Intestinal Adenocarcinoma with Pancreas and Lymph Node Metastases in a Captive Cotton-Top Tamarin (Saguinus oedipus)

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ABSTRACT. A case of intestinal adenocarcinoma with metastases to the pancreas and regional lymph node was found in a 9-year-old, captive female cotton-top tamarin (Saguinus oedipus) with intermittent diarrhea. At necropsy, the tumor mass was located in the ileo-cecal junction causing circumferential thickening and annular stenosis. Microscopically, the lesions at primary and metastatic sites showed typical features of mucinous adenocarcinoma as seen in humans, including intracellular and extracellular mucin production and characteristic appearance of a signet ring of the tumor cells. The diagnosis was confirmed by histological evaluation, positive cytokeratin immunostaining, and mucin production demonstrated by PAS and Alcian blue stain. It is speculated that the development of intestina l carc inoma was partly attributable to the excessive absorption of a diet of refined food, unbalanced nutrition, and the nature of these animals to develop stress easily.

KEY WORDS: cotton-top tamarin, intestinal adenocarcinoma, metastasis.

A female, 9-year-old cotton-top tamarin (Saguinus oedipus) was found dead. The animal had a six-year history of intermittent diarrhea or soft stool, but hematological data on complete blood count and serum biochemistry profiles for liver and kidney function were within normal limits. Fecal flotation and smear were negative for intestinal parasites. Proteus mirabilis, E. coli, Moraxella spp. and K. terrigena had been previously isolated from stool. The animal had failed to respond to treatment with oxytetracycline, imodium, kapectin, or trimeterin. One week prior to death, abdominal ultrasonography revealed hyperechoic regions surrounding the intestinal lumen and radiography showed unidentified intestinal boundary with mist image in the abdominal cavity.

At necropsy, a circumscribed and firm mass, measuring 1.5 × 2 × 1 cm, was found in the ileo-cecal junction which tightly adhered to the pancreas and a portion of small intestine (Fig. 1). On cut surface, the affected intestine showed circumferential thickening extending from the mucosa to the muscular layer resulting in annular stenosis (Fig. 2). Other organs examined showed no marked gross lesions. Tissue samples from the tumor masses and representative tissues including the liver, pancreas, kidneys, spleen, heart, ovary, urinary bladder, lung, and mesenteric lymph node were fixed in neutral buffered 10% formalin, embedded in paraffin, sectioned at 5 µm, and stained with hematoxylin and eosin (HE). In addition, selected sections obtained from the tumor tissue were stained with periodic acid-Schiff (PAS) and Alcian blue (pH 0.4) for demonstration of mucin substance. Immunohistochemical studies were also performed on the sections by an avidin-biotin complex (ABC) immunoperoxidase technique using diaminobenzidine (DAB) chromogen (Vector Laboratories, Burlingame, CA) with cytokeratin antibody (AE1/AE3; 1:50) (Vector Laboratories, Burlingame, CA). Paired tissue sections from a variety of canine tissues known to express the relevant antigen were immunostained in parallel.

