Systemic *Toxoplasma gondii* Infection in a Cat with Incidental Cholangioma

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ABSTRACT

A ten year old castrated male domestic short haired cat was presented to the Veterinary teaching hospital of the Koret School of Veterinary Medicine with a history of relapsing icterus, anemia, and lethargy. A diagnosis of disseminated toxoplasmosis (*Toxoplasma gondii*) was made on histopathological examination and confirmed by immunohistochemical studies. The immune status of this cat was unknown and therefore it could not be concluded that the disseminated infection was due to immunodeficiency. The presence of a cholangioma in the liver of this cat was regarded as an incidental finding.

Keywords: Feline; *Toxoplasma gondii*; Disseminated Toxoplasmosois; Cholangioma

INTRODUCTION

This case report describes a cat with a *Toxoplasma gondii* infection and a hepatic tumor. Coincidences of this type are usually unrelated and have no relationship to each other. Toxoplasmosis is common in cats however the presence of a cholangioma is relatively rare (1, 2). The coincidence of both a tumor and a *T. gondii* infection in this cat was considered of interest in the light of other studies carried out in mice and humans indicating that *T. gondii* may be a factor in suppressing or slowing the development of various types of cancers (3). This case represents a rare occurrence of two conditions in the same cat, the incidence of which is rarely reported.

CASE REPORT

A ten year old castrated male domestic short haired cat was presented to the Veterinary teaching hospital of the Koret School of Veterinary Medicine with a history of relapsing icterus, anemia, and lethargy. The last episode was recorded 2 months prior to presentation.

On presentation the cat was mildly dehydrated (estimated at 8%), with hypothermia (36.8°C), tachycardia (pulse 220 bests/minute) and a tachypnea (32 breaths/minute). On clinical examination the abdomen was dilated and painful during palpation. Hematology and blood chemistry demonstrated a mild anemia (PCV/TS = 22/9). Serum albumin levels were reduced and the concentration of total gamma globulins was at the high end of the normal range.

Ultrasound examination revealed a splenomegaly with suspicion of the presence of a splenic and hepatic infiltration. In addition two tumors were seen in the liver. These masses were biopsied, examined cytologically and found to contain cells representing a granulomatous reaction without the presence of neoplastic cells.

No free fluid was visualized in the abdominal cavity.

The cat was treated with supportive care and showed minor improvement. However, due to a relapse and deteriorating condition the cat was euthanized and submitted to the Kimron Veterinary Hospital for a post mortem examination.

POST MORTEM

Gross pathology

Pale yellow mucous membranes and severe flea infestation

was present. A small amount of transparent pericardial fluid was noted. The liver was diffusely yellow with an irregular rugged surface, multifocal nodules and a single 2 cm slightly firm, roughly spherical mass in the right central lobe. The adrenal glands were bilaterally symmetrically enlarged. The mesenteric lymph nodes were moderately enlarged but appeared to retain their normal form.

During the post mortem examination tissue samples were taken and fixed in 10% neutral buffered formalin for histopathology. Serum samples were sent for toxoplasma antibody testing.

Toxoplasma antibody test

Indirect Immunofluorescence antibody (IFA) laboratory results for T*oxoplasma gondii* antibodies revealed a strong positive titer of 1:1024.

Histological description

Routine histopathological evaluation of formalin-fixed tissues was carried out. In the liver a well demarcated unencapsulated, expansile neoplastic mass was seen. The mass was formed of cuboidal to polygonal cells closely packed supported by a small amount of fibrous stroma resembling tubular structures (Figure 1). The neoplastic cells were cuboidal to polygonal having variably distinct cell borders and small to moderate amounts of eosinophilic cytoplasm. The nuclei of the neoplastic cells were intermediate to large in size, centrally located with finely stippled chromatin and 1-2 inconspicuous nucleoli. Anisokaryosis and anisocytosis graded as mild to moderate were present with a mitotic index of 10 at a high power magnification.

Within the neoplastic areas and the adjacent liver parenchyma there were multiple randomly distributed foci of coagulative necrosis, admixed with small numbers of neutrophils, macrophages, lymphocytes and plasma cells most prominent at the periphery of the necrotic foci (Figure 2 and 3). Within the necrotic foci there were numerous 20-30 µm in diameter, round to oval parasitic cysts, each one with a thin 0.5 µm basophilic cyst wall containing numerous 2-3 µm, basophilic round to banana shaped bradyzoits. Occasional tachyzoits could be visualized within macrophages and hepatocytes.

