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Abstract

Case summary A 9-month-old intact female domestic mediumhair cat presented with a 5-month history of obtundation, lethargy, hypernatremia (181 mmol/l; reference interval [RI] 151–158 mmol/l), hyperchloremia (142 mmol/l; RI 117–126 mmol/l), azotemia (blood urea nitrogen 51 mg/dl; RI 18–33 mg/dl), creatinine 3.0 mg/dl (RI 1.1–2.2 mg/dl), hyperphosphatemia (8.3 mg/dl; RI 3.2–6.3 mg/dl) and total hypercalcemia (11.4 mg/dl; RI 9–10.9 mg/dl), with concurrent polyuria with adipsia. Neurologic evaluation revealed proprioceptive deficits, and this finding paired with a history of focal seizure-like activity despite improving sodium concentrations suggested a cerebrothalamic lesion. For this reason, and historical and biochemical findings consistent with adipsic diabetes insipidus (DI), MRI of the brain was performed, which revealed a lesion of the hypophyseal fossa consistent with a pituitary cyst. Given the patient's age and the timeline of clinical signs, a congenital pituitary cyst was strongly suspected. The patient was managed initially with intravenous fluids to correct the hypernatremia, then managed for more than 4 years with topical ocular desmopressin acetate administration and free water administered through a feeding tube. This cat's clinical diagnosis included a congenital pituitary cyst with subsequent central DI and primary adipsia.

Relevance and novel information The clinical presentations of primary adipsia or central DI are both rare in cats. This is the first report to describe these conditions occurring in a cat owing to a congenital pituitary cyst and describes successful long-term management of this condition.

Keywords: Feline congenital abnormality; polyuria; feline endocrinopathy; pituitary tumor; electrolyte abnormality

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Introduction

Diabetes insipidus (DI) is characterized by absent secretion or diminished response to antidiuretic hormone (ADH). ADH binding to renal tubular cell V2 receptors promotes renal water resorption, while its binding to V1 blood vessel receptors stimulates vasoconstriction to promote renal reabsorption of water and maintain blood volume and pressure.¹ Two broad categories of DI are described: central and nephrogenic. Central DI (CDI) is caused by decreased or absent production of ADH from the magnocellular neurons of the hypothalamic supra-optic and paraventricular nuclei.¹ In contrast, in nephrogenic DI, ADH secretion is appropriate, but the distal and collecting tubule response to ADH is diminished.¹

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DI typically manifests clinically as polyuria and polydipsia, which is the result of the kidney's inability to conserve water appropriately. Free water loss results in hyposthenuric or isosthenuric urine, while the resultant hyperosmolar state induces polydipsia.¹

Identifiable causes of CDI in cats are due to perturbation or disruption of normal anatomy of the hypothalamus and/or pituitary gland and include head trauma, neoplasia, ischemic damage, and hypothalamic or pituitary malformations.²⁻⁶ Idiopathic CDI has also been reported in the cat.^{7,8} Additionally, non-structural causes of CDI that have been reported in other species include genetic mutations and hypoxic damage.^{9,10} Factors such as the location damaged and size of the area affected influence whether the resulting DI is transient or permanent and, if transient, the time frame, duration and severity of clinical signs.¹ Studies in humans and veterinary species report that pituitary lesions are much more common than previously thought.^{1,11,12} One study observed a prevalence of pituitary lesions in 15.3% of cats sampled at routine necropsies, with no clinical signs of pituitary disease identified.¹² Cystic changes were the most common lesions, existing in 12.3% of cats. Despite this prevalence, the literature suggests that the majority of these pituitary lesions are incidental findings.¹² Although there are various identifiable etiologies for the development of CDI, idiopathic CDI is still the most common, with an unidentified autoimmune etiology suggested as the actual underlying cause. However, this assertion has not been tested or documented formally.¹³

