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NEOPLASTIC DISEASE

Concurrent Gliosarcoma and Choroid Plexus Carcinoma in a Cow

A. Ortloff*, J. Neumann* and O. Illanes†

** Escuela de Medicina Veterinaria, Facultad de Recursos Naturales, Núcleo de Producción Alimentaria, Laboratorio de Anatomía Patológica, Universidad Católica de Temuco, Chile and † Department of Biomedical Sciences, Ross University School of Veterinary Medicine, PO Box 334, Basseterre, St. Kitts, Saint Kitts and Nevis*

Summary

Brain tumours in cattle are uncommon and the spontaneous development of primary brain tumours of different histological types is rare in both man and animals. In man, multiple concurrent primary tumours of different types are occasionally described. We report the rare simultaneous occurrence of two different primary brain tumours, gliosarcoma and choroid plexus carcinoma, diagnosed by microscopical and immunofluorescence evaluation in an 8-year-old cow with a 2-month history of neurological disease. Gliosarcoma is a rare variant of glioblastoma multiforme, characterized by the presence of malignant glial cells and mesenchymal tissue. This tumour has not been reported previously in animals.

Keywords: choroid plexus carcinoma; cow; gliosarcoma

With the exception of the dog, primary neoplasms of the nervous system in domestic animals are relatively uncommon (Koestner and Higgins, 2002) and have been only rarely reported in cattle (Hoenerhoff *et al*., 2006). In addition, the simultaneous development of histologically different primary brain tumours is rare and in man is usually seen in patients with phacomatosis or in those undergoing cranial irradiation therapy (Tokunaga *et al*., 1991).

An 8-year-old Holstein cross cow developed slowly progressive depression, ataxia, drowsiness, teeth grinding and left head tilt over a period of 2 months. It was presented to the teaching hospital of the School of Veterinary Medicine, Universidad Católica de Temuco, Chile, where a complete neurological examination also revealed medial strabismus and lack of menace response in the left eye, decreased menace response in the right eye and partial paralysis of the left side of the face characterized by loss of motility and drooping of the left ear and loss of sensitivity of the skin of the left side of the face. Serum biochemical analysis, haematological analysis and microbiological examination of blood and cerebrospinal fluid revealed no abnormalities. Due to the poor prognosis, the cow was humanely destroyed and submitted for post-mortem examination.

Gross post-mortem findings were confined to the brain. A sagittal section of the brain near the midline revealed two moderately firm, closely apposed space-occupying lesions within the dorsal mesencephalon (Fig. 1). These masses, up to 5 cm in the largest dimension, caused effacement of the normal architecture of the midbrain, focal compression and stenosis of the mesencephalic aqueduct and moderate secondary dilation of the lateral ventricles (i.e. acquired hydrocephalus). The larger mass (later diagnosed as a choroid plexus carcinoma [CPC]) was round, relatively well demarcated and had a grey, granular cut surface containing scattered white and yellow foci of discolouration up to 3 mm in size. The smaller mass (later diagnosed as a gliosarcoma) was less defined, approximately 3 cm in the largest dimension and

Correspondence to: A. Ortloff (e-mail: aortloff@uct.cl).

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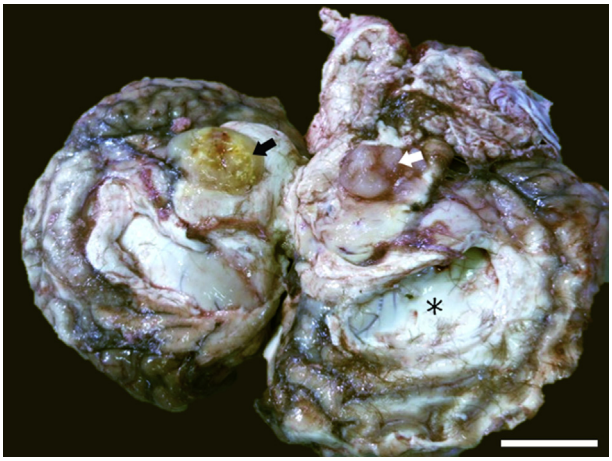

Fig. 1. Sagittal section of the brain showing two mesencephalic space-occupying lesions (arrows) causing mesencephalic aqueduct stenosis and moderate dilation of the lateral ventricles (asterisk). Note the lobulated and chondromatous appearance of the tumour (gliosarcoma) on the right (white arrow). Choroid plexus carcinoma (black arrow). HE. Bar, 5 cm.

was multilobulated, with glassy areas of chondromatous appearance and consistency.

