Aplasia of the gallbladder in a dog

A young, female Maltese dog was presented with intermittent vomiting of bile. Biochemical evidence of persistent mild hepatopathy had been present for 11 months. Exploratory celiotomy was performed. Absence of the gallbladder with malformation of the quadrate lobe of the liver was identified. There was histological evidence of bile duct proliferation and portal fibrosis.

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INTRODUCTION

Aplasia of the gallbladder is a rare entity in humans which can either be familial or congenital and is caused by abnormal development of the pars cystica during embryogenesis (Sterchi and others 1970, Nadeau and others 1972, Becker and Mastroni 1979, Noden and de Lahunta 1985). At the time of writing, the condition does not appear to have been reported in the English veterinary literature. This report describes the presenting signs, diagnosis and treatment of gallbladder aplasia in a dog.

CASE HISTORY

An 11-month-old entire female Maltese dog of 2·2 kg bodyweight was presented with a two-month history of intermittent retching and vomiting of bile. The dog was clinically normal between vomiting episodes. Elevations in alkaline phosphatase (ALP) (243 U/litre, reference range 1 to 120 U/litre), alanine aminotransferase (ALT) (1794 U/litre, reference range 1 to 70 U/litre) and aspartate aminotransferase (644 U/litre, reference range 1 to 80 U/litre) suggested the presence of a hepatopathy, but urea (4·1 mmol/litre, reference range 1·7 to 6·5 mmol/litre) and protein (55 g/litre, reference range 53 to 75 g/litre) were within normal ranges and cholesterol (9·6 mmol/litre, reference range 3·6 to 8·8 mmol/litre) was elevated. Abdominal radiographs were normal. Enlargement of mesenteric lymph nodes and mild thickening of the gastric and small intestinal walls were identified on abdominal ultrasonography. The liver parenchyma appeared normal.

Clinical signs persisted and the dog was presented for further examination and neutering 11 months later. The dog's weight had increased to 2·6 kg and no obvious abnormalities were detected on clinical examination. Serum biochemical analysis revealed persistent elevations of ALP (245 U/litre) and ALT (1003 U/litre). The dog was premedicated with methadone (Physeptone; GlaxoWellcome) 0·5 mg intravenously, and general anaesthesia was induced with propofol (Diprivan; Zeneca) 18 mg intravenously, and maintained using gaseous isoflurane (Forthane; Abbott) with oxygen and nitrous oxide.

A ventral midline abdominal celiotomy was performed. The quadrate lobe of the liver was malformed and the gallbladder could not be visualised or palpated. An antimesenteric duodenotomy was performed opposite the duodenal papilla. The bile duct appeared patent and a continuous flow of bile was observed into the duodenum. A sample of bile was collected for laboratory examination. The abdominal viscera were otherwise normal and tissue specimens from the liver, stomach and duodenum were collected for histopathological examination. Ovariohysterectomy was performed.

Histologically, the hepatocytes were normal, but there was variable central fibrosis with some light bridging fibrosis. The portal areas appeared abnormal, with increased numbers of fibrocytes, bile duct epithelial cells and hepatic artery branches. Portal vein branches were absent in some portal areas (Fig 1). These changes are consistent with a congenital hepatic and biliary malformation (Kelly 1985). Mild chronic gastritis was present and the duodenum was normal. The sample of duodenal bile had a bile acid concentration of 41,700 µmol/litre (reference range 119,500 to 140,800 µmol/litre) and a bilirubin concentration of 30·7 µmol/litre (reference range 1840 to 4000 µmol/litre).

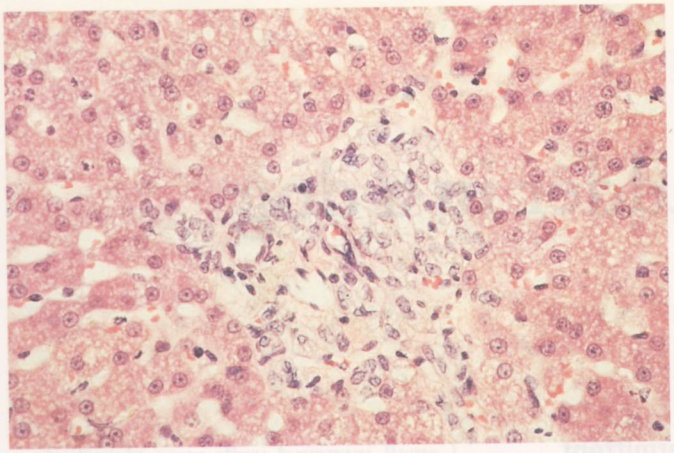

FIG 1. Biopsy from the liver of a Maltese dog with gallbladder aplasia. The portal area is abnormal with absence of normal portal vein branch, an increased number of hepatic artery branches and poorly organised bile duct epithelial cells. Haematoxylin and eosin × 400

