CASE REPORT
Central diabetes insipidus in a cat with central nervous system B cell lymphoma

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A 6-year-old male neutered cat presented with blindness, lethargy, polydipsia, hyposthenuria and severe hypernatraemia. Central diabetes insipidus was demonstrated by means of a low measured anti-diuretic hormone (ADH) concentration in the face of hypernatraemia, and clinical response to supplementation with desmopressin. Magnetic resonance imaging of the brain showed a discrete mass in the region of the hypothalamus. The cat was euthanased and post-mortem histological examination demonstrated B cell lymphoma involving the brain, optic nerves, urinary bladder wall and diaphragm. To the authors’ knowledge, this case report is the first to describe central diabetes insipidus caused by central nervous system lymphoma in the cat.

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### Table 1. Results of pathology tests.

| Haematology                                      | Result | Reference range | Biochemistry | Result | Reference interval |
|--------------------------------------------------|--------|-----------------|--------------|--------|-------------------|
| Haemoglobin (g/dl)                               | 13.0   | 10.0—15.0       | Sodium       | 178    | 150—165           |
| Packed cell volume (PCV) (l/l)                   | 0.41   | 0.30—0.45       | Potassium    | 4.7    | 3.5—5.8           |
| Red cell count (× 10¹²/l)                        | 7.7    | 5.0—10.0        | Chloride     | 141    | 112—129           |
| Mean cell volume (MCV) (PCV/RCC) (fl)            | 58     | 37—49           | Calcium      | 3.14   | 1.75—2.50         |
| Mean corpuscular haemoglobin (MCH) (Hb/RCC) (pg)| 17     | 13—17           | Phosphate    | 2.4    | 1.3—2.3           |
| White cell count (× 10⁹/l)                       | 2.50   | 5.5—19.5        | Urea         | 13.6   | 5.4—10.7          |
| Bands (× 10⁹/l)                                  | 0.15   | 0—0.13          | Creatinine   | 0.28   | 0.07—0.16         |
| Neutrophils (× 10⁹/l)                            | 2.23   | 2.5—12.5        | Glucose      | 2.8    | 3.9—7.5           |
| Lymphocytes (× 10⁹/l)                            | 0.10   | 1.5—7.0         | Cholesterol  | 4.7    | 1.9—3.9           |
| Monocytes (× 10⁹/l)                              | 0.02   | 0—0.9           | Total bilirubin | 2     | 0—15              |
| Eosinophils (× 10⁹/l)                            | 0.02   | 0—1.5           | ALT          | 115    | 5—80              |
| Basophils (× 10⁹/l)                              | Rare   | ALP             | CK           | 2603   | 50—400            |
| Platelets (× 10⁹/l)                              | Adequate 300—700 | Total protein | 83     | 56—80            |
| Reticulocytes (/100 RBC)                         | 0—0.4 | Albumin         | 39           | 22—35  |                   |

| Endocrinology                                    | Result | Reference | Serology                                      | Result |
|--------------------------------------------------|--------|-----------|-----------------------------------------------|--------|
| Basal cortisol* (nmol/l)                         | <27    | 28—120    | FIV antibody*a                                 | Negative |
| Cortisol 30 min post ACTH*                       | 120    | <200      | FeLV antigen*b                                 | Negative |
| Cortisol 60 min post ACTH*                       | 120    | <200      | Toxoplasma IgG IFAT**                          | 1:128  |
| Endogenous ACTH† (pg/ml)                         | 23     | 20—40     | Toxoplasma IgM IFAT**                          |        |
| Total thyroxine† (nmol/l)                        | 15     | 20—45     | Coronavirus IFAT†                               | <1:10  |
| Free T₄ (MED)† (pmol/l)                          | 16.1   | 15.0—48.0 |                                               |        |
| Thyroid stimulating hormone (TSH)‡ (ng/ml)       | 0.03   | 0.03—0.15 |                                               |        |
| Anti-diuretic hormone (ADH)§ (pmol/l)            | 0.1    | See text  |                                               |        |

| Time post admission                               | 0 h    | 8 h      | 12 h   | 18 h   | 26 h   | 30 h   | 34 h   | 40 h   |
|--------------------------------------------------|--------|---------|--------|--------|--------|--------|--------|--------|
| Sodium                                           | 178    | 182     | 185    | 182    | 171    | 169    | 172    | 166    |
| Chloride                                         | 141    | 147     | 149    | 146    | 131    | 132    | 135    | 128    |
| Urine specific gravity (USG)                      | 1.005  | 1.003   | —      | 1.005  | 1.010  | —      | 1.012  | 1.014  |

ACTH = adrenocorticotropic hormone, ALT = alanine aminotransferase, ALP = alkaline phosphatase, CK = creatine kinase.

