

Cholangiocarcinoma in a Doe

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Case Report

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Abstract

Cholangiocarcinoma is a rare neoplasm in goats with only four cases reported since 1977 and only one report of cholangioma in 1995. Clinical signs that have been described are non-specific, and included loss of condition and diarrhoea. All the reported cases of cholangiocarcinoma have had similar histological characteristics including the presence of ductules and gland-like structures, a desmoplastic/prominent connective tissue stroma and intrasinusoidal/parenchymal invasion. The aetiology of this neoplasm in humans, dogs and cats is documented but the cause of the disease in goats remains unknown. Very little has been described about the prognosis of these tumors. Three previously reported cases have had intrahepatic metastasis and in one report the neoplasm was found to have led to peritonitis. In this case, a 5-year-old Anglo Nubian mixed doe was submitted for necropsy. The liver was enlarged to approximately two times its normal size, with the left lobe being effaced by multiple, coalescing, irregular moderately circumscribed, firm, whitish, raised foci with 10-15 similar variably sized scattered foci being present in the right lobe. The remaining parenchyma had an accentuated lobular pattern. No metastatic foci were found elsewhere. All of the neoplastic foci had similar histological characteristics consisting of multiple variably sized, well formed to irregular, tubular and acinar structures arranged within a moderately expansive but loose connective tissue stroma.

Keywords: Cholangiocarcinoma; Goat; Doe; Anglo-Nubian

Introduction

Since 1977, there have only been four reported cases of cholangiocarcinoma in goats [1,2,3,4] and only one report of a cholangioma [5]. Those described have similar histological characteristics including; the presence of ductules and gland-like structures, a desmoplastic/prominent connective tissue stroma and intrasinusoidal/parenchymal invasion [1,2,3,4]. A common feature in two of these cases [3,1], is the presence of mucin producing cells that are demonstrated with PAS staining. Invasion into the sinusoids or the parenchyma was also a feature in two

of these reported cases [3,4]. Very little has been described about the prognosis of these tumors with intrahepatic metastasis occurring in three cases [1,2,4] and in one report the neoplasm was found to have led to peritonitis [4]. Clinical signs that have been described are non-specific, and include loss of body condition and diarrhea [4].

Immunohistochemistry performed by Rodriguez, et al [4], showed that the neoplasm was positive for intermediate filament keratin and negative for vimentin. In a recent case of cholangiocarcinoma in a llama, it was found to be diffusely and intensely positive

for panCK and CK20, weakly positive for CK 19 and negative for TTF1, CK7 and CEA [6].

In humans, predisposing factors for cholangiocarcinomas are primary sclerosing cholangiohepatitis, Hepatitis B and Hepatitis C infection, liver flukes, bile duct stones, chemical carcinogens, mycotoxins choledochal cysts, abnormalities where the bile duct meets the pancreatic duct, cirrhosis, polycystic liver disease, Caroli syndrome, inflammatory bowel disease, ulcerative colitis, Crohn's disease, age, ethnicity, obesity, family history, diabetes, alcohol consumption and drugs such as anabolic steroids [7]. Cholangiocarcinoma in the dog and cat are associated with the Chinese liver fluke [8], and prolonged exposure *o*-aminoazotoluene and aramite, a sulphur-containing containing compound used for insecticide purposes [9].

Here we present the first case of cholangiocarcinoma in a goat in Trinidad.

Case Presentation

A 5-year-old Anglo Nubian Mixed doe was euthanized and submitted for necropsy at the School of Veterinary Medicine, University of the West Indies. The referring veterinarian indicated that the animal had a history of diarrhoea for 4 months which was unresponsive to antimicrobial therapy, decreased appetite, losing condition and not doing well. Upon physical examination by the referring veterinarian two days prior to euthanasia, the animal was found to have pale mucous membranes and a poor body condition. A faecal sample was taken, and blood was collected for haematological and biochemical analysis. Faecal examination revealed the presence of GIN eggs 3+.

The complete blood count (CBC) revealed that the animal had a leukocytosis ($21.1 \times 10^9/L$; reference interval (RI) $6-14 \times 10^9/L$) due to a neutrophilia ($17.3 \times 10^9/L$; RI $1.2-7 \times 10^9/L$) and a slight monocytosis ($0.63 \times 10^9/L$; RI $0-0.5 \times 10^9/L$). These changes were consistent with inflammation. It also had a regenerative anaemia (HCT $0.09L/L$; RI $22-38 L/L$; reticulocyte count 8%) and a hypoproteinemia (50g/L), possibly due to gastrointestinal blood loss and protein-losing enteropathy from gastrointestinal nematodes. Serum biochemistry results revealed the presence of hypoalbuminemia (18g/L; RI 29-43), increased CK (498 U/l, RI 0-100), hyponatremia (132 mmol/L; RI 135-156), hypocalcemia (1.72 mmol/L, RI 2.3-2.9), and a marked increase in GGT (227 U/L; RI 0-30). The hypoalbuminemia and hyponatremia were likely due to losses in the gastrointestinal tract. The increase in CK was indicative of acute muscle injury. The hypocalcemia was most likely secondary to the hypoalbuminemia present, but true hypocalcemia could not be ruled out as ionized calcium testing was unavailable. The increase in GGT indicated that cholestasis was present. Two days after being examined, the animal became completely anorexic, laterally recumbent, listless, had very pale mucous membranes, and was subsequently euthanized.