Less commonly in CDI patients, polyuria may exist with hypodipsia or adipsia owing to disease of the osmoreceptors in prosencephalon and corpus callosum. A case of hypodipsic hyponatremia was reported in a 7-month-old cat in association with hypopituitarism and hydrocephalus. Hypothalamic dysfunction, possibly related to the hydrocephalus, was suggested to have induced both hypodipsia and transient hypopituitarism.¹⁴ Cases of cats with concurrent hypodipsia and DI due to structural brain lesions such as a neuroendocrine pituitary macroadenoma, holoprosencephaly and hydrocephaly have been reported.¹⁴⁻¹⁷ Similarly, reports in human medicine describe cases of hypodipsia with DI owing to structural brain diseases such as holoprosencephaly, cranial trauma, trauma secondary to intracranial surgery, pituitary adenoma, astrocytoma, hypothalamic hamartoma, craniopharyngioma and neurosarcoïdosis.¹⁸⁻²³

This report describes the diagnosis and medical management of an adipsic cat diagnosed with DI secondary to a congenital pituitary cyst, which has never been described in the literature.

Case description

A 9-month-old intact female domestic mediumhair cat presented to the University of California–Davis William

R Pritchard Veterinary Medical Teaching Hospital with a lifelong history of polyuria and adipsia and a 5-month history of intermittent obtundation, lethargy and pelvic limb ataxia. The cat was examined by the referring veterinarian 5 months prior to presentation due to obtundation and lethargy, and severe hypernatremia (>180 mmol/l; reference interval [RI] 150–165 mmol/l) was recorded. The cat was initially treated with subcutaneous fluids and then hydration was maintained by administering water orally by syringe. The cat was adopted as a kitten and was an indoor-only cat. It had no history of trauma.

On initial presentation to the authors, the cat appeared to be adequately hydrated but lethargic, with a body condition score of 4/9 and mild pelvic limb ataxia. The cat was generally unthrifty, with a greasy haircoat, generalized scaling and small stature, with proportional dwarfism. It displayed anisocoria, with the left pupil smaller than the right, and it had a grade I/VI parasternal systolic murmur. A paroxysmal episode of diffuse muscle twitching, involuntary urination, ataxia and compulsive circling was witnessed.

Laboratory abnormalities at presentation included hypernatremia (sodium 181 mmol/l; RI 151–158 mmol/l), hypernatremia (chloride 142 mmol/l; RI 117–126 mmol/l), azotemia (blood urea nitrogen [BUN] 51 mg/dl; RI 18–33 mg/dl), creatinine 3.0 mg/dl (RI 1.1–2.2 mg/dl), hyperphosphatemia (phosphorous 8.3 mg/dl; RI 3.2–6.3 mg/dl) and hypercalcemia (total calcium 11.4 mg/dl; RI 9–10.9 mg/dl). Potassium concentration was 4.6 mmol/l (RI 3.6–4.9 mmol/l) and glucose was 101 mg/dl (RI 63–118 mg/dl). The cat's serum osmolarity was calculated using the formula $(2[\text{Na}^+] + \text{glucose} [\text{mg/dl}]/18 + \text{BUN} [\text{mg/dl}]/2.8)^{24}$ and determined to be markedly elevated at 385.8 mOsm/l (reference value <330 mOsm/l). A urinalysis was performed revealing a urine specific gravity of 1.011, with no other abnormalities noted. An abdominal ultrasound was unremarkable.

Urine concentrations of sodium, potassium and chloride were 27 mmol/l, 38.4 mmol/l and <20 mmol/l, respectively. Urinary percent free water excretion was calculated with the following formula and resulted in a positive number, indicating free water excretion:²⁵

$$\text{Urinary free water excretion (\%)} = 100 * \left(1 - \frac{\left(\frac{[\text{urinary sodium}] + [\text{urinary potassium}]}{[\text{serum sodium}]} \right)}{\right)$$

The urinary free water excretion (%) at this time was positive at 64%, indicating a deficiency in, or diminished response to, ADH. Therefore, DI was diagnosed based on inappropriate positive free water excretion in the face of hypernatremia.

