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Triaditis in a Cat with Suspected Malignant Hepatobiliary Tumor

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Abstract : A nine-year-old spayed female Turkish angora cat presented for evaluation of anorexia, lethargy, vomiting, ptyalism and jaundice. Based on clinical examinations including laboratory examinations, concurrent inflammatory condition of the biliary system, pancreas and intestines (triaditis) was suspected. The cat was under antibiotic and immune-suppressive therapy, but there was no response. Further examination revealed the possibility of malignant hepatobiliary tumor with pulmonary metastasis. The condition of the cat continued to deteriorate and the cat died 3 weeks after the diagnosis. This case demonstrates the clinical findings of triaditis combined with suspected malignant hepatobiliary tumor.

Key words **:** Feline, malignant hepatobiliary tumor, triaditis, pulmonary metastasis.

Introduction

The prevalence of hepatobiliary tumors varies from 1.5% to 2.3% of feline neoplasms (2,9), and approximately 50% of cats are symptomatic (11). Among the primary hepatobiliary tumors, cholangiocarcinoma (bile duct adenocarcinoma) is the most common malignant hepatobiliary tumor in cats and human beings, and the second most common in dogs (5,7,8). Cholangiocarcinoma has an aggressive biologic behavior which is a locally invasive and highly metastatic, spreading within the liver and to local lymph nodes, lungs, abdominal organs and peritoneum (11). In cats, diffuse intraperitoneal and generalized metastasis occurs in 67% to 80% of cases (8,11) and there is no known effective treatment with nodular or diffuse bile duct carcinoma (11).

Triaditis is a condition encompassing concurrent inflammatory infiltration of the hepatobiliary system, pancreas and small intestine (1). Bacterial infection, immune-mediated and idiopathic mechanisms are thought to be the potential roles of these inflammatory stimuli and the temporal development of triaditis (6). Although the etiology of the disorder is largely unknown, evidence suggests that intestinal inflammation could promote dysbiosis and the translocation of enteric bacteria to the pancreas and liver (1,6,10). However, the pathogenesis of which one occurs first and how this disease has an effect on other two disorders are not clear (13). In many cases, additional immune-suppressive drugs with antibiotics are often required to successfully manage the patients (6). A recent report suggests that from 50 to 85% of cats with one syndrome have all three diseases (3).

This report describes a cat with triaditis caused by suspected malignant hepatobiliary tumor. It is necessary to consider malignant hepatobiliary tumor in the differential diagnosis of triaditis in cats.

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Case

A nine-year-old spayed female Turkish angora cat was presented with anorexia, lethargy, vomiting, and ptyalism. The cat showed progressive clinical signs for 10 days ago and was tentatively diagnosed with triaditis in a local hospital and treated with metronidazole and amoxicillin for 3 days. However, the cat's condition deteriorates gradually. On physical examination, the cat had body condition score (BCS) 2/5, mildly delayed skin turgor, tachypnea (respiratory rate 32/min; reference interval, 20-30 breaths/min) and jaundice seen at bilateral sclera, gingiva and generalized skin.

The complete blood count revealed mild regenerative anemia (HCT 24.2%; reference interval, 30.3-52.3%, the absolute reticulocyte counts 50.6) and leukocytosis (WBC 29.09 $\times 10^9$/L; reference interval, 2.87-17.02 $\times 10^9$/L). Serum biochemistry profile presented elevation of alanine aminotransferase (140U/L; reference interval, 12-130U/L), aspartate aminotransferase (126U/L; reference interval, 0-48U/L), alkaline phosphatase (501U/L; reference interval, 14-111U/L), gamma glutamyltransferase (12U/L; reference interval, 0-1U/L) and total bilirubin (7.8 mg/dL; reference interval, 0-0.9 mg/dL) and decrease of blood urea nitrogen (10 mg/dL; reference interval, 16-36 mg/dL).

Thoracic radiograph showed mild broncho-interstitial pattern and circumscribed, multiple interstitial nodules in the lungs (Fig 1). Decreased serosal detail with gas-filled intestines was found at abdominal radiograph. There were no significant findings in echocardiograph and hypertrophic cardiomyopathy was ruled out. On abdominal ultrasonographic examination, thickened gall bladder wall was detected and intrahepatic and common bile duct wall was also thickened and dilated (Fig 2). Moreover, there was free fluid near the

