# Veterinary Science

## **Case Report**

## Hepatocellular adenoma in a Eurasian otter (Lutra lutra)

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A 7-year-old female Eurasian otter (Lutra lutra) at the Seoul Grand Park, Korea, died after displaying depression, anorexia, weight loss and rough skin for several days. At necropsy, a solitary friable round mass, which was approximately  $12 \times 9 \times 5$  cm and mottled dark red and yellow, was found bulging from the right hepatic lobe. Microscopically, the nonencapsulated, poorly circumscribed mass was composed of solid sheets of neoplastic hepatocytes. In addition, numerous small tan foci, ranging from 0.5 to 1.0 cm in diameter, were evenly scattered throughout the pancreatic tissue. These foci were found to be nonencapsulated, well-demarcated hyperplastic nodules of the exocrine pancreatic gland. We observed neither intrahepatic nor extrahepatic metastases. Based on the gross and microscopic changes, we diagnosed the animal as having a hepatocellular adenoma accompanied by exocrine pancreatic nodular hyperplasia.

**Key words:** Eurasian otter, hepatocellular adenoma, *Lutra lutra*, tumor

Hepatocellular adenoma is a benign neoplastic proliferation of hepatocytes, and it is uncommon in animals, although it has occasionally been reported in dogs, cats, sheep, pigs, primates and exotic avian species [4,10]. Although hepatocellular adenoma generally occurs in older animals, it has been described in pigs under 6 months of age and in sheep less than 1 year old [2]. In dogs, it is less frequently diagnosed than its malignant counterpart [9,15]. In humans, hepatocellular adenoma develops more frequently in women than in men [11], but no comprehensive breed and gender predisposition has been identified in animals.

Numerous cases of tumor have been reported in ferrets. In contrast, there have been a far smaller number of cases reported in otters, including hepatocellular carcinoma [16], lymphosarcoma [5], malignant seminoma [12], malignant ovarian teratoma [17], concurrent cholangiocellular carcinoma, leiomyoma, pheochromocytoma [14] and differentiated

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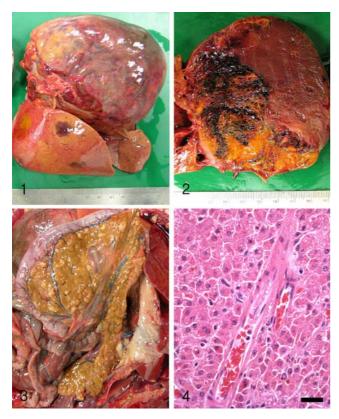
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basal cell carcinoma [8]. We describe here a spontaneous hepatocellular adenoma with exocrine pancreatic nodular hyperplasia in a Eurasian otter (*Lutra lutra*) in Korea.

A 7-year-old female Eurasian otter, which was kept in an outdoor exhibit at the Seoul Grand Park, Korea, died suddenly after several days of displaying depression, anorexia, weight loss and rough skin. At necropsy, a solitary friable, mottled, dark red to yellow mass that was approximately  $12 \times 9 \times 5$ cm in size with a pale and dull margin was found bulging from the right hepatic lobe (Fig. 1). On cut section, the neoplastic mass had a widespread area of focal red or yellow discoloration that was associated with hemorrhage and necrosis, respectively (Fig. 2). No metastasis to the other parenchymal organs was noted. Numerous small tan foci that ranged from 0.5 to 1.0 cm in diameter were found to be evenly scattered throughout the pancreas (Fig. 3). Representative tissue samples, including the hepatic mass and pancreas, were fixed in 10% phosphate-buffered formalin, routinely processed, embedded in paraffin, sectioned at 3 µm, stained with hematoxylin and eosin and then they were examined by light microscopy.

Microscopically, the neoplastic mass was non-encapsulated and poorly circumscribed, and it consisted of neoplastic hepatocytes arranged in solid sheets. There was moderate anisocytosis and anisokaryosis. The neoplastic cells had distinct borders, moderate to abundant amounts of eosinophilic cytoplasm that contained glycogen and lipid droplets, and centrally located round nuclei with one to 2 prominent nucleoli. There were 0-1 mitotic figures per high power field (× 400). The majority of portal triads were obliterated by invasion of neoplastic cells (Fig. 4), with only a few remnants of the portal triads being recognizable. Neither intrahepatic nor extrahepatic metastases were observed. In the pancreas, we observed nonencapsulated, well-demarcated foci of hyperplastic nodules of the exocrine pancreatic glands.

Gross and histologic examinations resulted in the differential diagnosis of hepatic nodular hyperplasia, hepatocellular adenoma and hepatocellular carcinoma. The presence of destroyed portal triads by neoplastic cell invasion was helpful in discriminating the current case from nodular hyperplasia. It may be difficult to distinguish between



**Fig. 1.** Liver. Note a solitary friable large round mass approximately  $12 \times 9 \times 5$  cm in the right hepatic lobe.

**Fig. 2.** Cut surface of mass in Fig. 1. Confluent areas of necrosis and hemorrhage were noted.

**Fig. 3.** Pancreas. Numerous small tan foci ranging from 0.5 to 1.0 cm in diameter were evenly scattered throughout the pancreatic tissue.