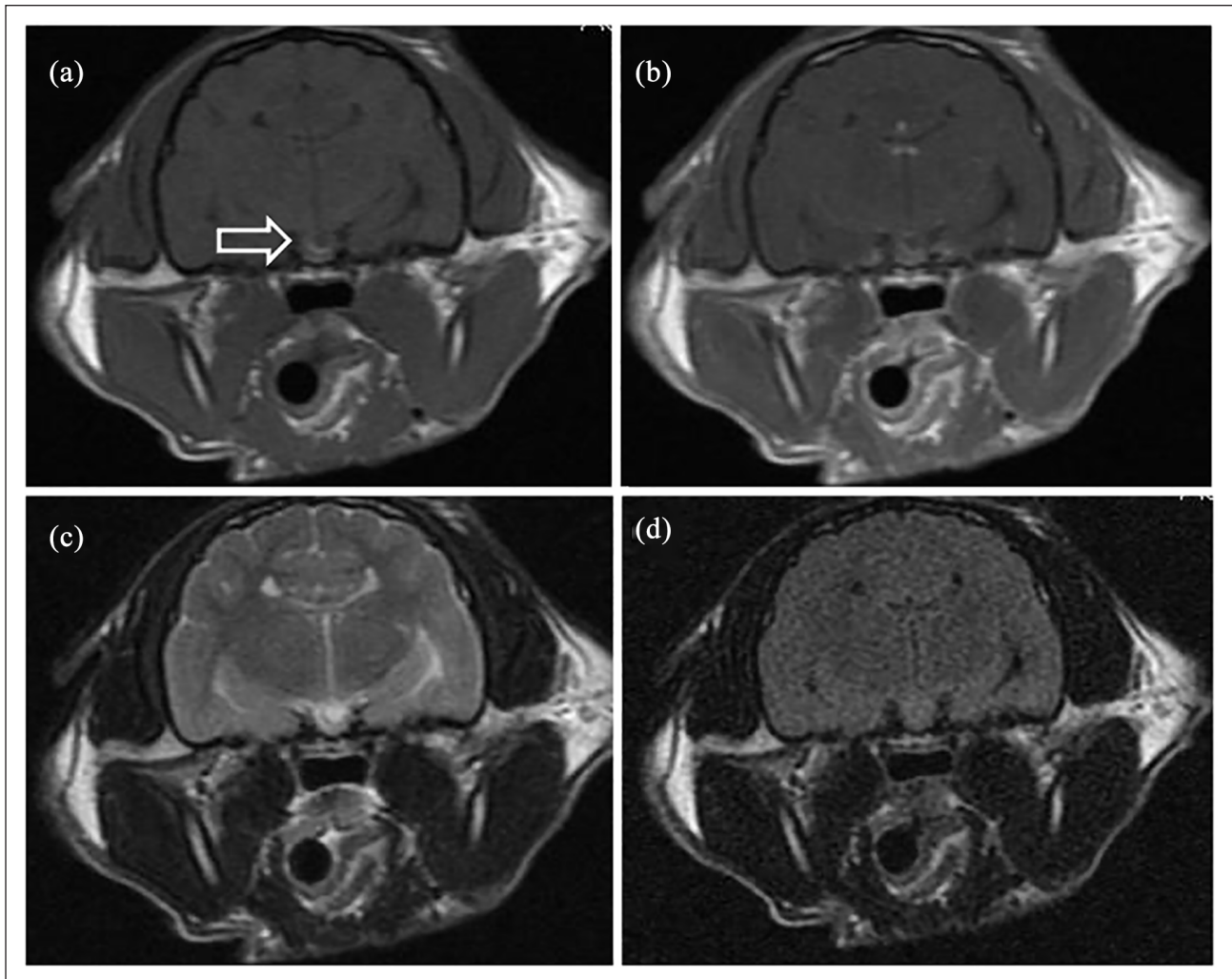


Figure 1 (a) T1-weighted, (b) T1-weighted post-contrast, (c) T2-weighted and (d) T2 fluid-attenuated inversion recovery axial MRI images. The arrow (a) indicates the location of a T1 hypointense, T2 hyperintense 1 mm × 2 mm structure within the hypophyseal fossa that is consistent with a pituitary cyst. A T1 hyperintense, T2 hyperintense crescent structure is noted in the caudal aspect of the fossa, consistent with the region of the posterior pituitary gland