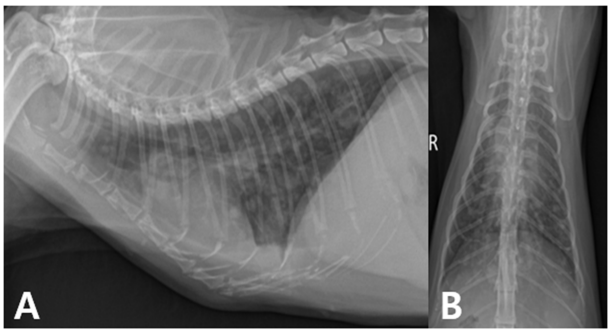

Fig 1. Thoracic radiographs of a cat with malignant hepatobiliary tumor and pulmonary metastasis. Mild broncho-interstitial pattern and circumscribed, multiple interstitial nodules are shown in the lungs. (A: lateral view, B: dorsoventral view).

liver and pancreas were edematous. Speckles within the mucosa are identified in transverse section of small intestine, indicating the presence of intestinal inflammation. Serum feline pancreatic lipase immunoreactivity was increased (4.6 μg/L; reference interval, 0-3.5 μg/L) indicating pancreatitis. Ultrasound-guided fine needle aspiration (FNA) biopsy of the hyperechoic hepatic region near gall bladder showed cytoplasmic hepatocellular vacuolar changes (demarcated, large and small discrete clear lipid-filled vacuoles) with increased neutrophils. Moreover, there were bile duct epithelial cells with marked cytological atypical features such as nuclear pleomorphism, obvious nucleoli, marked anisocytosis and anisokaryosis (Fig 3).

Based on clinical examinations including laboratory examinations, malignant hepatobiliary tumor with pulmonary metastasis and triaditis were suspected in this cat. Histopathological examination for definite diagnosis could not be performed because further evaluation was denied by the owner.

The cat was under antibiotic therapy (metronidazole and amoxicillin) for 3 days but no improvement was noted. Therefore, immune-suppressive therapy was initiated with prednisolone (2 mg/kg, SC, bid; Daesung, Korea). Other medications for controlling pancreatitis and cholangiohepatitis were also administrated. Treatment with prednisolone (2 mg/kg, SC, bid; Daesung, Korea), metronidazole (15 mg/kg, IV, bid; Daehan, Korea), amoxicilline (12.5 mg/kg, IV, bid; Kuhnil, Korea), marbofloxacin (2 mg/kg, SC, sid; Vetoquinol, U.S.A.), taurine (1 ml, IV, bid; Samyang, Korea), ornipural (1 ml, IV, bid; Vetoquinol, U.S.A.), famotidine (5 mg/cat, IV, bid; Donga, Korea), cobalamin (1 mg/cat, SC, sid; Daehan, Korea), lefotil (0.25T/divided, PO, bid; CMG pharm co., Korea), zentonil (0.1T/divided, PO, bid; Vetoquinol, U.S.A.) was also initiated. Vitamin K (1 mg/kg, SC, bid; Daehan, Korea) was used for the prevention of coagulopathy by pancreatitis and cholangiohepatitis. Parenteral nutritional sup-

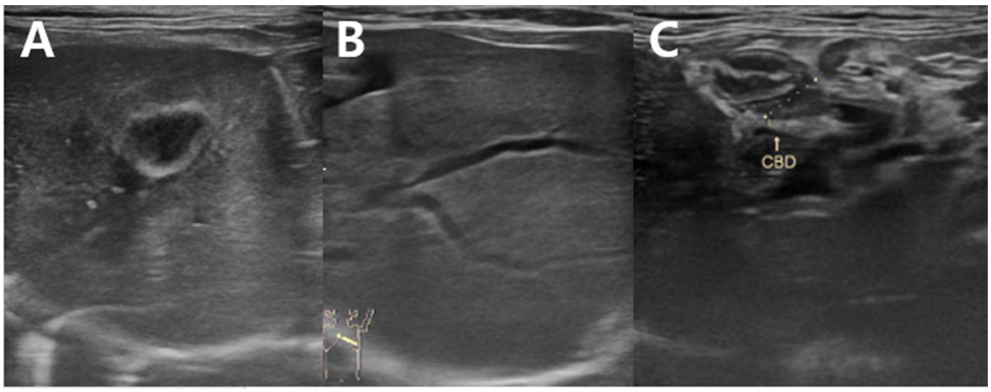

Fig 2. Ultrasonographs from a cat with malignant hepatobiliary tumor and triaditis. Increased thickness of gall bladder wall is detected (1.9 mm; reference range, < 1 mm) and hyperechoic region is seen surrounding the gall bladder (A). Intrahepatic bile ducts are thickened and dilated (B) and the width of common bile duct (CBD) is increased (C, 6.2 mm; reference range, < 4 mm). CBD; common bile duct.

