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## Uterine Adenocarcinoma with Abdominal Carcinomatosis in a Beluga Whale

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**ABSTRACT:** A case of uterine adenocarcinoma is reported in a 26-yr-old, free-ranging beluga whale (*Delphinapterus leucas*) from the St. Lawrence estuary (Quebec, Canada). This neoplasm appeared as a segmental stenotic thickening of the left uterine horn composed of well differentiated, but disorganized and infiltrative, glandular structures surrounded by an extensive scirrhous stroma. Abdominal carcinomatosis was observed on the mesosalpinx and on the serosal aspect of the gastric compartments. This is the first report of a malignancy originating in the uterus of a cetacean.

**Key words:** Adenocarcinoma, beluga whale, cetaceans, *Delphinapterus leucas*, marine mammals, neoplasm, pathology, reproduction, uterus, whales.

Cancer is rare in free-ranging mammals and particularly in wild cetaceans. The relatively short life-span of wild mammals compared to their captive counterparts might partly explain this rarity (Fowler, 1987). Less than 40 cases of cancer have been reported worldwide in whales (Martineau et al., 1998). In contrast, cases of neoplasia are regularly diagnosed in a free-living population of Beluga whales (*Delphinapterus leucas*) inhabiting the St. Lawrence estuary (Martineau et al., 1998). Of 93 necropsies performed on adult whales from this population over a 14 yr period (1983–96), 17 malignant neoplasms have been diagnosed in 16 animals (17% of animals examined) (Martineau et al., 1998; D. Martineau, S. Lair, and I. Mikaelian, unpubl. data). The purpose of this report is to describe a case of uterine adenocarcinoma in a beluga whale from this population.

An adult female beluga whale, was found stranded on 21 May 1995 at Rivière Ouelle

(Québec, Canada; 47°26'N, 70°01'W). The carcass was transported the following day to the Faculté de Médecine Vétérinaire (University of Montreal, St. Hyacinthe, Quebec) for a complete standard necropsy (see Martineau et al., 1988 for detailed procedure). Age was determined by counting dentinal growth layers on longitudinal sections of teeth (Sergeant, 1973), adopting the standard of two growth layer groups per year (Brodie, 1982).

This female whale was estimated to be >26-yr-old, weighed 582 kg, and was 331 cm long. Autolytic changes were moderate. Examination of the abdominal cavity revealed a focally extensive, circumferential thickening of the uterine wall which involved the medial third of the left uterine horn, and resulted in a marked, 9 cm long segmental stenosis of the uterine lumen (Fig. 1). On section, the affected wall was white and firm. The uterine mucosa was irregular, extensively ulcerated, and protruded into the uterine lumen.

In addition, a well-circumscribed mass, 2 cm in diameter, was attached to the mesosalpinx caudally to the right oviduct. Its texture and color were similar to those of the thickened uterine wall. Numerous, irregular, slightly raised, and often coalescent plaque-like areas, 5 to 15 mm in diameter, were scattered on the serosa of the third and fourth gastric compartments. The mucosa of all gastric compartments appeared macroscopically normal.

The uterine wall was diffusely thickened by numerous disorganized well differentiated acinar glandular structures that infiltrated the muscular layer and that were

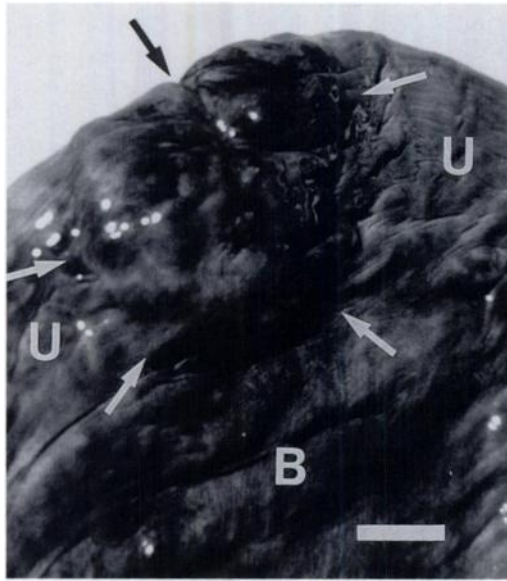


FIGURE 1. Uterine adenocarcinoma in an adult female beluga whale showing focally extensive, and circumferential thickening of the wall (arrows) of the left uterine horn (U). Broad ligament (B). Bar = 2 cm.

separated in pseudolobules by an abundant scirrhous stroma. Areas of necrosis were commonly observed in the neoplastic tissue. The neoplastic glandular structures were lined by one to two layers of disorganized, low columnar, highly pleomorphic epithelial cells (Fig. 2). Direct continuity between the neoplastic tissue and normal adjacent uterine mucosa was observed.

Neoplastic cells were characterized by a moderately abundant acidophilic cytoplasm with clearly distinct cytoplasmic borders, and their nuclei showed marked anisokaryosis and loss of polarity (Fig. 3). Nucleoli were usually prominent, abnormal mitotic figures were common, and multinucleated giant cells were frequent. Sections of the irregular uterine mucosa were characterized by a complex network of numerous papillomatous projections supported by a thin, highly vascularized, fibrous stroma, and lined by one or two layers of highly pleomorphic columnar to cuboid, often ciliated, epithelial cells similar to the neoplastic cells infiltrating the uterine wall (Figs. 2, 3).