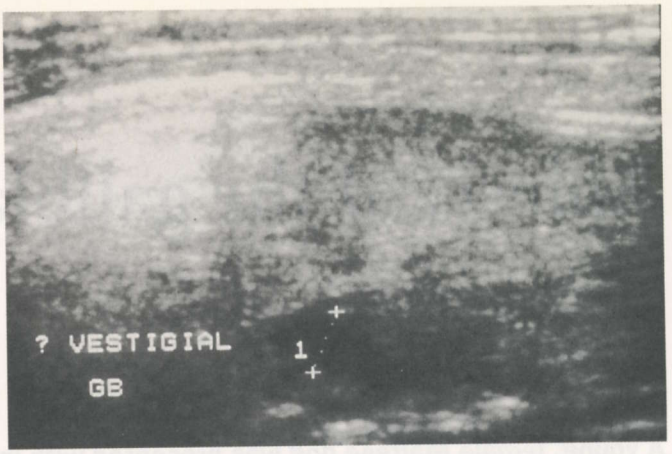

FIG 2. Abdominal ultrasonogram. A small, hypoechoic structure, 3·7 mm in diameter, was detected immediately caudal to the liver. This structure may be a vestigial gallbladder

Reference ranges for the bilirubin and bile acid concentrations in bile have previously been published (Washizu and others 1990, Ludwig and others 1997), but not in the units used in the present laboratory, and conversion tables were not available. Hence, the reference ranges used in the present study were based on samples of gallbladder bile collected from nine anaesthetised, young mature, female dogs used in student practical classes with grossly normal livers and gallbladders. Approximately 5 ml of bile was collected by direct needle aspiration of the gallbladder, stored at −18°C for 14 days, and analysed individually using a Roche Cobas-Mira analyser. Bile acid concentrations were calculated using a commercial kit (Enzabile; Nycomed) and bilirubin levels were analysed using a modification of the Jendrassik and Grof technique adapted for the Roche Cobas-Mira analyser.

The dog recovered uneventfully from surgery. It was discharged with instructions for the owner to feed small amounts of a low fat diet frequently. Repeat abdominal ultrasonography at the time of suture removal confirmed the absence of a normal gallbladder and the presence of a small, hypoechoic structure, 3·7 mm in diameter, just caudal to the liver, which may have represented a vestigial gall bladder (Fig 2). A rectal ammonia tolerance test was normal.

At the time of writing, the dog had been maintained on a low fat diet fed in small amounts at least four times daily, but was continuing to vomit bile intermittently every three to five days.

DISCUSSION

Aplasia of the gallbladder is rare in humans and has not previously been reported in the English veterinary literature. In humans, the condition is recognised as two separate syndromes occurring in either neonates or adults. The neonatal presentation is invariably fatal, with a high incidence of concurrent abnormalities in the genitourinary, gastrointestinal, cardiovascular and musculoskeletal systems (Turkel and others 1983, Rutledge and others 1984). There is no sex predilection (Satpathy 1966, Orava and Leiviskä 1972). Reported causes of human gallbladder aplasia include thalidomide toxicity (Kreipe 1967) and familial disease (Sterchi and others 1970, Nadeau and others 1972, Becker and Mastroni 1979).

The adult presentation of human gallbladder aplasia is not commonly associated with other organ abnormalities and is more common in females (Satpathy 1966, Orava and Leiviskä 1972, Turkel and others 1983). The cystic duct and gallbladder fossa are usually absent. As seen in the present case, the condition may be accompanied by structural abnormalities of the liver lobes, such as aplasia or atrophy, hypertrophy and extra liver lobes (Satpathy 1966, Orava and Leiviskä 1972). Compensatory dilation of the hepatic ducts or common bile duct may be caused by concurrent cholelithiasis (Satpathy 1966).

The liver and gallbladder develop separately during embryogenesis. The hepatic diverticulum develops two outgrowths called the pars hepatica and pars cystica. The pars hepatica develops into the hepatic parenchyma and the pars cystica forms the gallbladder (Noden and de Lahunta 1985). The pars hepatica differentiates into hepatocytes and the intrahepatic biliary system, while the common stem of the pars hepatica and cystica forms the common bile duct (Noden and de Lahunta 1985). Hence, absence of the gallbladder results from failure of development or vacuolisation of the pars cystica. However, as there was a malformation of the quadrate lobe of the liver and histological evidence of abnormal development of the intrahepatic biliary system and liver parenchyma in the present case, the embryological abnormality may have resulted from a common failure of normal development of the hepatic diverticulum or a concurrent abnormality in development of both the pars hepatica and cystica.