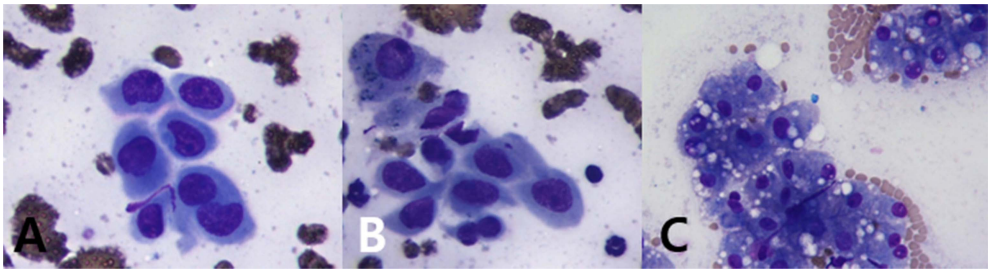

Fig 3. Cytology from ultrasound-guided fine needle aspiration (FNA) biopsy of the hyperechoic hepatic region near gall bladder in a cat with malignant hepatobiliary tumor and triaditis. The presence of bile duct epithelial cells with marked cytological atypical features such as nuclear pleomorphism, obvious nucleoli, marked anisocytosis and anisokaryosis is revealed (A, B). Moreover, there are demarcated and clear lipid-filled vacuoles in hepatocytes indicating hepatic lipidosis (C). (Diff-Quick stain, A, B; × 630, C; × 400).

port using a naso-esophageal feeding tube was applied to prevent the development of hepatic lipidosis because the cat had intractable anorexia.

The cat was not responded to the treatment and deteriorated gradually. The cat died 3 weeks after the diagnosis.

Discussion

Malignant hepatobiliary carcinoma, especially cholangiocarcinoma has high metastatic rate in dogs and cats and 80% have metastasized at the time of diagnosis in cats (3). In this case, metastasis to the lungs was also confirmed at the time of diagnosis. The diagnosis of triaditis and hepatobiliary tumor could not be proven by histological examination of the cat's liver, pancreas and intestine. However, clinical signs including the results of the laboratory findings and the FNA of the liver led to the presumptive diagnosis of malignant hepatobiliary tumor. The prognosis of malignant hepatobiliary tumor is poor, and the majority of cats treated with liver lobectomy have died within 6 months due to local recurrence and metastatic disease (3,6,11). The prognosis of this cat was extremely poor like previous reports (3,6,11).

Triaditis has been reported in 50-56% of cats diagnosed with pancreatitis (10). Pancreatic and bile ducts are combined prior to their entry in the feline small intestine, whereas these ducts have separate channels of entry in canine small intestine (1,10). This anatomic feature makes high prevalence of triaditis, which is concurrent inflammatory infiltration of the hepatobiliary system, pancreas and small intestine in cats. In this case, the cat had elevated hepatobiliary enzymes and feline pancreatic lipase immunoreactivity. Moreover, thickened gall bladder and common bile duct with speckle signs in small intestine were found through clinical examinations. Feline pancreatic lipase immunoreactivity is an assay that specifically quantifies lipase that originates from pancreatic acinar cells, and its sensitivity for the diagnosis of pancreatitis has been estimated to be 67% and it has 91% of specificity in cats with gastrointestinal disease (1). Moreover, hepatic lipidosis shown in this case is often associated with cholangitis, pancreatitis or IBD (1).

Triaditis is associated with likelihood of developing secondary hepatic lipidosis in cats. The presence of hepatic lipidosis can affect hepatic function and consequently the clinical and laboratory variables of the disease. In addition, chronic inflammatory liver disease mostly affects the biliary tree and portal areas (1). Chronic biliary tract diseases such as primary sclerosing cholangitis, choledocholithiasis, and choledochal cysts are major risk factors for cholangiocarcinoma in both human beings (12) and cats (10). Bile duct obstruction caused by cholelithiasis or hepatobiliary/pancreatic tumors can induce pancreatitis, intrahepatic cholestatis, and finally developed to triaditis (4,10).

This report describes a rare case of combined triaditis and suspected malignant hepatobiliary tumor in a cat. In this case, triaditis could lead to sclerosing cholangitis that progressed to malignant hepatobiliary tumor. Otherwise, malignant hepatobiliary tumor may trigger the concurrence of triaditis because of duct obstruction or release of inflammatory cytokines.

Conclusions

In conclusions, this report describes the diagnostic features and clinical management in a cat with suspected malignant hepatobiliary tumor combined with triaditis. Even though the pathogenesis of the link between malignant hepatobiliary tumor and triaditis can only be speculated, there is high possibility that one has an influence to occur the other. When the response to general therapies for the triaditis is poor, other concurrent diseases including neoplasia should be considered like this case and appropriate differential diagnosis should be considered.

Acknowledgements

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