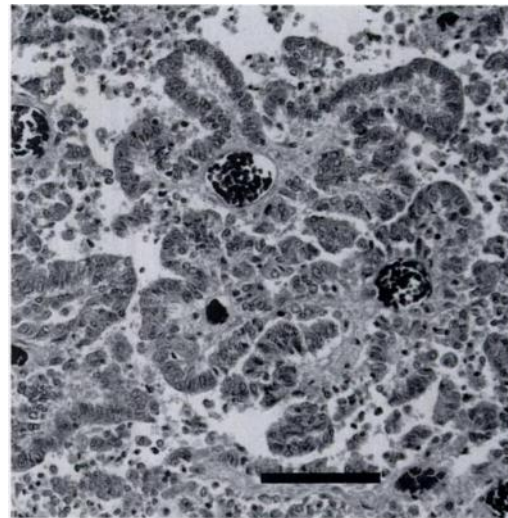


FIGURE 2. Uterine adenocarcinoma in an adult female beluga whale. Numerous papillomatous projections lined by highly pleomorphic epithelial cells. H&E. Bar = 100  $\mu$ m.

The mass observed on the mesosalpinx was similar to the uterine mass: it was not encapsulated and it was composed of numerous glandular structures separated by an abundant fibrous stroma. Tumor cells were occasionally observed in the lumen of blood vessels adjacent to the tumor

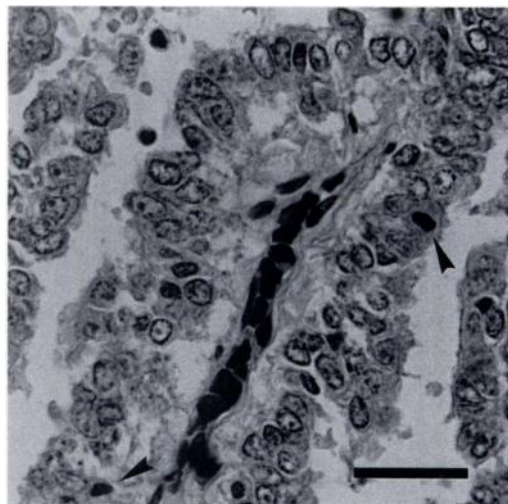


FIGURE 3. Uterine adenocarcinoma in an adult female beluga whale. Columnar to cuboidal neoplastic epithelial cells with marked anisokaryosis and frequent mitotic figures (arrowheads). H&E. Bar = 400  $\mu$ m.

masses. The plaque-like areas seen on the gastric serosa consisted of numerous glandular structures similar to previous lesions.

Paraffin embedded tissues and histological sections of this tumor have been deposited in the Registry of Comparative Pathology (Armed Forces Institute of Pathology, Washington, D.C., USA; accession number 2573966-5). The macroscopic and microscopic examinations of other organs were unremarkable.

The location and histological appearance of the largest mass indicate that this tumor was derived from the uterine mucosa. The masses observed on the mesosalpinx and on the gastric serosa most likely resulted from implantation of neoplastic cells from the primary uterine tumor into the abdominal cavity. Accordingly, a stenotic, scirrhous uterine adenocarcinoma with abdominal carcinomatosis was diagnosed. This malignant neoplasm may have contributed to the stranding of this animal, and may have affected its reproductive capacity.

Although reproductive organs of whales have been extensively examined in order to evaluate productivity for commercial exploitation purposes, only five cases of uterine tumors, all leiomyomas (and thus benign), have been described in cetaceans (Geraci et al., 1987). This report is the first case of uterine malignant neoplasia in a whale, and apparently in free-ranging animals.

Several cases of uterine carcinomas have been reported in captive wild felids, and it has been proposed that long-term exposure to megestrol acetate associated with the use of progestin contraceptives in these animals is a significant risk factor in the development of uterine malignancies (Munson et al., 1995).

With the exception of cows, rabbits, and one colony of rats, uterine adenocarcinomas also have been rarely reported in domestic species (McEntee, 1990). Isolated cases have been described in horses (Gunsen et al., 1980), dogs (Murphy et al., 1994), cats (O'Rourke and Geib, 1970),

sheep (Fecteau et al., 1993) and pigs (Werdin and Wold, 1976). Although several cases of uterine adenocarcinomas have been described in cows, this neoplasm remains uncommon in this species (McEntee, 1990). An unusually high prevalence (91%) of uterine adenocarcinomas was described in a colony of Hans: Wistar rats. The cause of this very high frequency was not determined (Kaspereit-Rittinghausen et al., 1987). Adenocarcinomas of the uterus are commonly seen in domestic aged rabbits, where prevalence may reach 60% (Burrows, 1940). It is believed that the constantly high estrogen/progesterone ratio observed in female rabbits housed individually is causally associated with this cancer (Elsinghorst et al., 1984). In rabbits however, unlike the case reported in this beluga whale, uterine adenocarcinomas are usually multiple and affect both horns (Elsinghorst et al., 1984).

Carcinomas of the *corpus uteri* are also relatively common in humans, where they account for approximately 13% of all malignant tumors in females (Perez et al., 1985). They are usually single, and as for rabbits, have been associated with endometrial hyperplasia (Ashley, 1978) and with excessive endogenous or exogenous estrogenic stimulation (Gambrell et al., 1983).

Beluga whales from the St. Lawrence population are known to accumulate high levels of organochlorinated compounds including DDT, PCBs, and mirex (Martineau et al., 1987; Muir et al., 1990). Estrogenic activities have been recognized for several of these industrial chemicals and their metabolites (for a review see Colborn et al., 1993). However, this potential exposure to endocrine-disrupting compounds in the etiology of this single uterine tumor case can be only speculative.

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