

# *Taenia taeniaeformis*-induced Metastatic Hepatic Sarcoma in a Pet Rat (*Rattus norvegicus*)

Armando R. Irizarry-Rovira, DVM, PhD

Alexander Wolf, DVM

Matthew Bolek, PhD

## Abstract

An approximately 683-g intact adult male pet rat (*Rattus norvegicus*) of unknown age was presented to the veterinarian by its owner with a complaint of lethargy and anorexia. Physical examination findings consisted of an enlarged abdomen and a large cranial abdominal mass strongly suggestive of neoplasia. Because of a poor prognosis, the owner refused additional diagnostic tests and the rat was euthanized. A necropsy was performed, and the findings consisted of a large, irregularly shaped mass that replaced a large portion of the liver. Multiple metastases were present on the peritoneal surfaces of other abdominal organs. Cestode larvae consistent with *Taenia taeniaeformis* were within cystic cavities in the center of the hepatic mass and in the remaining liver tissue. The clinical and postmortem gross and microscopic findings were consistent with metastatic hepatic sarcoma induced by *T taeniaeformis*. Copyright 2007 Elsevier Inc. All rights reserved.

**Key words:** sarcoma; rat; cytology; *Taenia taeniaeformis*; parasite; liver

**T***aenia taeniaeformis* is a cestode parasite of cats that uses rodents as intermediate hosts.<sup>1-3</sup> *T taeniaeformis* was initially described in the 1700s; however, an association between the implantation of larvae and the formation of liver tumors in rats was not postulated until the early 1900s.<sup>4,6</sup> Previous reported cases have been in laboratory or wild rats.<sup>2-7</sup> Here, we present a case of *T taeniaeformis*-induced metastatic hepatic sarcoma in a pet rat.

## Case Description

An approximately 683-g intact adult male pet rat (*Rattus norvegicus*) was presented by its owner with a complaint of lethargy and anorexia. Physical examination findings consisted of an enlarged abdomen and a large cranial abdominal mass strongly suggestive of neoplasia. Because of a poor prognosis, the

owner refused additional diagnostic tests and the rat was euthanized. At necropsy, a large, irregularly shaped, hemorrhagic, red to tan-colored firm mass replaced a large portion of the liver (Fig 1). The mass extended to the stomach, spleen, and diaphragm. Multiple small metastases were found throughout the mesenteric fat (Fig 1) and on the peritoneal surfaces of the kidney, small intestines,

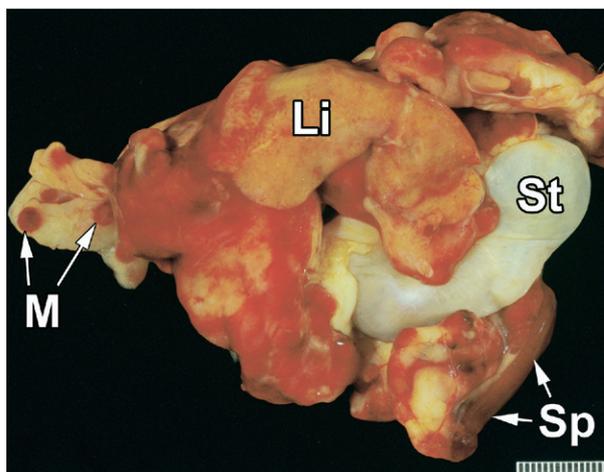
*From the Department of Pathology, Eli Lilly and Company, Greenfield, IN 46140 USA, the Avian and Exotic Animal Clinic of Lafayette, Lafayette, IN 47904 USA, and the School of Biological Sciences, University of Nebraska, Lincoln, NE 68588-0118 USA.*

*Address correspondence to: Dr. Armando R. Irizarry-Rovira, PO Box 708, Greenfield, IN 46140. E-mail: irizarryar@lilly.com*