**Fig. 4.** Liver. Portal triads were not clearly recognizable due to invasion of neoplastic hepatocytes. The bile ducts were completely obliterated by neoplastic cells. H&E stain. bar =  $20 \mu m$ .

hepatocellular adenoma and well-differentiated hepatocellular carcinoma. Although a hepatocellular carcinoma may be large in size before metastasizing, indications of malignancy such as metastases to other parenchymal organs, cellular atypia and invasiveness to the normal adjacent hepatic parenchyma are useful for the differential diagnosis [3]. On the basis of the absence of these indications, a diagnosis of hepatocellular adenoma was made in the present case.

Hepatocellular tumors are caused by several factors. In humans, hepatitis B virus is an epidemiologically proven risk factor, with individuals in Asia and the sub-Saharan region having a higher probability of contact with the hepatitis virus than do those individuals in Western countries [6]. Similarly, chronic infection with hepadnavirus and *Helicobacter hepaticus* can lead to hepatocellular carcinoma in woodchucks [13] and mice [4], respectively. No evidence of chronic hepatitis or cirrhosis was noted in the present case. In addition to the infectious agents, genetic, dietary,

aging and environmental factors are etiologically related to hepatocellular tumors in animals and humans [1,7]. In animals, however, no regional prevalence or interspecies differences in incidence have been identified due to the limited number of reported cases. In the present study, the diagnosis of hepatocellular adenoma could be established histologically in a Eurasian otter that was kept in an outdoor exhibit, but the exact etiology and pathogenesis of this disease are not known.

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#### References

- Adamson RH. Induction of hepatocellular carcinoma in nonhuman primates by chemical carcinogens. Cancer Detect Prev 1989, 14, 215-219.
- 2. Anderson LJ, Sandison AT. Tumors of the liver in cattle, sheep and pigs. Cancer 1968, 21, 289-301.
- 3. **Cullen JH, Popp JA.** Tumors of the liver and gall bladder. In: Meuten DJ (ed.). Tumors in Domestic Animals. 4th ed. pp. 483-508, Iowa State University Press, Ames, 2002.
- Fox JG, Li X, Yan L, Cahill RJ, Hurley R, Lewis R, Murphy JC. Chronic proliferative hepatitis in A/JCr mice associated with persistent *Helicobacter hepaticus* infection: a model of helicobacter-induced carcinogenesis. Infect Immun 1996, 64, 1548-1558.
- 5. **Kim JH, Kim BH, Kim JH, Yoo MJ, Kim DY.** Lymphosarcoma in a sea otter (*Enhydra lutris*). J Wildl Dis 2002, **38**, 616-617.
- McGlynn KA, Tsao L, Hsing AW, Devesa SS, Fraumeni JF Jr. International trends and patterns of primary liver cancer. Int J Cancer 2001, 94, 290-296.
- 7. McKillop IH, Schrum LW. Alcohol and liver cancer. Alcohol 2005, 35, 195-203.
- Nakamura K, Tanimura H, Katsuragi K, Shibahara T, Kadota K. Differentiated basal cell carcinoma in a Cape clawless otter (*Aonyx capensis*). J Comp Pathol 2002, 127, 223-227.
- Patnaik AK, Hurvitz AI, Lieberman PH. Canine hepatic neoplasms: a clinicopathologic study. Vet Pathol 1980, 17, 553-564.
- 10. Pettan-Brewer KC, Lowenstine LJ. Intrahepatic cysts and hepatic neoplasms in felids, ursids, and other zoo and wild animals. In: Fowler ME, Miller RE (eds.). Zoo and Wild Animal Medicine: Current Therapy. 4th ed. pp. 423-428, Saunders, Philadelphia, 1999.
- 11. Reddy KR, Kligerman S, Levi J, Livingstone A, Molina E, Franceschi D, Badalamenti S, Jeffers L, Tzakis A, Schiff ER. Benign and solid tumors of the liver: relationship to sex, age, size of tumors, and outcome. Am Surg 2001, 67, 173-178.

- 12. **Reimer DC, Lipscomb TP.** Malignant seminoma with metastasis and herpesvirus infection in a free-living sea otter (*Enhydra lutris*). J Zoo Wildl Med 1998, **29**, 35-39.
- 13. **Snyder RL, Tyler G, Summers J.** Chronic hepatitis and hepatocellular carcinoma associated with woodchuck hepatitis virus. Am J Pathol 1982, **107**, 422-425.
- 14. **Stetzer E, Williams TD, Nightingale JW.** Cholangiocellular adenocarcinoma, leiomyoma, and pheochromocytoma in a sea otter. J Am Vet Med Assoc 1981, **179**, 1283-1284.
- 15. **Trigo FJ, Thompson H, Breeze RG, Nash AS.** The pathology of liver tumours in the dog. J Comp Pathol 1982, **92**, 21-39.
- 16. Wadsworth PF, Jones DM, Pugsley SL. Primary hepatic neoplasia in some captive wild mammals. J Zoo Anim Med 1982, 13, 29-32.
- 17. **Zachary JF, McDonald SC.** Malignant ovarian teratoma in a spot-neck otter. J Am Vet Med Assoc 1981, **179**, 1279-1283.