*Solid phase chemiluminescent competitive immunoassay on Immulite, Siemens Healthcare, Gwynedd, UK.
†ACTH DA Kit, MP Biomedicals, Solon, OH.
‡Solid phase chemiluminescent, competitive immunoassay on Immulite, Siemens Healthcare, Gwynedd, UK.
§Nichols method of equilibrium dialysis, Idexx laboratories, Brisbane, QLD, using radioimmunoassay, Antech, Irvine, CA.
¶Chemiluminescent competitive immunoassay on Immulite, Siemens Healthcare, Gwynedd, UK.
∥Double antibody radioimmunoassay, Buhlmann, Schonenbuch, Switzerland.
*SensPERT FeLV Ag/FIV Ab test kit, VetAll, Kyunggi-Do, Korea.
**Immunofluorescent antibody test, Mt Pleasant laboratory, Launceston, TAS, using Anti-Feline fluorescent conjugate, Kirk Garden Perry, Gaithersburg, MD.
††Feline infectious peritonitis virus immunofluorescent antibody kit, Fuller, Fullerton, CA.
pure water loss include primary hypodipsia/adipsia, lack of access to water, fever, burns, panting, secondary nephrogenic diabetes insipidus (NDI), central diabetes insipidus (CDI), or primary NDI (rare). Of these differentials, only diabetes insipidus would account for hypernatraemia and hyposthenuria.

Intravenous fluid therapy was commenced at 5 ml/kg/h. The fluid type initially chosen was lactated Ringer’s solution (LRS) with 2.5% dextrose supplemented with additional NaCl to produce a sodium concentration of 160 mmol/l. This was undertaken with the aim of decreasing the serum sodium concentration at a rate no faster than 0.5 mEq/l/h. Electrolytes were rechecked repeatedly during this infusion (see Table 1). After the first 2 h, the sodium concentration increased to 182 mmol/l, and oscillated between 182 and 185 mmol/l throughout the first 24 h of treatment. For this reason the sodium concentration of the intravenous fluid was serially decreased. The cat remained clinically the same throughout this phase of the treatment.

Blood was submitted for anti-diuretic hormone (ADH) assay. The serum sodium of the same sample was 185 mmol/l. The ADH concentration of this sample was 1.0 pmol/l. Although no published reference interval is available for the cat, one study demonstrated a mean ADH value in water restricted cats of 78 pmol/l. Accordingly, the result in this case was inappropriate in the face of hypernatraemia and supported a diagnosis of CDI.

Exogenous desmopressin was administered (Minirin solution; Ferring AB, Sweden) one drop (1.5–4 mg) in the conjunctival sac. Two hours later sodium was 171 mmol/l and the urine specific gravity (USG) of a free-catch urine sample was 1.010. Although the rate of decrease in sodium concentration was undesirably rapid, there was no clinical deterioration immediately or over the subsequent 24 h. The sodium concentration 6 h after vasopressin administration was 169 mmol/l, with a USG of 1.012, and 12 h after administration the sodium was 166 mmol/l. The same dose of vasopressin was subsequently administered twice daily, and the sodium concentration remained between 157 and 165 mmol/l over the subsequent 24 h.

At the same time as desmopressin was commenced a single dose of dexamethasone sodium phosphate 0.1 mg/kg was given by intravenous injection. The cat’s vision returned, there was a partial return of the pupillary light responses, its demeanour improved, and it began to eat voluntarily.

Magnetic resonance imaging (MRI) of the brain was performed on the following day (Fig 1). This showed a rounded mass lesion, approximately 10.5 mm diameter, ventral to the thalamus, rostro-dorsal to and apparently continuous with the pituitary gland. The mass was causing dorsal displacement of the thalamus; on the sagittal plane there was caudodorsal displacement of the interthalamic adhesion. Differentials considered were neoplasia, particularly meningioma or pituitary macroadenoma, or granuloma.

Based on the MRI findings, and despite the clinical improvement, the owners elected to have the cat euthanased and consented for necropsy. At necropsy, grossly there was a round mass bulging from the base of the brain at the level of the optic chiasm (Fig 2).

Other pertinent gross findings were that the adrenal cortices were thinned with a cortical to medullary ratio of 1:4, and there were depressions in the surface of both kidneys, with loss of parenchyma and replacement with fibrous tissue.