*© 2007 Elsevier Inc. All rights reserved.*

*1557-5063/07/1601-\$30.00*

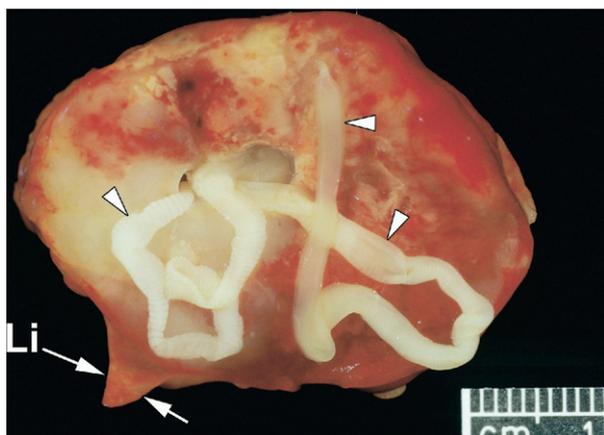
*doi:10.1053/j.jepm.2006.11.008*



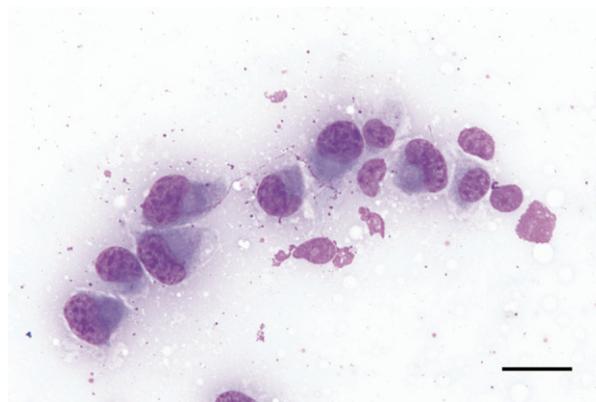
**Figure 1.** Image of excised abdominal viscera from a rat with *Taenia*-induced hepatic sarcoma. *Li*, liver; *St*, stomach; *Sp*, spleen; *M*, metastases in the mesenteric fat. Ruler = 1.5 cm.

large intestines, pancreas, and seminal vesicles. On cut section, the primary mass and the metastases were firm and red to tan colored, with few areas of pale discoloration (Fig 2). At the center of the primary hepatic mass, an elongate, pale white, translucent, segmented cestode larva was found within a fluid-filled cavity (Fig 2). A second cestode larva within a fluid-filled, encapsulated cyst was present in the remaining liver tissue (not shown). These larvae were morphologically consistent with the larvae of *T taeniaeformis*, an intestinal cestode parasite of cats.

Air-dried, cytologic preparations of the abdominal mass and metastases were obtained at necropsy, stained with an automated staining system (Hematek; Bayer Diagnostics, Elkhart, IN USA), and evaluated cytologically. The samples were of high cellularity and con-



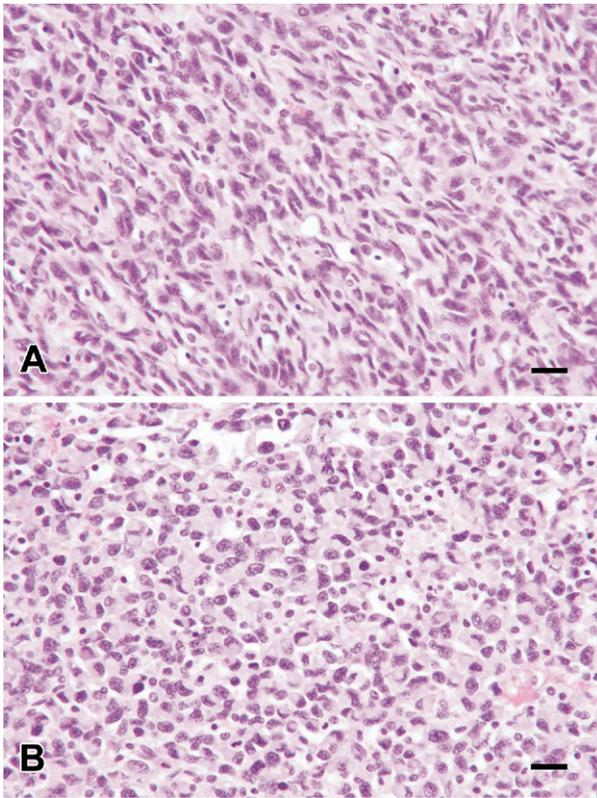
**Figure 2.** Image of the excised tumor from a rat with *Taenia*-induced hepatic sarcoma. A long cestode larva was within a cystic cavity within the hepatic tumor. *Li*, remaining liver tissue; arrowheads, cestode larva. Ruler = 1.0 cm.