On necropsy, the doe was in poor body condition with limited subcutaneous and abdominal fat stores and had pale pink oral and conjunctival mucus membranes. The liver was enlarged to approximately two times its normal size, with over 90% the left lobe being effaced by multiple (1-7cm x 1-5cm) coalescing irregular moderately circumscribed, firm, whitish, raised foci (Figure 1) with 10-15 similar variably sized (1x1cm to 4x7cm), scattered foci being present in the right lobe. The remaining parenchyma had an accentuated lobular pattern. No metastatic foci were found elsewhere.



Figure 1: An enlarged liver with the left lobe effaced by multiple (1-7cm x 1-5cm) coalescing foci, with similar scattered foci in the right lobe.

Samples of the liver lesions were fixed in 10% buffered formalin for 48 hours, embedded in paraffin and prepared for staining with haematoxylin and eosin [10]. Tissue samples were fixed in 10% buffered formalin for 48 hours, embedded in paraffin and stained with haematoxylin and eosin [10].

All of the neoplastic foci had similar histological characteristics consisting of multiple variably sized, well formed to irregular, tubular and acinar structures arranged within a moderately expansive but loose connective tissue stroma (Figure 2). These structures

were lined by single to multiple layers of cuboidal to columnar epithelial cells with indistinct borders which displayed moderate anisocytosis and anisokaryosis. The cells had moderate amounts of amphophilic cytoplasm, often containing clear intracytoplasmic vacuoles in the cytoplasm (Figure 3). Nuclei were rounded and predominantly basilar with heterochromatin and indistinct nucleoli. Mitoses averaged 2 per 10hpf. The neoplasm invaded into the adjacent parenchyma (Figure 4) and there was variable necrosis in adjacent areas with multiple lymphocytic aggregates.

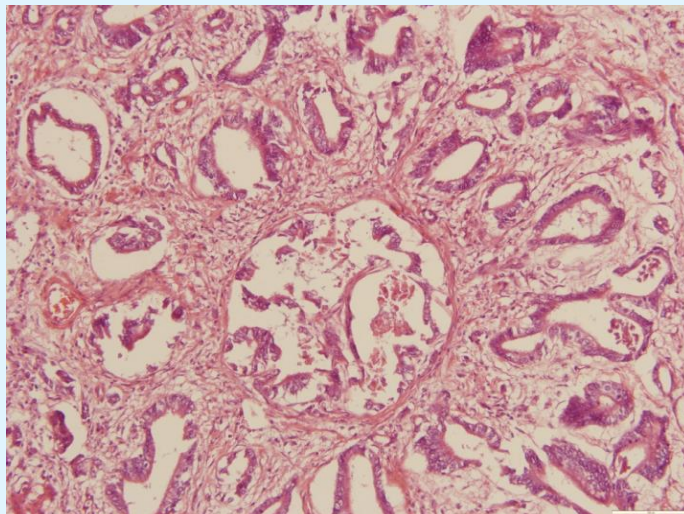


Figure 2: Multiple variably sized neoplastic bile ducts on a moderately expansive but loose connective tissue stroma. H&E stain, 20X.

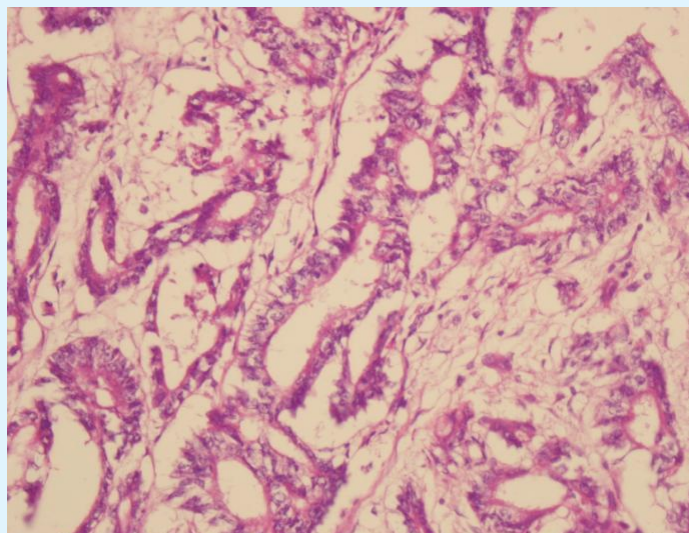


Figure 3: Neoplastic cells cytoplasmic vacuolation. H&E stain, 40X.

