegaly, or ascites.

There are numerous types and subtypes of biliary atresia and choledochal cysts (Wildhaber, 2012; Singham *et al*., 2009; Hartley *et al*., 2009) and based on the appearance of the biliary system during exploratory laparotomy, this kitten most likelyhad a type 1 cystic congenital biliary atresia or a type 1 choledochal cyst as both are identical morphologically.

Abdominal ultrasonography is the first choice and gold standard non-invasive imaging modality (Wildhaber, 2012) generally used for the biliary tree. However it is often difficult to distinguish a choledochal cyst from biliary atresia on ultrasound (Singham *et al*., 2009).In this case, it was challenging to differentiate the distended gallbladder from the dilated bile duct during abdominal ultrasonography and therefore a diagnosis could not be made. As the kitten's condition was deteriorating, the next best diagnostic and possibly therapeutic procedure available was an exploratory laparotomy.

Many theories have been put forth regarding the aetiology of these congenital anomalies. The most popular theory of choledochal cyst development is by Babbitt in 1969 where an abnormal pancreaticobiliary duct junction meeting outside the ampulla of Vater forms a long common channel that allows chronic mixing of digestive juices which activates the pancreatic enzymes causing inflammation and deterioration of the biliary duct wall leading to subsequent dilatation. The aetiopathogenesis of biliary atresia still remains unknown although infectious, immune, genetic, and morphogenic origins have been invoked (Perlmutter and Shepherd, 2002; Wildhaber, 2012; Hartley *et al*., 2009).

Due to the limited diagnostic modalities available, the type of congenital anomaly could not be confirmed in this case. Regardless whether it was a choledochal cyst or partial cystic biliary atresia, the delayed bile emptying is believed to have resulted in chronic inflammation and irritation of the biliary system. The production of exudate or mucin which forms protein plug can cause further obstruction and interference of bile flow. Lack of bile acids in the intestine causes impaired fat digestion and malabsorption (Hampson *et al*., 1987; Williams, 2009) resulting in failure to thrive and severe emaciation as seen in this case. Chronic inflammation and irritation could lead to further weakening of the bile duct wall increasing the risk of spontaneous rupture, bile peritonitis and septicaemia (Singham *et al*., 2009)

Retrograde flow and bile stasis in the liver and biliary ducts could also occur with interference of bile flow which increases the risk of ascending cholangitis, liver abscess, and septicaemia (German, 2009). In this case, pure growth of *E. coli* was cultured from the kitten's liver as well as lung indicating septicaemia. Toxemia could have occurred following that leading to respiratory failure as the kitten required assisted ventilation for 5 hours prior to death.

Due to the caustic nature of bile fluid, retention of bile can cause significant tissue damage leading to secondary cholangiohepatitis and sometimes pancreatitis. Over time, secondary cholangiohepatitis can result in secondary biliary cirrhosis causing portal hypertension (Schulze *et al*., 2000) leading to ascites and splenomegaly while the impaired liver function can result in jaundice, toxins circulation in the system, hepatic encephalopathy, and vitamin deficiencywhich was present in this case.

In veterinary medicine, three biliary diversion techniques for the treatment of biliary atresia and choledochal cysts (Monnet, 2008) have been described. Cholecystoduodenostomy is often the procedure of choice as it is said to be more physiologic than cholecystojejunostomy (Williams, 2009) and the former was successfully carried out in a Border Collie dog with extra-hepatic biliary atresia (Schulze *et al*., 2000) while the latter was performed with successful outcome in a cat with suspected choledochal cyst (Best *et al*., 2010). Choledochoduonenostomy, that is the surgical anastomosis of the bile duct and the duodenum, was performed in this case, however it is not commonly performed in animals.

CONCLUSION

In conclusion, biliary anomalies are uncommon in animals and are rarely described in veterinary literature. A definitive diagnosis of biliary anomaly is often challenging with limited diagnostic modalities and the treatment options in veterinary medicine are unlike those of human medicine as they have conducted extensive research in this particular area due to the importance of biliary anomalies in neonatal patients. Therefore, the prognosis of veterinary patients having these conditions is usually poor.

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CONFLICT OF INTEREST

None of the authors have any potential conflicts of interest to declare.

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