**Figure 3.** Photomicrograph of the cytologic preparation from the hepatic mass. Discrete plump to elongate mesenchymal cells. Wright's stain. Bar = 20  $\mu$ m.

sisted of individualized and dense aggregates of discrete pleomorphic neoplastic mesenchymal cells (Fig 3). The discrete neoplastic cells varied from polygonal to plump spindle shapes and had low to moderate amounts of well-demarcated, finely granular blue to deep blue cytoplasm. Low numbers of cells had an elongate spindle shape. The cells had perinuclear clear zones that indented the nuclei. The nuclei were oval to indented and had coarsely clumped chromatin and single to multiple small nucleoli. Binucleate and trinucleate cells were rarely seen. Anisokaryosis and anisocytosis were moderate in severity. The morphology of the cells was consistent with sarcoma, possibly of histiocytic and/or fibrocytic differentiation.

The histopathologic findings were consistent with sarcoma of fibrohistiocytic differentiation (Fig 4). The neoplasm and metastases were nonencapsulated and densely cellular, and consisted of closely packed, pleomorphic plump polygonal to spindle-shaped cells arranged in dense sheets and ill-defined interlacing bundles (Fig 4). Multifocal to coalescing areas of necrosis occurred within the primary tumor. There was no significant neoplastic deposition of collagen or other extracellular matrix by the neoplastic cells. Perinuclear clear zones frequently occurred in some areas of the tumor and metastases, and, when present, would often indent the nucleus. Nuclei were oval to indented to irregularly shaped with coarsely clumped, irregularly distributed chromatin and small, indistinct, round nucleoli. The mitotic rate varied from 1 to 7 per high-power field. The cells of the primary tumor aggressively dissected into compressed and distorted adjacent remnant hepatic tissue and the diaphragmatic muscle. The metastases were primarily localized to the peritoneal surface of the other organs, with focal infiltration of adjacent parenchyma. The lungs were congested and col-



**Figure 4.** Photomicrographs of the histologic sections from the hepatic mass. *A*, area of the tumor with spindle cell morphology; *B*, area of the tumor with discrete, plump cellular morphology. Many cells have perinuclear clear areas. Wright's stain. Bar = 20  $\mu$ m.

lapsed and contained small, multifocal, microscopic metastatic islands of neoplastic cells similar to those seen in the primary tumor and the abdominal metastases. The *T taeniaeformis* larva found within the tumor had all the typical histologic characteristics of taeniid cestodes: scolex with hooks, suckers, and calcareous corpuscles.<sup>8</sup>

## Discussion

The postmortem findings in the pet rat were consistent with *Taenia*-induced hepatic sarcoma. The microscopic findings were consistent with sarcoma of fibrohistiocytic differentiation and are similar to previously reported *Taenia*-induced hepatic tumors. There are no published descriptions of the exfoliative cytologic features of these tumors, and the present report addresses this gap in the scientific literature.

*T taeniaeformis* is a cestode parasite of cats that uses rodents as intermediate hosts. The parasite has been previously referred to in the adult stage as *Taenia crassicollis* and in the larval stage as *Cysticercus fasciolaris*, *Hydatagera fasciolaris*, *Strobilocercus fascio-*

*laris*, and *Cysticercus taeniaeformis*.<sup>1-3</sup> *T taeniaeformis* was initially described in the 1700s; however, the association between the implantation of the larvae and the formation of liver tumors in rats was not postulated until the early 1900s.<sup>4,6</sup> *T taeniaeformis* mainly localizes to the liver of rodents, and experimental studies have demonstrated the causal relationship between implantation of the larvae and the development of neoplasms in the liver.<sup>9,10</sup> The overwhelming majority of the hepatic tumors are sarcomas with locally aggressive growth and a tendency to metastasize.<sup>2,3,7,11</sup> Hepatic tumors are first detected microscopically at 8 months postinfection, but the majority of tumors form between 11 to 17 months postinfection.<sup>9</sup> The tumors are believed to arise from the host capsule that forms around the encysted larvae. Encysted larvae and associated sarcomas rarely occur in other anatomical locations.<sup>6</sup> In contrast to the pet rat of the present report, naturally occurring cases typically occur in laboratory or wild rats.<sup>2,7</sup> Although other rodents are susceptible to infection with *T taeniaeformis*, tumors are exceedingly rare in other infected rodents, suggesting that susceptibility to oncogenesis is partly dependent on the host species.<sup>3,12</sup>