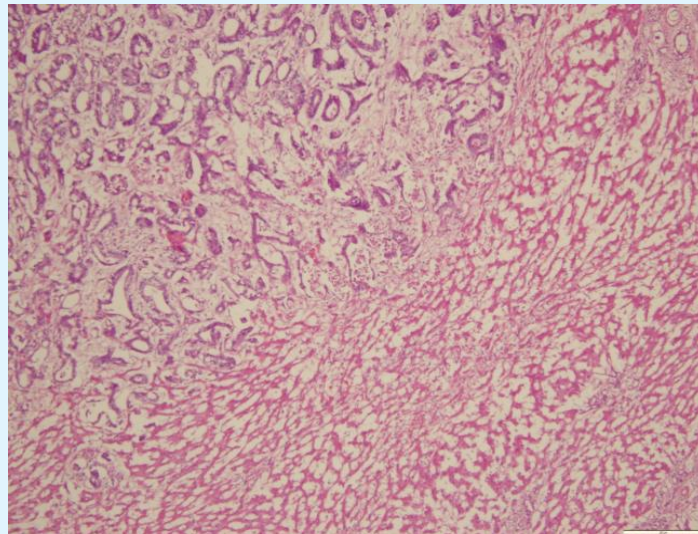


Figure 4: Invasion into the adjacent hepatic parenchyma. H&E stain, 20X.

Discussion

The cholangiocarcinoma in this goat had similar histological characteristics to those previously described, including the presence of ductules and gland-like structures, a desmoplastic/prominent connective tissue stroma and intrasinusoidal/parenchymal invasion [1-4]. Intrahepatic metastasis was grossly present in this case but there was no evidence of distant metastasis or peritonitis. We concluded that this goat's condition was a likely result of the combination severe endoparasitism and the systemic consequences of the presence of the large hepatic neoplasm, which would likely have affected hepatic function, with emaciation and diarrhea contributing to its clinical status.

Clinical signs described previously have included loss of condition and diarrhea, [4] which were also seen in this case. The chronic diarrhea with poor body condition and lack of response to conventional antimicrobial therapy initially suggested a diagnosis of Jöhnes disease; however, there were no characteristic gross or histological changes in the ileum and ileocecal lymph node. Mycobacterial infection was also considered but again no lung, intestinal or mesenteric lymph node changes were detected.

The aetiology of cholangiocarcinomas in goats is unknown. There are only a small number of reported cases, the sporadic nature of the disease and the wide geographical occurrence, would make the determination of the cause of this neoplasm difficult. The neoplasm occupied over 90% of the left lobe and a smaller area of the right lobe, which may indicate an

aetiological agent similar to the mycotoxin, sporodesmin, which predominantly affects the left lobe of the liver in sheep in New Zealand. There are no known caprine liver flukes present in Trinidad and the clinical history could not adequately indicate possible exposure to other carcinogens.

Conclusion

The clinical, gross and histopathological findings in this case were consistent with previously described cases. The aetiology of cholangiocarcinomas in goats remains unknown.

References

1. Dominguez M, Chávez G, Trigo F, Rosales M (2001) Concurrent cholangiocarcinoma, peritonitis, paratuberculosis, and aspergillosis in a goat. *Can Vet J* 42(11): 884-885.
2. Ivoghli B, Cheema H (1977) Bile duct carcinoma in a goat. *Vet Pathol* 14(5): 538.
3. Movassaghi A, Asiani M (2000) The first report of cholangiocarcinoma in a goat in Iran. *Journal of the Faculty of Veterinary Medicine, University of Tehran* 55(3): 63-64.
4. Rodríguez F, Herráez P, Rodríguez J, Orós J, Zaera J, et al. (1996) Cholangiocarcinoma in a goat. *Vet Rec.* 139(6): 143-144.

5. Puette M, Hafner S (1995) Cholangioma in a Goat. *J Vet Diagn Invest* 7(4): 574-575.
6. Taulescu M, Bolfa P, Buiga R, Gal A, Sevastre B, et al. (2012) Metastatic cholangiocarcinoma in a llama (*Lama glama*). *J Vet Diagn Invest* 24(5): 986-989.
7. American Cancer Society (2016) Bile Duct Cancer (Cholangiocarcinoma). 1st (Edn).
8. Choi BI, Han JK, Hong ST, Lee KH (2004) Clonorchiasis and Cholangiocarcinoma: Etiologic Relationship and Imaging Diagnosis. *Clin Microbiol Rev* 17(3): 540-542.
9. Cullen JM, Poop JA (2002) Tumours of the liver and gallbladder. In: Meuten DJ (ed.): *Tumours in Domestic Animals*. 4th (Edn). Iowa State Pres, Iowa, USA, 495-499.
10. Luna L (1960) *Manual of Histologic Staining Methods of the Armed Forces Institute of Pathology*. 3rd (Edn), McGraw- Hill, New York, USA, pp: 12-46.