Primary Uterine T-cell Lymphoma with Metastasis in an Atlantic Spotted Dolphin (*Stenella frontalis*), Canary Islands, Spain

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**ABSTRACT:** We describe gross, histopathologic, and immunocytologic features of a primary uterine T-cell lymphoma with multiple metastases in an adult female Atlantic spotted dolphin (*Stenella frontalis*). Neoplastic T-cell lymphocytes (CD3+) partially effaced the uterus, ovaries, mesosalpinx, and urinary bladder and variably infiltrated abdominal and thoracic organs. Herpesvirus and morbillivirus PCR were negative.

Lymphoma is a widely reported neoplasm in humans and animals. Two major types are recognized in humans, Hodgkin’s lymphoma and non-Hodgkin’s lymphoma (Kumar et al. 2014). In cetaceans, reported lymphoid neoplasms include Hodgkin’s lymphoma in a fin whale (*Balaenoptera physalus*; Stolk 1962); Hodgkin’s lymphoma in a killer whale (*Orcinus orca*; Yonezawa et al. 1989); metastatic thymic lymphosarcoma in a beluga whale (*Delphinapterus leucas*; De Guise et al. 1992); sclerosing malignant lymphoma in a Pacific white-sided dolphin (*Lagenorhynchus obliquidens*; Howard et al. 1983); immunoblastic malignant lymphomas in three bottlenose dolphins (*Tursiops truncatus*), an Atlantic spotted dolphin (*Stenella frontalis*), and a pantropical spotted dolphin (*Stenella attenuata*) (Bossart et al. 1997); hepatosplenic large-cell immunoblastic lymphoma in a bottlenose dolphin (Jaber et al. 2005); and a primary central nervous system T-cell lymphoma in a common dolphin (*Delphinus delphis*; Arbelo et al. 2014). Here we report gross, microscopic, and immunocytologic features of a primary uterine T-cell lymphoma with multiple metastases in an adult female Atlantic spotted dolphin.

A 96-kg, 191-cm, adult female Atlantic spotted dolphin was necropsied after being found stranded dead in Morro Jable, Fuerteventura (Canary Islands; 28°02′38″N, 14°20′52″W) in fair nutritional condition in August 2007. There was mild, ventral cutaneous erosion and erythema at the level of the sternum and pectoral fins and a small amount of sand in the upper digestive system. Grossly, the uterus was diffusely enlarged (Fig. 1), measuring 12, 13.5, 14, and 14.5 cm in diameter at the level of the neck, body, and left and right uterine horns, respectively. While walls of the neck and body of the uterus were diffusely thickened (2.5 and 1.7 cm, respectively), the walls of both uterine horns were thinned, measuring 2.5 mm at their widest lumen section. Ovaries were markedly enlarged (5×4×2.5 cm and 3.5×2×1.5 cm, left and right, respectively) and the mesosalpinx was markedly thickened, up to five times, with multiple fibrous adhesions involving the serosa of uterine body and neck, the abdominal wall, and fusing the urinary bladder. On section, the uterine walls were mottled white to pink and soft with occasional, well-delineated, firm areas rimmed by a red halo, mostly at the level of the neck and body. These areas of necrosis occasionally spanned the entire wall thickness. The endometrium was diffusely roughened with patchy, dull red areas and frequent mats of pale yellow, friable, loosely attached material and scattered areas of denuded mucosa and hemorrhage. The vagina was dilated (14-cm diameter) with congestion and submucosal hemorrhages around the fornix. The adjacent peritoneum had variable, 0.5–2.5-cm diameter, white to pink, firm nodules and plaque-like masses. A 2-cm diameter, well-demarcated plaque was in the serosa of the thoracic aorta, 6 cm from the aortic...
bulb. Mesenteric and mediastinal lymph nodes were up to three times enlarged and mesenteric lymphangiectasia was moderate. For histopathology, samples from selected organs were collected and preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned at 5 μm, and stained with H&E.

Histologically, the normal cytoarchitecture of the uterus was distorted by a multifocal to coalescing, poorly demarcated, unencapsulated, densely cellular and infiltrative transmural neoplasm, frequently extending into the endometrium and serosa. It was composed of a monomorphic population of round cells arranged in dense sheets dissecting through a pre-existing fibrovascular stroma (Fig. 2). Neoplastic cells were 10–23 μm and had scant, light eosinophilic cytoplasm with indistinct cell borders. Nuclei were central, round, frequently cleaved with hyperchromatic to euchromatic and coarsely stippled chromatin and inconspicuous nucleoli. Anisocytosis and anisokaryosis were mild, and there were up to four mitotic figures per high-power field. These neoplastic cells disrupted adjacent collagen bundles and myofibers with variable degeneration, necrosis, atrophy, and loss of myofibers. Within areas of neoplastic infiltration there was multifocal subacute hemorrhage, edema, moderate deposition of fibrin, and rare viable and degenerate neutrophils. Fibrinosuppurative endometritis with necrosis was observed in the uterine neck and body. The neoplastic cell population diffusely infiltrated the mesosalpinx and showed variable, multifocal, metastatic infiltration into the muscular layers of the keratinized gastric compartment, peritoneum, lung parenchyma, serosa of the thoracic aorta, pituitary gland, and adrenocortical layers. No neoplastic invasion of main lymph nodes was observed.

For immunohistochemistry, a mouse monoclonal anti-CD79a antibody (clone HM57) for B-cells (1:100), and a rabbit polyclonal anti-CD3 antibody for T-cells (1:100) (DAKO, Carpinteria, California, USA), were utilized. Approximately 95% of the lymphoid neoplastic population showed moderate, diffuse, granular cytoplasmic immunopositivity for CD3 in
uterine sections (Fig. 2, inset) whereas CD79a was negative. Based on gross and microscopic severity and extension of the neoplasm, along with immunophenotype, it was determined to be a T-cell lymphoma of likely primary uterine origin with subsequent metastasis likely via blood and lymphatic vessels to abovementioned organs.

Molecular detection (PCR) of Cetacean morbillivirus (Reidarson et al. 1998) and herpesviruses (VanDevanter et al. 1996, Ehlers et al. 1999) in lung, brain, mesenteric lymph nodes, and spleen was performed according to previously reported methodologies and all were negative.

Bossart et al. (1997) detected immunoblastic lymphomas in five dolphins from the same geographic region in a 24-mo period, leading the authors to speculate about genetic, environmental, or infectious etiologies. However, none of these hypotheses were further evaluated. In our case, no histologic evidence suggested viral infection, and PCR detection of herpesviruses and morbilliviruses were negative.

In veterinary medicine, T-cell lymphomas have been associated with simian T-cell leukemia virus-1; Marek’s disease (alphaherpesvirus) and leucosis-sarcoma group (retroviruses) in poultry; type C retrovirus in swine; feline leukemia virus or feline immunodeficiency virus; and bovine leukemia virus. Oncogenic retroviruses have been suspected to play a role in the development of large cell lymphomas of harbor seals (*Phoca vitulina*) (Griner 1971).

After pathologic examination of 236 of 320 cetaceans stranded in the Canary Islands during 2006–12 (results will be published elsewhere), the present case constitutes the only identified lymphoma wherein disseminated presentation with chronic, multiorgan failure was considered the most likely cause of stranding and eventual death. This report contributes to
current knowledge of cetacean pathology. Lymphoma should be added to the differential diagnoses of female genital system disorders in spotted dolphins.

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