NOTE Internal Medicine

Gallbladder Agenesis in a Chihuahua

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ABSTRACT. A 4-year-old neutered male Chihuahua was presented with a history of anorexia and vomiting. Continuous elevation of liver enzymes was found on repeated blood examinations and the dog was referred to us for further evaluation. The absence of gallbladder was suspected on ultrasonography. Exploratory laparotomy and retrograde cholangiography confirmed gallbladder agenesis and a possible hypoplasia of the right medial and lateral liver lobes. Histologically, proliferation of bile ductules associated with portal fibrosis and pseudolobular formation were apparent in the liver lobes.

KEY WORDS: cholangiography, canine, gallbladder agenesis, liver, ultrasonography.

Gallbladder agenesis (GBA) is an extremely rare condition in dogs and there have been only two reports in young female Maltese dogs [2, 15]. It is also a rare condition in humans, reported in both newborns and adults, with a reported incidence between 0.01% and 0.075% [3, 18, 19]. In human adults, most cases are found incidentally during either abdominal surgery or autopsy. In newborns, it is often associated with other life incompatible anomalies [5, 6, 10]. Two of the reported dogs with GBA were relatively young when diagnosed (11-month-old and 7-month-old) [2, 15]. The etiology of GBA is unknown both in dogs and humans, but in humans it is generally thought to be a developmental failure of the pars cystic from which the gallbladder arises during embryogenesis. It is also suggested in humans that there are familial hereditary forms of GBA [21, 24]. In this report, we present a Chihuahua with progressive hepatopathy possibly due to GBA which was suspected based on ultrasonographic findings and subsequently confirmed by exploratory laparotomy and retrograde cholangiography.

A 4-year-old, 3.5 kg, castrated male Chihuahua was examined by the referring veterinarian for a 3-day history of anorexia and vomiting. Blood examination revealed increased alanine transferase (ALT, 372 IU/l) and alkaline phosphatase (ALP, 1,020 IU/l). The results of complete blood count were unremarkable. Amoxicillin, ursodeoxycholic acid, S-adenosylmethionine, and glutathione were prescribed. At follow-up evaluations, the owner claimed that the clinical signs had resolved; however, the liver enzymes continued to elevate (at 3 months after the first admission; ALT >1,000 IU/l, AST 318 IU/l, ALP 1,020 IU/l).

The dog was referred to the Veterinary Teaching Hospital of Iwate University three months after the clinical onset. On presentation, the dog was alert and the physical examinations revealed no abnormalities. The results of complete blood count were within normal limits. Serum biochemistry panels revealed marked elevations of liver enzymes; ALT 961 IU/l (reference range 11–69 IU/l), AST 500 IU/l (reference range 7–49 IU/l), ALP 1,022 IU/l (reference range 14–193 IU/l), and gamma-glutamyl transpeptidases (GGT) 26 IU/l (reference range <9.0 IU/l). Fasting and postprandial ammonia levels were 18.0 and 40.2 µg/dl, respectively (reference range 15–88 µg/dl). Activated partial thromboplastin time, prothrombin time, and fibrinogen level were within normal limits. The total protein, albumin, and total bilirubin levels were also within normal limits. Fasting bile acids were elevated (>250 µmol/l, reference range 0–5 µmol/l), but the postprandial bile acids were normal (8 µmol/l). Thoracic and abdominal radiographs were unremarkable. On abdominal ultrasonography, the morphology and echogenicity of the liver appeared normal; however, the gallbladder was not visualized from any plane. Other abdominal organs were considered normal.

Based on the results of elevated liver enzymes and abdominal ultrasonography, GBA was suspected, and therefore exploratory laparotomy and retrograde cholangiography were performed. The gallbladder could not be visualized or palpated around the normal or ectopic locations. The right medial and lateral liver lobes were clearly smaller than other lobes. Duodenotomy was performed and the outer needle of a 24-gage indwelling needle was inserted into the major duodenal papilla. Retrograde cholangiography revealed dilation of common bile duct (estimated to be 9 mm in diameter) and the absence of a gallbladder (Fig. 1). Approximately 2 ml of a contrast agent (Iothalamate Meglumine, Conray, Daiichi Sankyo Company, Tokyo, Japan) filled the right and left hepatic ducts and the bifurcating intrahepatic bile ducts (Fig. 1). It was
Gallbladder agenesis (GBA) is an extremely rare condition both in humans and dogs. In symptomatic human cases, the most common clinical signs are right upper quadrant abdominal pain, nausea, vomiting, fatty food intolerance, dyspepsia, and jaundice [3, 23]. These clinical signs could be a result of biliary dyskinesia or secondary to ascending cholangitis [1, 4, 12]. Common duct stones have been often found in human GBA which could lead to symptoms associated with biliary dyskinesia. In a previous report of a dog with GBA, retching and vomiting were the only clinical signs [15]. In the case presented here, anorexia and vomiting were the chief complaint when the dog was first presented to the referring veterinarian. These clinical signs improved after administration of antibiotics, ursodeoxycholic acid, S-adenosylmethionine, and glutathione, and the use of low-fat diet despite persistent elevated liver enzymes.

