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NEOPLASTIC DISEASE

Pituitary Null Cell Adenoma in a Domestic Llama (*Lama glama*)

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Summary

Pituitary gland neoplasia has been reported rarely in camelids. A 12-year-old neutered male llama (*Lama glama*) presented with lethargy, inappetence and neurological signs. On physical examination, the llama was mentally dull and exhibited compulsive pacing and circling to the left. Complete blood count and serum biochemistry revealed haemoconcentration, mild hypophosphataemia, hyperglycaemia, hypercreatininaemia and hyperalbuminaemia. Humane destruction was elected due to rapid clinical deterioration and poor prognosis. Post-mortem examination revealed a pituitary macroadenoma and bilateral internal hydrocephalus. Microscopically, the pituitary tumour was composed of neoplastic chromophobic pituitary cells. Ultrastructural studies revealed similar neoplastic cells to those previously described in human null cell adenomas. Immunohistochemically, the neoplastic cells were strongly immunoreactive for neuroendocrine markers (synaptophysin and chromogranin A), but did not exhibit immunoreactivity for epithelial, mesenchymal, neuronal and all major pituitary hormone markers (adrenocorticotropic hormone, follicle stimulating hormone, growth hormone, luteinizing hormone, melanocyte-stimulating hormone, prolactin and thyroid stimulating hormone), consistent with the diagnosis of a pituitary null cell adenoma. This is the first report of pituitary neoplasia in a llama.

Keywords: camelid; llama; null cell adenoma; pituitary gland

Neoplastic diseases are relatively common in camelids (Valentine and Martin, 2007); however, pituitary neoplasia has been reported rarely (Gilsenan *et al.*, 2012). In contrast, primary pituitary neoplasia is well documented in several other animal species, in particular, dogs, horses and cats (Capen, 2002), budgerigars (Langohr *et al.*, 2012) and rats (Percy and Barthold, 2007). Adenomas of the adenohypophysis are the most prevalent pituitary tumours in animals. Adenohypophyseal pituitary adenomas are a heterogeneous group of tumours for which subclassification is based on the hormone(s) produced and/or secreted by the constituent neoplastic cells (Kiupel *et al.*, 2008). Null cell adenomas of the adenohypophysis are non-functional tumours composed of chromophobic cells that lack immunoreactivity for any of the major pituitary hormones (Kiupel *et al.*, 2008). Because complete immunohistochemical and ultrastructural characterization of non-functional pituitary adenomas is lacking in many reports, the true prevalence of null cell adenomas in animals is difficult to determine. Comparatively, human null cell pituitary adenomas are fairly well characterized and comprise a significant portion of pituitary macroadenomas (Lloyd *et al.*, 2009). To our knowledge, the current case represents the first report of pituitary adenoma in a llama. Comprehensive clinical, morphological, ultrastructural and immunohistochemical characterization of the tumour allowed subclassification as a null cell pituitary adenoma.

A 12-year-old, 146 kg, neutered male llama (*Lama glama*) was presented for assessment of acute onset neurological signs. The llama was reportedly lethargic for 13 days prior to presentation. The

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evening prior to presentation, the llama paced constantly to the left and was unable to lie down. Muscle fasciculations and a left-sided full-body lean were noted. Treatment with ivermectin, fenbendazole and flunixin meglumine yielded no improvement. The llama resided in a herd of 12 other camelids with no in-contacts affected.

The llama was referred to the University of Minnesota Large Animal Hospital. On physical examination, the llama was mentally dull, but responsive to stimulation. Vital parameters were within normal limits; however, the llama was estimated to be 5% dehydrated. The llama exhibited intermittent compulsive circling and a full-body lean, both to the left. The head and neck were often held towards the left side; however, there was no notable head tilt. Cranial nerve reflexes were present and normal. Gait analysis revealed a wide-based stance in all limbs, with asymmetrical hypermetria of the hindlimbs. Placing reactions appeared to be normal and limited spinal reflexes were considered normal. With these neurological deficits a forebrain lesion was suspected.

