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DISEASE IN WILDLIFE OR EXOTIC SPECIES

Mixed Glioma (Oligoastrocytoma) in the Brain of an African Hedgehog (*Atelerix albiventris*)

S. S. Benneter*, B. A. Summers†, W. J. Schulz-Schaeffer‡, W. Härtig§, J. Mollidor‖ and S. Schöniger*

** Institute of Pathology, Faculty of Veterinary Medicine, University of Leipzig, An den Tierkliniken 33, 04103 Leipzig, Germany, † The Royal Veterinary College, Department of Pathology and Pathogen Biology, Hawkshead Lane, North Mymms, Hatfield, Herts AL9 7TA, UK, ‡ Department of Neuropathology, University Medical Center Göttingen, Georg-August University of Göttingen, Robert-Koch-Str. 40, 37075 Göttingen, § Paul-Flechsig-Institute for Brain Research, University of Leipzig, Jahnallee 59, 04109 Leipzig and ‖ Tierarztpraxis Dr. J. Mollidor, Niehler Str. 68, 50733 Köln, Germany*

Summary

This report describes an oligoastrocytoma in the brain of a 3.5-year-old female pet African hedgehog (*Atelerix albiventris*) that showed progressive central nervous system signs for 6 months. Microscopical examination of the brain revealed a widely infiltrative, deep-seated glioma within the white matter of the cerebral hemispheres, basal nuclei, hippocampus, thalamus, midbrain, pons and the medulla of the cerebellum with extension of neoplastic cells into the cerebral cortex and overlying leptomeninges. Morphological features of the neoplastic cells, together with variable immunohistochemical expression of glial fibrillary acidic protein, Olig-2 and Nogo-A, indicated the presence of intermingled astrocytic and oligodendroglial tumour cells with an astrocytic component of approximately 40% consistent with an oligoastrocytoma. The distribution of the tumour is consistent with gliomatosis cerebri.

Keywords: African hedgehog; brain tumour; immunohistochemistry; oligoastrocytoma

Gliomas in man and domestic animals are subclassified according to their histopathological features. Astrocytic and oligodendrocytic tumours are most frequent (Koestner *et al.*, 1999; Koestner and Higgins, 2002; Burger and Scheithauer, 2007; Louis *et al.*, 2007). Diffuse infiltrating astrocytic tumours include low-grade astrocytoma, anaplastic astrocytoma and the most aggressive variant, glioblastoma multiforme. For subclassification the following features are evaluated: hypercellularity, cellular pleomorphism, nuclear atypia, mitotic activity, glomeruloid vascular or endothelial proliferation and presence of necrotic areas (Koestner *et al.*, 1999; Koestner and Higgins, 2002; Burger and Scheithauer, 2007; Louis *et al.*, 2007).

Diffuse and anaplastic astrocytomas lack glomeruloid vascular or endothelial proliferation and/or necrotic areas. These findings together with marked nuclear atypia are diagnostic for glioblastoma multiforme (Koestner *et al.*, 1999; Koestner and Higgins, 2002; Burger and Scheithauer, 2007; Louis *et al.*, 2007).

Oligodendrogliomas are composed of neoplastic oligodendroglial cells. In formalin-fixed paraffin wax-embedded tissue sections the cells commonly show perinuclear shrinkage artefacts in the form of clear halos and are intermingled with branching capillaries. They can occur as relatively benign tumours or as anaplastic variants (Koestner *et al.*, 1999; Koestner and Higgins, 2002; Burger and Scheithauer, 2007; Louis *et al.*, 2007).

Oligoastrocytomas are composite tumours formed of neoplastic astrocytes and oligodendrocytes. These two cell populations may be intermingled (diffuse variant) or located in separate clusters (biphasic or compact variant) (Koestner *et al.*, 1999; Louis *et al.*, 2007). In human medicine, whether or not the glioma is an astrocytoma, oligodendroglioma or

Correspondence to: S. Schöniger (e-mail: Sandra.Schoeniger@vetmed.uni-leipzig.de).

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oligoastrocytoma has prognostic and therapeutic significance (Louis *et al.*, 2007).

The most common tumours reported in the African hedgehog (*Atelerix albiventris*) are mammary gland carcinomas, lymphomas and oral squamous cell carcinomas (Raymond and Garner, 2001; Heatley *et al.*, 2005). Primary tumours of the central nervous system (CNS) appear to be rare; reported cases include astrocytomas located in the cerebellum ($n = 2$), hippocampus ($n = 1$), brainstem ($n = 4$), medulla oblongata and cervical spinal cord ($n = 1$) or spinal cord ($n = 1$) as well as a cerebral microglioma (Gibson *et al.*, 2008; Garner *et al.*, 2010; Nakata *et al.*, 2011). The present case report describes an oligoastrocytoma with extensive spread in the brain of an adult African hedgehog.