Clinical signs in humans are variable and usually caused by cholelithiasis. They include upper abdominal pain, nausea, vomiting and intolerance of fatty foods, with occasional icterus, fever, anorexia and pruritus (Satpathy 1966, Orava and Leiviskä 1972, Bennion and others 1988).

The serum biochemical changes in the present case were suggestive of a hepatopathy. These abnormalities have not been reported in human cases of gallbladder aplasia without concurrent cholelithiasis (Orava and Leiviskä 1972, Richards and others 1993). Cholelithiasis was not evident in the present case. The elevations of ALP and ALT were probably caused by a low-grade cholangiohepatitis or cholestasis resulting from reflux of bile and intestinal contents into the common bile duct. The increase in bile duct epithelial cells may also account for the mild increase in ALP (Cornelius 1987). Other causes include drug-induced hepatopathy or early chronic active hepatitis (Cornelius 1987). The initial mild elevation in cholesterol probably resulted from a recent meal as the cholesterol level was normal on subsequent serum biochemical evaluation.

Bile is formed in the liver and drains from the intrahepatic lobar ducts into the cystic and common bile duct, and is stored and concentrated in the gallbladder. Secretion of bile by the liver provides a source of bile acids for fat digestion and

absorption, an excretory route for endogenous metabolites and drugs, and buffers to neutralise hydrogen ions in the proximal duodenum. Bile is secreted continuously in all species, but a continuous flow of bile is unnecessary in animals which feed intermittently. This has resulted in the development of anatomical and physiological mechanisms permitting intermittent delivery of bile into the duodenum during feeding (Argenzio 1984).

Gallbladder aplasia and cholecystectomy result in the continuous excretion of bile into the duodenum. The concentration of bile salts is therefore low due to the lack of storage and absorption of bile in the gallbladder (Krondl and others 1964). The concentrations of bile acids and bilirubin in the sample of bile collected from the duodenum in the present case were very low when compared to the authors' normal laboratory ranges for gallbladder bile. However, the secretion of dilute bile apparently has a minimal effect on fat digestion and absorption (Krondl and others 1964). Following cholecystectomy, adaptive changes occur which increase the number of daily circulations of bile salts and alter the proportion of bile salts due to increased bacterial synthesis (Pomare and Heaton 1973). The absence of a postprandial bolus of bile from the gallbladder may, however, result in fat maldigestion when dietary fat exceeds a certain limit (Brydon and others 1982). A low fat diet was probably unnecessary in the present case due to the above compensatory mechanisms and may have increased the risk of fat malabsorption and fat-soluble vitamin deficiency.

In the absence of a gallbladder, the flow of bile is not mediated by the presence of food. This may predispose to enteritis, as bile salts are chemical irritants (Walker and Ellis 1978), and duodenal ulceration due to inability of the buffering system to neutralise gastric acids during feeding periods (Argenzio 1984). Histological examination of the duodenal biopsy in the present case did not show any evidence of either inflammation or ulceration.

Two types of aplasia of the gallbladder have been reported in humans. Type I is classified as failure of the gallbladder and cystic duct to develop and type II is a rudimentary gallbladder with congenital biliary atresia (Orava and Leiviskä 1972). Contrast cholangiography, which was not performed in the present case, is required for classification of gallbladder aplasia. The abnormality in the present case could be classified as type II due to the presence of a vestigial structure identified ultrasonographically; biliary atresia was not, however, present.

In humans, gallbladder aplasia is usually only confirmed when operative findings are supported by cholangiography, as the position of the gallbladder can be highly variable, with reported locations including the left liver lobe, falciform ligament, liver parenchyma, retroperitoneal space, abdominal wall, epiploic foramen and as a free-floating structure (Orava and Leiviskä 1972). The same variation in gallbladder location has not been described in animals. Ultrasonography is not considered a reliable diagnostic tool in humans as aplasia and gallbladder shrinkage due to inflammation are difficult to differentiate (Richards and others 1993). In the present case, direct observation and palpation during exploratory celiotomy was used to detect absence of the gallbladder, continuous flow of bile into the duodenum and to differentiate between gallbladder aplasia and shrinkage. Postoperative ultrasonography confirmed aplasia of the gallbladder by failing to detect a gallbladder in a normal, intraparenchymal or ectopic location.

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