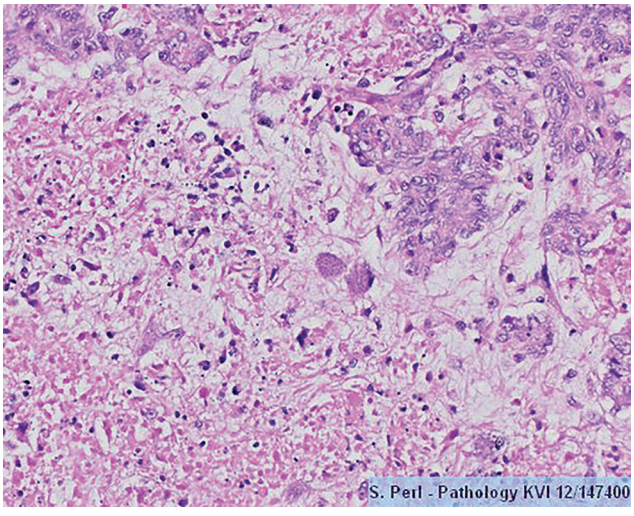

Figure 1: Liver – Neoplastic area adjacent to necrotic areas and parasitic cysts are present H&E. x20.

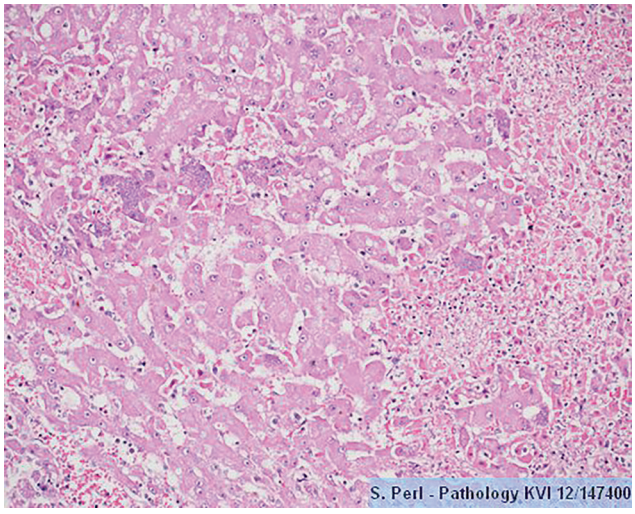

Figure 2: Liver: Foci of coagulative necrosis admixed with a small number of inflammatory cells and parasitic cysts containing numerous basophilic zoites. H&E. x10.

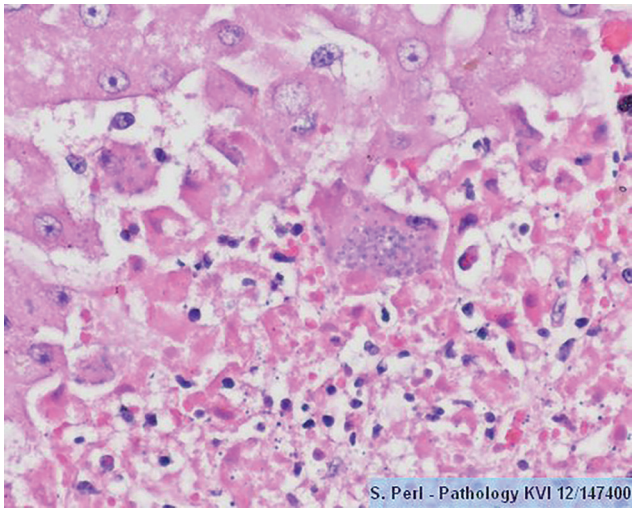

Figure 3: Liver: H&E x40 Enlargement of figure 1.

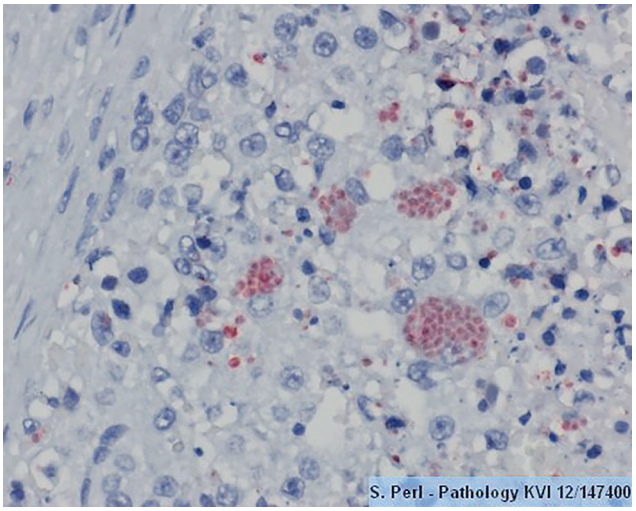

Figure 4: Liver x40 – immunohistochemistry positive for *Toxoplasma gondi*.

Lesions in other organs include a severe necrotizing adrenalitis with the presence of protozoal cysts; mild lymphocytic myocarditis; mild interstitial pneumonia with edema and mild multifocal interstitial nephritis.