Complete blood count (CBC), serum biochemistry and free-catch urine sample were assessed. Serum hormone concentrations were not evaluated and endocrine functional tests were not performed. The CBC revealed a mildly elevated packed cell volume (42%; reference range 27–40%); white blood cell counts and fibrinogen were within the normal ranges. The serum biochemistry panel showed hypercreatininaemia (248 μmol/l; reference range 115–221 μmol/l), hypophosphataemia (1.10 mmol/l; reference range 1.58–2.52 mmol/l), hyperalbuminaemia (39 g/l; reference range 25–38 g/l), hypokalaemia (3.6 mmol/l; 4.0–5.1 mmol/l) and elevated muscle-related enzymes (creatine kinase [CK]: 11,739 U/l; reference range 30–334 and aspartate transaminase [AST]: 864 U/l; reference range 117–225 U/l). Hyperglycaemia was also present (14.32 mmol/l; reference range 5.66–12.10 mmol/l). The urine specific gravity (USG) was appropriately concentrated at 1.047 and a urine dipstick analysis was unremarkable. The elevated PCV, creatinine and albumin were attributed to the dehydration. The hypokalaemia and hypophosphataemia were likely due to reduced food intake. The elevated CK and AST were attributed to the compulsive walking and transportation to the hospital. The mild hyperglycaemia was likely secondary to stress and/or concurrent disease.

Based on the history, physical examination and laboratory results a space-occupying lesion (e.g. neoplasia, abscessation or granuloma), encephalitis (viral [e.g. rabies, equine viral encephalitides or West Nile virus] or bacterial), polioencephalomalacia and parasitic migration (e.g. *Parelaphostrongylus tenuis*) were the main differential diagnoses. Treatment for a presumptive intracranial abscess (ceftiofur, 2.2 mg/kg intravenously q12h) and parasitic migration (fenbendazole, 50 mg/kg per os q24h) were administered. A constant rate infusion of crystalloid fluids was given to correct the dehydration, to provide maintenance fluid requirements and to correct the hypokalaemia (4 mg/kg/h intravenously, with KCl 20 mEq/l supplementation). Thiamine hydrochloride (10 mg/kg subcutaneously q12h) was administered to help treat or prevent possible polioencephalomalacia. Free-radical scavenging medication (dimethyl sulphoxide, 1 g/kg intravenously q12h) was given in an attempt to reduce further neuronal damage.

The llama continued intermittently to walk compulsively while hospitalized. A fever developed, so non-steroidal anti-inflammatory medication (flunixin meglumine, 1.1 mg/kg intravenously q24h) was given. After 16 h of therapy, the llama experienced two grand-mal seizures, which were temporarily abated with anticonvulsant therapy (diazepam, 0.1 mg/kg intravenously). Between and following the seizures, the llama was unresponsive with fixed, dilated pupils. Hypertonic saline administration (4 ml/kg intravenously) did not improve the neurological status of the llama. Given the poor prognosis, the llama was humanely destroyed and subsequently submitted to the University of Minnesota Veterinary Diagnostic Laboratory for necropsy examination.

The most significant post-mortem finding was a well-demarcated, 3.5 × 3.0 × 1.2 cm, roughly spherical, beige and dark red mottled, soft to friable mass markedly expanding and partially replacing the

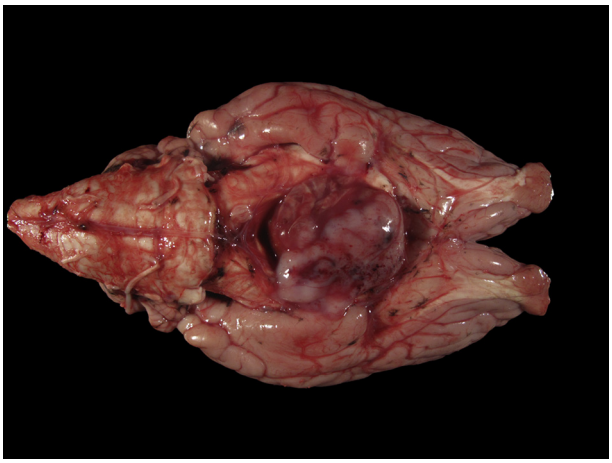

Fig. 1. Ventral brain showing marked expansion of the pituitary gland by a spherical, beige and dark red mottled, neoplastic mass.

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