The brain and tumour samples were fixed in 10% neutral buffered formalin, processed routinely and embedded in paraffin wax. Sections (5 μm) were stained with haematoxylin and eosin (HE) and periodic acid–Schiff (PAS) stain. Additional slides were processed for immunofluorescence labelling (Sternberger *et al.*, 1970). Primary reagents used in these procedures included antibodies specific for beta IV tubulin (Abcam, Cambridge, UK), glial fibrillary acidic protein (GFAP; Sigma, St. Louis, Missouri, USA), transthyretin (TTR; Sigma), S-100b (Abcam, Cambridge, UK) and aquaporin-1 (AQP1; Sigma). Antibodies were diluted in a buffer containing 0.1 mol/l Tris buffer, pH 7.8, 0.7% nongelling seaweed gelatin, lambda carrageenan and 0.5% Triton X-100 (Sigma). Incubation with primary reagents was carried out for 18 h at room temperature. Omission of the primary antibody during incubation served as the negative control. The normal choroid plexus and brain tissue of the same cow was used as a positive control. Secondary antibodies were conjugated with Alexa Fluor 488 or 594 (1 in 500 dilution; Invitrogen, Carlsbad, California, USA). Slides were examined under an epifluorescence microscope using Zeiss multidimensional acquisition software AxioVision Rel (version 4.6) (Zeiss, Aalen, Germany) or a confocal microscope (Leica SP5 II, Leica, Mannheim, Germany).

Microscopic evaluation of the larger midbrain tumour revealed a well-demarcated but non-encapsulated neoplasm composed of variably sized, irregularly shaped tubular structures lined by a single layer of moderately to highly anaplastic cuboidal epithelium. Intratubular polypoid and papillary projections of neoplastic epithelium supported by small amounts of fibrovascular connective tissue stroma were often seen and interpreted as consistent with choroid plexus origin. Due to the significant degree of anaplasia of the neoplastic cells, evidenced by marked anisokaryosis, anisocytosis, karyomegaly and the presence of a few multinucleated tumour cells, this neoplasm was diagnosed as a CPC. Immunofluorescence examination revealed that most of the neoplastic cells were positive for beta IV tubulin, especially within the apical cytoplasm (Fig. 2). The beta IV tubulin antibody is a good marker of multiciliated cells (Guerra *et al.*, 2015) and is the major beta-isotype in motile and non-motile bovine cilia (Renthal *et al.*, 1993). Ultrastructural cilia have been observed in human choroid plexus tumours, but have not been previously reported in animal tumours of choroid plexus origin. The CPC from this cow did not express S100b protein, AQP1 and TTR. Data from studies of AQP1 (Boassa *et al.*, 2006) and TTR (Herbert *et al.*, 1986) suggest that both proteins are important in the production of cerebrospinal fluid; therefore, they can be used as indicators of normal choroid plexus functionality. It is likely that the lack of expression of AQP1 and TTR within the tumour cells of the CPC of this cow was due to the significant degree of anaplasia and dedifferentiation. Similar results have been observed in CPC of dogs (Cantile *et al.*, 2002). Tumour cells in this neoplasm stained positively with PAS, which is considered a reliable and

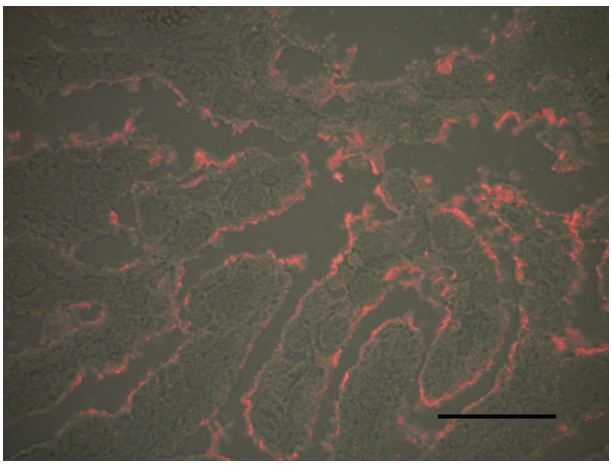

Fig. 2. Positive immunofluorescence labelling of beta IV tubulin throughout the apical surface of neoplastic epithelial cells lining papillary projections supported by fibrovascular stroma. Choroid plexus carcinoma. HE. Bar, 100 μm.

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