Paraffin sections of liver, lung, kidney, intestine and mesenteric lymph node were sent for immunohistochemistry using the avidin-biotin peroxidase technique of Haines and Chelack using rabbit polyclonal antibodies (Novus Biologicals, Littleton, CO., USA) (4). Immunohistochemistry for *Toxoplasma gondii* showed strong positive staining in the liver, lung, adrenal and mesenteric lymph nodes (Figure 4).

DISCUSSION

A morphologic diagnosis was made of hepatic cholangioma and severe multifocal to coalescing acute necrotizing hepatitis with the presence of myriad protozoal cysts and tachizoites consistent in with *Toxoplasma*.

T. gondii is a zoonotic obligate intracellular protozoon. Infection of cats is by ingesting of asexual stages in tissues or by ingesting oocysts. Felidae the definitive host of *T. gondii* (1) can serve also as an intermediary host of the parasite. In intermediate hosts asexual development with multiplication of parasites occurs in various organs and tissues. *T. gondii* (and *Neospora caninum*) has the ability to parasitize a wide range of hosts. Natural infection occurs in birds, rodents, insectivores, herbivores, carnivores and primates including humans.

Systemic toxoplasmosis occurs most often in immunologically immature or immunocompromised animals although cases of fatal disseminated toxoplasmosis has been recorded in immunocompetent cats and humans (5). In the cat, intestinal and systemic infection occurs almost simultaneously. It can spread via lymphocytes to the lymph nodes and from there to the blood\lymph and portal circulation to the liver. In the case of this cat feline immunodeficiency virus (FIV), status was not examined although there was no history of pharmaceutical immunosuppression and therefore there is a lack of information regarding the immune status of the cat.

The possibility of infection by a virulent strain of *T. gondii* should be considered. In North America and Europe three *T. gondii* clonal lineages of different levels of virulence designated I, II and III have been found based on polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) (6, 7). Furthermore, the possibility of differing feline genotypes of differing sensitive to *Toxoplasma* infection has also been investigated and also remains an option for the explanation for the reason for systemic severe toxoplasmosis in immunocompetent cats (8).

Focal necrosis where tachyzoites are present is common and appears to be related to the rapid replication of tachyzoites. Immune animals develop a chronic or dormant form of toxoplasma infection that is characterized by the formation of cysts containing bradyzoites. In the liver irregular foci of coagulative necrosis are usually scattered randomly and there is usually only little inflammation associated with the necrotic area. Variable number of tachyzoites may be present in hepatocytes and Kupffer cells usually at the periphery of the lesions. In the adrenals vast area of necrosis are usually seen in the adrenal cortex with minimal inflammation.

The adverse clinical signs which lead to the decision to euthanize the cat were probably due to the disseminated toxoplasmosis which resulted in severe liver disease and hypoabluminemia. The hypothermia present was indicative of a poor prognosis. The hepatic neoplasm in this case was considered as an incidental finding.

Three differential diagnoses that were considered regarding the liver tumor were: Cholangiocarcinoma, biliary cystadenoma (congenital biliary cysts) and cholangioma. The small size, demarcation, low cellular pleomorphism, lack of invasion or metastases, lack of substantial desmoplasia, and lack of aggregates of hepatocytes between the neoplastic tubules favored a diagnosis of cholangioma.

Chloangiomas have been reported in dogs, cats, sheep, cows and pigs (2). This benign tumor is uncommon and there are a limited number of reports in the literature. Cholangiomas are considered to be the most common hepatobiliary neoplasm in cats in two studies (2, 8, 9). Clinical signs in cats are non-specific and the tumor may not be detected at an early stage as they are clinically silent and only detected when affected animals are examined for other clinical conditions (9, 10, 11). Cholangiomas develop in cats of 10-12 years of age and older, which was the case in this cat. One survey found that males were overrepresented compared to females with cholangiomas and that the results suggested that domestic short haired cats may have a higher rate for hepatic neoplasia than pure bred cats (12).

The incidental finding in this cat with an hepatic tumor concomitantly with toxoplasmosis raises the question of the relationship between these two events. *Toxoplasma* has been demonstrated to have antitumor effects (3). Protein extracts from *Toxoplasma* have shown quantifiable effects in slowing the development of various tumors such as fibrosarcoma, melanoma, sarcoma and chemically induced tumors (3). Most studies have been carried out in mice and humans. No literature is available regarding cats. Whether there was any interaction between the development of the cholangioma and the presence of a *T. gondii* infection remains unknown.

The diagnosis of toxoplasmosis (*T. gondii*) was made by histopathological examination and confirmed by immunohistochemical studies. The immune status of this cat is was unknown and therefore it cannot be concluded that the disseminated infection was due to immunodeficiency. The presence of a cholangioma in the liver of this cat is regarded as an incidental finding.

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