The specific pathogenesis for the formation of tumors is not known; however, several causal hypotheses have been proposed including microbial infection, larval-derived oncogenic substances, chronic irritation/inflammation, and oxidative damage.<sup>2,3,11</sup> It is possible that *Taenia*-induced immunosuppression could also play a contributory role.<sup>13</sup>

Clinical signs associated with *T taeniaeformis*-induced hepatic tumors are nonspecific and may include lethargy, weight loss, anorexia, and sudden death.<sup>2,3</sup> Nonspecific laboratory changes in infected rats include mild decreases in serum cholesterol concentration, increases in the serum activity of alanine aminotransferase, sorbitol dehydrogenase, and/or aspartate aminotransferase, decreased concentration of glucose, and increases in the numbers of peripheral blood neutrophils, lymphocytes, and/or eosinophils.<sup>14-17</sup> Rats infected with larvae of *T taeniaeformis* may develop unique lesions consisting of inhibited gastric acid secretion, hypergastrinemia, and gastric and intestinal mucosal hyperplasia.<sup>18,19</sup> Experimental studies have demonstrated that these gastrointestinal changes are secondary to substances secreted by the larvae.<sup>20</sup> The gastrointestinal tract of the rat in this report was not evaluated for mucosal hyperplasia due to autolysis. *T taeniaeformis* may also have negative effects on reproductive function in the rat.<sup>21</sup>

A tentative diagnosis of *T taeniaeformis* infection in the laboratory rat may be achieved with the use of ultrasonography and/or radiology. In experimental

studies with laboratory rats, ultrasonography was used to detect parasitic cysts in the liver, and contrast radiography was used to detect hepatomegaly and gastric and intestinal mucosal changes.<sup>22,23</sup> Serology may also be a useful diagnostic tool for the diagnosis of *T taeniaeformis* in rats.<sup>22</sup> The clinical utility of ultrasonography, radiography, and serology for the diagnosis of *T taeniaeformis* in pet rats requires additional investigation.

Treatment options for pet rats infected with *T taeniaeformis* have not been adequately investigated. However, experimental studies indicate that praziquantel is effective at killing adults and larvae.<sup>24,25</sup> The safety of praziquantel for the treatment of encysted larvae in rats is unknown, and it is possible that killed larvae would elicit a marked host response that could be harmful to the rat. Vaccination of rats with inactivated oncospheres or oncosphere antigens protects laboratory rats from infection.<sup>26,27</sup>

The origin of the infection in the pet rat of the present report was undetermined. The owner did not own a cat and kept the rat indoor at all times with other rats. The rat was possibly infected in the breeding facilities or in the retail establishment where it was purchased.

## Acknowledgments

The work of Nancy Martin (Histopathology Service, Department of Veterinary Pathobiology at Purdue University) is acknowledged and greatly appreciated.

