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DISEASE IN WILDLIFE OR EXOTIC SPECIES

High-grade Astrocytoma (Glioblastoma Multiforme) in an Atlantic Spotted Dolphin (*Stenella frontalis*)

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Summary

This report describes the gross, microscopical and immunohistochemical features of a high-grade astrocytoma (glioblastoma multiforme) in an adult male Atlantic spotted dolphin (*Stenella frontalis*). On necropsy examination, a 5 × 2.5 × 2 cm, poorly demarcated, red, friable and locally expansile mass effaced the thalamus and the left periventricular region and extended to the left lateral ventricle of the brain. Microscopically, the mass consisted of haphazardly arranged bundles and rows of interweaving polygonal to spindle-shaped cells. These often palisaded along serpentine foci of necrosis and were surrounded by prominent vessels. Immunohistochemically, the neoplastic cells expressed glial fibrillary acidic protein, but not vimentin, S100 protein, neuron-specific enolase or neurofilament protein. A diagnosis of high-grade astrocytoma was made and this represents the first description of a glioma in a cetacean species.

Keywords: astrocytoma; Atlantic spotted dolphin; brain; immunohistochemistry

Reports of primary brain tumours in cetaceans are limited to a cerebral lipoma in a humpback whale (*Megaptera novaeangliae*) (Pilleri, 1966), a cerebral neurofibroma in a fin whale (*Balaenoptera physalus*) (Pilleri, 1968), a poorly differentiated carcinoma in the brainstem of a Beluga whale (*Delphinapterus leucas*) (Ridgway *et al*., 2002), a microcystic meningioma in a short-beaked common dolphin (*Delphinus delphis*) (Miclard *et al*., 2006), a primitive neuroectodermal tumour in a striped dolphin (*Stenella coeruleoalba*) (Baily *et al*., 2013) and a T-cell lymphoma in a common dolphin (Arbelo *et al*., 2014). Additionally, Siebert *et al*. (2010) described intracranial metastases of a gastric squamous cell carcinoma in a harbour porpoise (*Phocoena phocoena*).

Gliomas, including astrocytomas, oligodendrogliomas and ependymomas, are the most common group of primary brain tumours in man and dogs (Stoica *et al*., 2011; Kumar *et al*., 2014). Astrocytomas are among the most fibrillary of central nervous system (CNS) neoplasms and are challenging to diagnose, in particular in discerning low-grade astrocytoma from gliosis (McKeever, 2010). Astrocytomas contain glial fibrillary acidic protein (GFAP) and although the expression is variable, GFAP is the most reliable marker for distinguishing astrocytomas from non-glial neoplasms (McKeever, 2010). Recognition of areas of tumour cells that express phenotypic characteristics of astrocytes and the immunohistochemical detection of GFAP form the basis for classification. Histologically, astrocytomas may show diffuse infiltration or be more localized.

The World Health Organization (WHO) classifies human astrocytomas into grades I–IV (Louis *et al*.,

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2007). A grade I tumour is a more circumscribed pilocytic astrocytoma with bipolar piloid and multipolar cells, microcysts, Rosenthal fibres and granular bodies. Grade I tumours may or may not show mitoses, vascular proliferation and focal necrosis. Grade II (diffusely infiltrative) astrocytoma shows cytological atypia, with or without mitotic activity. Grade III (anaplastic) astrocytoma displays anaplasia, mitotic activity and infiltration, while those tumours showing microvascular proliferation and/or necrosis, crowded anaplastic cells and numerous mitoses are considered to be of grade IV (Louis *et al*., 2007; McKeever, 2010).

Three categories of astrocytoma are recognized in veterinary medicine (Baba and Câtoi, 2007). Low-grade (well-differentiated) astrocytomas include three major variants; fibrillary, protoplasmic and gemistocytic. These display slow growth, have uniform cell structures with differentiated cells, low pleomorphism, rare mitoses and variable GFAP expression. Medium-grade astrocytomas (anaplastic) have increased mitotic activity, anaplasia, variable GFAP expression and an absence of vascular proliferation and necrosis. High-grade astrocytomas (HGAs, glioblastoma multiforme) show cellular pleomorphism, a high mitotic index, necrosis, haemorrhage, a common perivascular palisading arrangement and, in the periphery of necrotic areas, there may be cysts, oedema, prominent microvasculature and variable GFAP and vimentin expression. These tumours tend to arise from particular areas of the brain (e.g. the subventricular zone of the lateral ventricles) and give rise to progressive, unilateral neurological deficits.