A 3.5-year-old female African hedgehog showed clinical signs of neurological disease that progressed over 6 months. Initially, manège movement (walking in circles to the right) was noted, but the hedgehog could be encouraged to walk in a straight line with assistance. Later, the animal was unable to walk without falling to the left. The animal was humanely destroyed because of the poor prognosis and submitted for necropsy examination.

The animal was in a good body condition. There was multifocal mild to moderate acute pulmonary alveolar emphysema and oedema. All other organs including the brain and spinal cord showed no significant gross changes. The brain, spinal cord, brachial plexus, sciatic nerves, skeletal muscle of the thoracic and pelvic limbs, as well as additional selected tissue samples, were fixed in 10% neutral buffered formalin and processed routinely. Microscopically, there was a widely infiltrative glioma within the white matter of the cerebellum, midbrain, thalamus, basal nuclei and both cerebral hemispheres. Neoplastic cells expanded the corpus callosum, infiltrated the cerebral cortex, extended along the white matter tracts into the hippocampus and pons, formed perivascular cuffs and spread via the cerebral leptomeninges. They integrated into and expanded the parenchyma without formation of a discrete tumour mass, although areas with a dense accumulation of tumour cells were observed. In areas with a higher tumour cell density, the parenchyma showed microvacuolation (Fig. 1).

Two distinct tumour cell populations were discerned. On the one hand, neoplastic cells had an oligodendroglial morphology with round or oval hyperchromatic nuclei surrounded by clear halos; some of these cells were clustered. On the other hand, there were tumour cells with larger, cigar-shaped or irregularly-shaped vesicular nuclei, indicating an astrocytic component (Fig. 1), of which a few were gemistocytic astrocytes; such cells were occasionally binucleate. Scattered tumour cells with nuclear features of oligodendrocytes, but an eccentrically located nucleus and a moderate amount of eosinophilic cytoplasm, were observed. These cells were consistent with minigemistocytes, which are regarded as a variant of neoplastic oligodendrocytes. There was an average of 10 mitotic figures in 10 high-power (×40 objective) fields; mitotic figures were observed in both neoplastic cell populations. A Gomori's reticulin stain revealed no basal lamina delineating the tumour cells. Intralesional blood vessels were proliferating, but did not show an endothelial or a glomeruloid vascular proliferation and no necrotic areas were observed. Additional findings were marked splenic extramedullary haemopoiesis and multifocal mild interstitial lymphoplasmacytic infiltrates within the renal parenchyma.

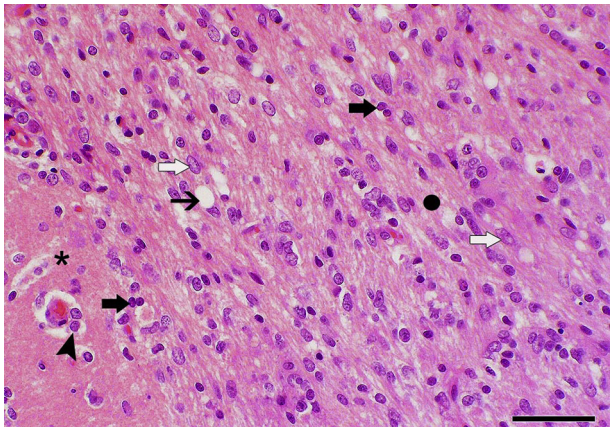

Fig. 1. Oligoastrocytoma, cerebrum. Mixed neoplastic glial cells are located predominately within the white matter (black dot), which fills the figure, except for the grey matter (lower left; asterisk) where neoplastic cells are located perivascularly (arrowhead). The white matter shows multifocal mild microvacuolation (thin black arrow). Neoplastic oligodendrocytes (thick black arrows) are intermingled with other neoplastic cells indicative of an astrocytic population (thick white arrows). HE. Bar, 50 μm.

Tumour cells were further characterized by immunohistochemistry (IHC) using a biotin–streptavidin technique (for evaluation of expression of vimentin, Nogo-A and glial fibrillary acidic protein [GFAP]) or the peroxidase–antiperoxidase method (for evaluation of Olig-2 and GFAP expression) with 3, 3′ diaminobenzidine as chromogen. Approximately 40% of the tumour cells expressed GFAP (antibody from Dako, Glostrup, Denmark, 1 in 1,000 dilution). The GFAP labelling was of varying intensity (mild, moderate or strong) with most immunolabelled cells having branching fibrillary processes (resembling fibrillary astrocytes), while a few had morphological features consistent with those of gemistocytes (Fig. 2). A similar cell population (interpreted as astrocytes) expressed