Preoperative diagnosis of GBA has been considered challenging in humans. Despite of its high-quality images and prevalence in practice, ultrasonography may not reliably differentiate GBA from other gallbladder abnormalities. Abnormalities in morphology such as gallbladder shrinkage or in location such as an ectopic gallbladder are common in humans. Therefore, most symptomatic cases are diagnosed by laparotomy. In our case, GBA was suspected at ultrasonography and subsequently confirmed by exploratory laparotomy as in the cases of previous reports [2, 15]. In addition, we performed retrograde cholangiography and found dilation of the common bile duct and a possible hypoplasia of the right liver lobes. The dilation of the common bile duct could be due to substitution of the common bile duct for the absence of gallbladder to take on its function [11]. Alternatively, it could be the result of biliary dyskinesia due to hypertrophic muscular retrograde contraction of the Oddi sphincter [16, 22] or simply the sequel of common duct stones that have passed [14]. In humans, GBA is known to accompany other anomalies of numerous organs including those of gastrointestinal, skeletal, cardiovascular, and genito-urinary systems [4, 8, 9, 13, 20]. We speculated in our case that the right liver lobes were hypoplastic. Because GBA is asymptomatic in most cases, it was possible that the dysfunction of right liver lobes was responsible for the clinical signs and the GBA was an incidental finding. Abnormalities of the right liver lobes in our case could have been congenital or acquired; however, this remained unknown without histopathological evidence. A previous dog case of GBA reported a concomitant malformation of the quadrant lobe [15]. A right liver lobe hypoplasia in association with GBA has been reported in humans as well [13]. Concomitant abnormalities of liver lobes, intrahepatic ducts, and a gallbladder are thought to arise from developmental failure of the hepatic diverticulum or failure of both pars hepatica and pars cystica [17]. Although a definitive association could not be made, our case had a history of an undescended testis which has also been reported in GBA in humans [20].

One consistent observation in dogs with GBA in previous reports and also in most human symptomatic patients is elevation of liver enzymes on serum biochemical panels. Two of the dog cases in previous reports both had marked elevation of ALT and variable increase of AST, ALP, and in one case GGT [2, 15]. Our case showed similar results of serum biochemical panels initially, but elevations of most enzymes progressed with time probably exceeding the degree of elevations found in previous reports. This may be because our case was older (4.5-year old) than the dogs in previous reports (7-month and 11-month old) and therefore had more progressed hepatopathy. However, the significance and mechanisms of elevated liver enzymes have not been completely understood in dogs with GBA. It has been suggested that the absence of gallbladder leads to failure of intermit-
tent excretion of bile into the duodenum, which is also regulated by the Oddi sphincter. This failure of bile excretion may result in biliary dyskinesia and, with dysfunctional Oddi sphincter, reflux of duodenal contents [5, 12], leading to cholangiohepatitis. Proliferation of intrahepatic bile ductules found on histopathology in our case was thought to be secondary to chronic cholestasis. Although most treatments are empirical, treatments of GBA are aimed at taking preventive measures for common sequelae of biliary dyskinesia and secondary hepatopathy [12]. In the present case, we used ursodeoxycholic acid to prevent progression of further biliary stasis and glutathione to protect hepatocytes from oxidative stress. Although its effects are not entirely clear for GBA patients S-adenosylmethionine may be used for the purpose of hepatoprotection [7]. In human symptomatic cases, cholelithiasis is frequently related to the symptoms; thus, cholelithotomy is performed. However, cholelithiasis is relatively rare in dogs and was not found in previous 2 reports and in the present case. In addition, for the dysfunctional Oddi sphincter and abdominal pain, smooth muscle relaxants and analgesics have been used in human patients with GBA [12]. These drugs have not been used for dogs with GBA. A low-fat diet was used in the present case because fatty food intolerance could develop due to inability of intermittent bile excretion into the duodenum during feeding. Prevention of duodenitis and duodenal ulceration may be necessary since the buffering effects of bile on gastric acids could also be compromised in GBA.

Fig. 2. Histopathology of a quadrate lobe of the liver. Proliferation of bile ductules were observed in the portal areas. Hematoxylin and eosin stain. (A, bar= 100 µm; B, bar=30 µm). Masson trichrome stain demonstrated portal fibrosis and pseudolobular formation (C and D, bar= 300 µm). Bile ductules were positive for cytokeratin. Immunohistochemical staining, hematoxylin counterstain. (E, bar= 300 µm; F, bar=50 µm).
patients. Long term prognosis of GBA in dogs remains unknown. The previous two reports in young Maltese dogs described only mild pathology in the biopsied liver samples; therefore, the prognosis of GBA was thought to be better than symptomatic human cases. In contrast, pathological findings of the liver in our case suggested the presence of progressive hepatopathy possibly due to chronic biliary dyskinesia. The long term prognosis of dogs with GBA remains to be investigated; however it is likely to be dependent on many factors such as the status of the Oddi sphincter, duration and extent of biliary dyskinesia, and presence of cholangiohepatitis.

REFERENCES