An adult male Atlantic spotted dolphin (*Stenella frontalis*), 194 cm in length, was presented for necropsy examination. The dolphin was in good body condition (Arbelo *et al*., 2013) and the carcase was fresh (Kuiken and Hartmann, 1991). The animal had been found stranded dead in Playa de Pozo Negro, Fuerteventura, Canary Islands, Spain (28°19′12″N, −13°53′24″W).

A complete necropsy examination was carried out using a standardized protocol (Kuiken and Hartmann, 1991). Grossly, the most relevant finding was the presence of a 5 × 2.5 × 2 cm, moderately well-demarcated, red, friable and locally extensive mass that effaced and expanded the thalamus (Fig. 1) and suprathalamic left periventricular region and communicated with the left lateral ventricle. Additional gross findings included a 4 × 3 cm focal submandibular haematoma, mild left pterygoid sinus parasitism by adult *Crassicauda* sp., moderate and multifocal chronic pyogranulomatous mesenteric lymphadenitis, diffuse hepatic congestion and a focal

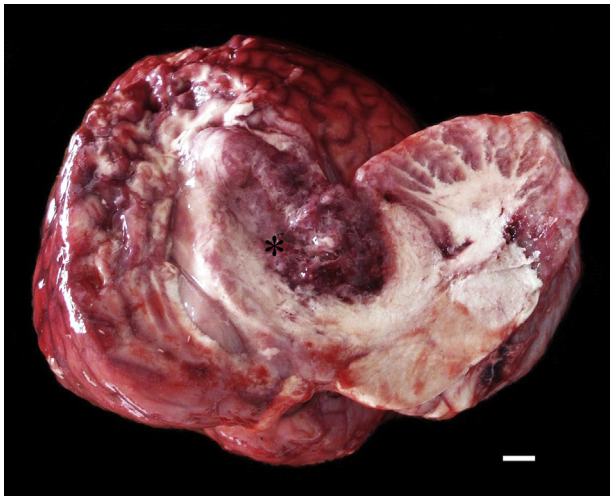

Fig. 1. Encephalon showing a moderately well-demarcated, red, friable and locally extensive mass effacing and expanding the thalamus (asterisk) and left periventricular region (not shown). Bar, 1 cm.

(5 × 4 cm) area of subcapsular haemorrhage and a single pancreatic granuloma (1 cm diameter). A small number of squid beaks, teleost lenses and otoliths were present in the keratinized area of the stomach.

Representative samples from skin, longissimus dorsi and rectus abdominis muscles, peritoneum, diaphragm, brain, pterygoid sinuses, tympanoperiotic complexes, tongue, oral mucosa, pharyngeal and laryngeal tonsils, oesophagus, gastric compartments, intestine, liver, pancreas, trachea, lungs, heart, aorta, kidneys, ureters, urinary bladder, lymph nodes, testicles, penis and prepuce were collected and fixed in 10% neutral buffered formalin. These tissues were processed routinely and embedded in paraffin wax. Sections (5 μm) were stained with haematoxylin and eosin (HE). Identification of parasites was based on their morphological features (Delyamure, 1955).

Microscopically, a nodular, moderately well-demarcated, unencapsulated, moderately cellular, locally expansile and infiltrative tumour expanded and distorted the normal architecture of the supraventricular neuroparenchyma and blended progressively with the adjacent parenchyma. It was composed of haphazardly arranged bundles and poorly cellular rows of interweaving polygonal to spindle-shaped cells, which occasionally clustered and were supported by a delicate vascular stroma (Fig. 2). Neoplastic cells had a mild to moderate quantity of pale eosinophilic cytoplasm, often with a fibrillary appearance, rare clear vacuoles and indistinct cell borders. Nuclei were central to paracentral, oval to elongate, with euchromatic and finely stippled to hyperchromatic chromatin and inconspicuous nucleoli. Anisocytosis and anisokaryosis were mild