## References

- Georgi JR, Georgi ME: Helminths, in Georgi JR, Georgi ME (eds): Parasitology for Veterinarians (ed 5). Philadelphia, PA, WB Saunders Co, 1990, pp 103-225
- Hanes MA: Fibrosarcomas in two rats arising from hepatic cysts of *Cysticercus fasciolaris*. Vet Pathol 32: 441-444, 1995
- Tucek PC, Woodard JC, Moreland AF: Fibrosarcoma associated with *Cysticercus fasciolaris*. Lab Anim Sci 23:401-407, 1973
- Roux ME: V. Sur travail de M. le Dr A Borrel, intitule: Tumeurs cancéreuses et helminthes Bull Acad Med 56:141-144, 1906
- Woolley PG, Wherry WB: Notes on twenty-two spontaneous tumors in wild rats (*R. norvegicus*). J Med Res 25:205-216, 1911
- McCoy GW: A preliminary report on tumors found in wild rats. J Med Res 31:285-296, 1909
- Jaquet J, Lemarinié M: Recherches sur un sarcome du rat induit primitivement par la larve d'un tenia du chat. Bull Acad Vet Fr 48:325-338, 1975
- Gardiner CH, Poynton SL: in An Atlas of Metazoan Parasites in Tissues. Morphological characteristics of cestodes in tissue sections. Washington DC, Armed Forces Institute of Pathology, 1999, pp 50-55
- Bullock FD, Curtis MR: A study of the reactions of tissues of the rat's liver to the larvae of *Taenia crassicolis* and the histogenesis of *Cysticercus* sarcoma. J Cancer Res 8:446-481, 1924
- Dunning WF, Curtis MR: Attempts to isolate the active agents in *Cysticercus fasciolaris*. Cancer Res 13: 838-842, 1953
- Bullock FD, Curtis MR: Types of cysticercus tumors. J Cancer Res 9:425-443, 1925
- Al-Sadi HI, Youkana SO, Dauod MS: Fibrosarcoma in association with *Cysticercus fasciolaris* (*Taenia taeniaeformis*) infection in laboratory mice. Iraqi J Vet Sciences 93:289-296, 2000
- Burger CJ, Rikihisa Y, Lin YC: *Taenia taeniaeformis*: inhibition of mitogen induced proliferation and interleukin-2 production by rat splenocytes by larval *in vitro* product. Exp Parasitol 62:216-222, 1986
- Mathur CS, Johnson S: Serum cholesterol in the house rat (*Rattus rattus*) naturally infected with some helminth parasites. Helminthologia 23:231-236, 1986
- Cook RW, Trapp AL, Williams JF: Pathology of *Taenia taeniaeformis* infection in the rat: hepatic, lymph node, and thymic changes. J Comp Pathol 91:219-226, 1981
- Ansari A, Williams JF: The eosinophilic response of the rat to infection with *Taenia taeniaeformis*. J Parasitol 62:728-736, 1976
- Konno K, Abella JA, Oku Y, et al: Histopathology and physiopathology of gastric mucous hyperplasia in rats heavily infected with *Taenia taeniaeformis*. J Vet Med Sci 61:317-324, 1999
- Oku Y, Yamanouchi T, Matsuda K, et al: Retarded gastric acid secretion in rats infected with larval *Taenia taeniaeformis*. Parasitol Res 88:872-873, 2002
- Konno K, Oku Y, Nonaka N, et al: Hyperplasia of gastric mucosa in donor rats orally infected with *Taenia taeniaeformis* eggs and in recipient rats surgically implanted with the larvae in the abdominal cavity. Parasitol Res 85:431-436, 1999
- Lagapa JT, Oku Y, Nonaka N, et al: *Taenia taeniaeformis* larval product induces gastric mucosal hyperplasia in SCID mice. Jpn J Vet Res 49:273-285, 2002
- Lin YC, Rikihisa Y, Kono H, et al: Effects of larval tapeworm (*Taenia taeniaeformis*) infection on reproductive functions in male and female host rats. Exp Parasitol 70:344-352, 1990
- Ito A, Sakakibara Y, Ma L, et al: Ultrasonographic and serologic studies of experimental cysticercosis in rats infected with *Taenia taeniaeformis*. Parasite Immunol 20:105-110, 1998
- Perry RL, Williams JF, Carrig CB, et al: Radiologic evaluation of the liver and gastrointestinal tract in rats infected with *Taenia taeniaeformis*. Am J Vet Res 55:1120-1126, 1994
- Eom KS, Kim SH, Rim HJ: Efficacy of praziquantel (Cesocide injection) in treatment of cestode infections in domestic and laboratory animals. Korean J Parasitol 26:121-126, 1988
- Thomas H, Andrews P, Mehlhorn H: New results on the effect of praziquantel in experimental cysticercosis. Am J Trop Med Hyg 31:803-810, 1982
- Ito A, Hashimoto A: Vaccination with hatched but non-activated, non-viable oncospheres of *Taenia taeniaeformis* in rats. J Helminthol 67:165-168, 1993
- Ito A, Bogh HO, Lightowers MW, et al: Vaccination against *Taenia taeniaeformis* infection in rats using a recombinant protein and preliminary analysis of the induced antibody response. Mol Biochem Parasitol 44:43-49, 1991