Histologically, areas of ileo-cecal thickening were composed of neoplastic glands and tumor emboli in distended lymphatics embedded in abundant fibrous stroma, extending from the mucosa to serosa. The predominant features of the tumor cells included single or multiple gobules of mucin in the cytoplasm, with a centrically placed nucleus, giving their characteristic appearance of a signet ring (Fig. 3). Mitotic figures were infrequently seen. Variable numbers of lymphocytes and plasma cells infiltrated into the tumor tissue. Large amounts of intracellular and extracellular mucin production by the tumor cells resulted in dilation of the ducts and tubules of glands. PAS and Alcian blue (pH 0.4) clearly demonstrated mucin substance in dilated ducts or tubules and in the cytoplasm of the signet-ring cells. Cytokeratin was strongly immunoreactive with the majority of tumor cells in the crypts of ileo-cecal mucosa, transmural penetration, and metastatic sites (Fig. 4). Based on histological, histochemical and immunohistochemical evidences, mucosal crypts were the most likely origin of tumor development. Invasion to the pancreas (Fig. 5) and the cortex of a regional lymph node were observed. Differential diagnosis of the present adenocarcinoma requires distinguishing from Cryptococcus neoformans infection, because the yeast form of Cryptococcus neoformans is round, typically encapsulated and 5–15 µm in diameter, and begins with a myxoid degeneration with the area of inflammation assuming a gelatinous appearance resembling mucin production in signet ring cells. Intestinal cryptococcosis has been reported in nonhuman primates through fecal-oral transmission. Systemic infection predisposing to immunosuppressive status may occur [9, 11]. Clinical signs may reveal gastrointestinal disorders and pathological diagnosis is frequently based on the demonstration of a typical organism associated with...
a flask-shaped colonic ulcer. Thus, PAS and Alcian blue will help eliminate the possibility of cryptococcosis by demonstrating positive stain in the mucinous pool and cytoplasm of signet ring cells. Positive cytokeratin staining can further identify the epithelial origin and help in distinguishing signet-ring tumor cells from Cryptococcus neoformans. In this case, immunohistochemistry commonly used in humans and dogs served as a rapid and definite diagnostic tool for identifying the tumor and distinguishing it from Cryptococcus neoformans.

Colonic adenocarcinoma is a common neoplasm in cotton-top tamarins from several different colonies in Europe and the United States [3]. It appears that initial ulcerative colitis (UC) predisposes to the development of colonic adenocarcinoma in this species [5]. The incidence of intestinal carcinoma in cotton-top tamarins is 20.5% of the population.
Approximately 50% of cotton-top tamarins develop active colitis, and in 25 to 40% of these animals further progress to colonic carcinoma after 2 to 5 years in captivity [4]. Although the relationship between UC and colonic adenocarcinoma is unknown, it is probably attributable to many factors including a species-related susceptibility and an infectious cause [1, 2], disorders of the immune system, and environmental stresses [14–16]. Coronaviruses and Campylobacter spp., and more recently, Helicobacter spp. have been considered as infectious agents causing UC in cotton-top tamarins [1, 2, 10]. In humans, environmental factors, particularly diet, obesity and physical inactivity are impli-
cated as risk factors for colon cancer. Dietary risk factors include intake of excessive energy, low fiber content, high carbohydrate content, intake of red meat, and decreased intake of protective micronutrients [6]. For the cotton-top tamarin, evidence shows that diet affects the incidence of chronic mucosal changes, which seems to be associated with the development of colon cancer. Evidences also suggest that some dietary components other than fat or fibers may play a role in the development or prevention of cancer [8]. In the native habitation, cotton-top tamarins may feed on fruits, insects, and are opportunistic feeders on sap, and occasionally on small birds, lizards, and eggs [7, 12, 13]. The tamarin housed in this zoo was regularly fed Tenebrio molitor larvae, bread, cookies, eggs, bananas, papayas, apples, guavas, sweet oranges, carrots, sweet potatoes, maize, tomatoes, chicken meat, raisins, and honey. Although the recipes prepared mimicked the wild tamarin's natural diet, it resulted in high intake of carbohydrate and protein, such as for the 31% fat and 56% protein content of Tenebrio molitor larvae consumed by the tamarin. As suggested by previous investigators [4, 5], chronic colitis may have an important role in intestinal carcinogenesis because it accelerates cell turnover which results in the occurrence of mutation. However, there was no macroscopic and histological evidence of ulcer in the intestinal mucosa of the present case. Therefore, chronic inflammation seems not to be involved in the tumor development. It is speculated that the development of intestinal carcinoma in this case was partly attributable to the excessive absorption of a diet of refined food, unbalanced nutrition, and the nature of these animals to develop stress easily.

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REFERENCES