The tissues were fixed in neutral buffered 10% formalin and embedded in paraffin, followed by routine sectioning and staining with haematoxylin and eosin (HE). Histologically, there was a fairly well...
Histologically intact. There was marked Wallerian degeneration of the optic tracts. Neoplastic lymphocytes were also detected in the diaphragm, urinary bladder wall and around the optic nerves, just caudal to the eyes. There was no histological evidence of toxoplastic chorioretinitis and histological changes within the eyes were minimal, showing only small areas of cataract formation.

The mechanisms that regulate thirst and ADH regulation in the mammalian brain have been reported in detail. Increased serum osmolarity triggers both thirst and ADH release in the normal animal. Sodium is the main determinant of osmolarity, and so hypernatraemia results in an increased cerebrospinal fluid osmolarity, and this is detected by a series of so-called circumventricular organs. These organs, located in the anterior wall of the third ventricle, are the organum vasculosum of the lamina terminalis (OVLT) and the SFO. The median preoptic nucleus (MnPO) is also involved in thirst detection, and is located inside the blood-brain barrier, but is not considered part of the circumventricular organ system. In rodent models, experiments have demonstrated connections between these organs and thirst centres elsewhere in the brain.

ADH is produced by the SON and PVN in the hypothalamus, from where it is transmitted to, and subsequently released from, the posterior pituitary. The SON and PVN are osmoreceptive, and hyperosmolarity directly stimulates ADH production. Additionally, the SON and PVN receive input from the circumventricular organs described above.

In summary, hypernatraemia results in two distinct but interrelated processes: the stimulation of thirst, and the release of ADH. In the normal animal, these responses occur simultaneously, but it is possible to experimentally decouple these processes, and cause a selective incapacity of either thirst or ADH production.

In this cat, severe hypernatraemia resulted in compulsive thirst, but not increased serum ADH concentrations. A lesion that destroyed the organs of ADH production, but preserved the mechanism of thirst, would be consistent with these observations. The identified tumour had obliterated the region containing the PVN and SON, as well as the ventral circumventricular region, but had preserved the more dorsal circumventricular region. It was hypothesised that part or all of the SFO or MnPO may have been spared, which would be sufficient to preserve the thirst response, a hypothesis supported by the finding of an histologically intact SFO. The MnPO could not be confidently identified histologically, which is unsurprising, as it is normally not a histologically distinctive structure.

A previous published report of CNS lymphoma in a cat described severe hypernatraemia with a concurrent lack of thirst. That case is probably best described as hypodipsic hyponatraemia (HH), which may or may not have had concurrent CDI as well. ADH was not tested, nor any supplementary ADH administered in that case. In order for thirst to be lacking in that case, we hypothesise that the OVLT, MnPO and SFO were damaged by that tumour.

Histologically, the optic chiasm, tuber cinereum, infundibulum (pituitary stalk) and ventral hypothalamus [including supraoptic nuclei (SON) and paraventricular nuclei (PVN)] were effaced by the tumour. The pars distalis remained, although was poorly demarcated from the neoplasm. The dorsal third of the hypothalamus was predominantly intact, while containing moderate numbers of large, white matter vacuoles. The subfornical organ (SFO) remained histologically intact. There was marked Wallerian degeneration of the optic tracts. Neoplastic lymphocytes were also detected in the diaphragm, urinary bladder wall and around the optic nerves, just caudal to the eyes. There was no histological evidence of toxoplastic chorioretinitis and histological changes within the eyes were minimal, showing only small areas of cataract formation.

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**Fig 3.** Hypothalamus of a 6-year-old neutered male domestic short hair cat with CDI: the infiltrative neoplasm is causing lateral deviation of the third ventricle. The small inset at the upper right shows a higher magnification of the neoplastic B cells (HE).
To the authors’ knowledge this is the first reported case of CDI caused by intracranial neoplasia in a cat. CDI has been associated with B cell lymphoma in a dog,7 and has also been described in several case series and reports in cats.8–15 The underlying cause of CDI in the feline cases has been reported as congenital,10,14 traumatic14,15 or idiopathic.9

The position of the lesion raised the possibility that other aspects of hypothalamopituitary function could be impaired. The results of an adrenocorticotropin hormone (ACTH) stimulation test, endogenous ACTH, thyroxine, and thyroid stimulating hormone (TSH) assessments were not supportive of this possibility. The testing of other hormones, including growth hormone and IGF-1 could also be considered in such a case but were not taken in this instance due to time, financial and sample handling constraints.

The blindness in this cat was likely due to direct injury to the optic chiasm and adjacent optic tracts. The retinal changes observed initially were consistent with toxoplasmal chorioretinitis, but that is not likely to have been the main cause of blindness in this patient. This is supported by the lack of a definitive improvement from medical management of toxoplasmosis with clindamycin, and a lack of supportive histological changes.

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