Neurologic examination revealed left thoracic limb conscious proprioceptive deficits, and bilaterally weak pelvic limb crossed extensor reflexes. These neurologic findings, along with the above-described episode consistent with a focal seizure, were suggestive of a cerebrothalamic lesion. Brain MRI was recommended for further evaluation. Brain MRI (General Electric, 1.5 tesla) revealed a 1 mm × 2 mm T2 hyperintense, T1 hypointense peripherally enhancing structure of the craniodorsal aspect of the hypophyseal fossa consistent with a pituitary cyst (Figure 1). A T1 hyperintense, T2 hyperintense crescent-shaped structure lined the caudal aspect of the hypophyseal fossa and was interpreted to be the region of the posterior pituitary gland with neurohypophyseal granules. There was also an absent septum pellucidum, suspected to be congenital.

The cat was diagnosed with CDI and primary adipsia as a consequence of a pituitary cyst with resultant severe hypernatremia. Given the clinical signs were present throughout life, this was suspected to be congenital.

At the time of hospitalization and 2 days after initial presentation, electrolytes were rechecked, and severe progressive hypernatremia was noted (sodium 201 mmol/l). The cat was treated with intravenous (IV) 5% dextrose in water (9 ml/kg/h) and lactated Ringer's solution (1.8 ml/kg/h). As the cat displayed signs of severe hypernatremia, including decreased mentation and possible focal seizure activity, the goal was to reduce the serum sodium concentration by no more than 1 mmol/l/h to achieve the levels measured 2 days prior. This was followed by a slow decrease of 0.5 mmol/l/h until the sodium concentration normalized. Electrolytes were assessed every 4–6 h, and a

gradual decrease in sodium was observed over 96h to 161mmol/l. On day 4 of hospitalization, the cat was noted to be persistently markedly polyuric, so treatment with 0.01% desmopressin acetate (DDAVP; Ferring Pharmaceuticals) was initiated (1 drop into the conjunctival sac of both eyes q12h). The observed polyuria improved, and the cat was weaned off of IV fluid therapy when serum sodium concentration remained stable at 157mmol/l. Recheck of serum (sodium 162mmol/l, potassium 5.4mmol/l, chloride 128mmol/l) and urine (sodium 177mmol/l, potassium 91mmol/l, chloride 188mmol/l) electrolytes on day 5 of hospitalization was performed, and the calculated urine percent free water excretion which was negative at -65%. Recheck of urine specific gravity was 1.028. This indicated improved ADH action on the kidney with the addition of desmopressin acetate therapy, further supporting the preliminary diagnosis of CDI.

For long-term management, an esophageal feeding tube was placed for home administration of free water. The cat was discharged to the owners with instructions to administer 80–90ml/kg/day of free water through the feeding tube and desmopressin acetate 1 drop into each eye q12h. Recheck examination at 1 month post-hospitalization showed that the cat was clinically well with a resolution of all neurologic signs. At the time of writing, 4 years post-diagnosis, the cat is clinically well and still maintained on free water through a feeding tube (transitioned to a gastrostomy tube 2 years into treatment) and desmopressin acetate q12h. No further episodes of severe hypernatremia have been noted. At 3.5 years into treatment, free water intake was reduced by 10% due to persistent mild hyponatremia (146mmol/l), which resolved (sodium 152mmol/l).

Discussion

This case report describes a cat diagnosed with a congenital pituitary cyst with subsequent adipsia and CDI that presented for severe hypernatremia. This case highlights a rare congenital condition that resulted in a constellation of clinical signs stemming from severe hypernatremia and its subsequent successful management with free water administration by a permanent feeding tube and desmopressin acetate therapy.

Hypodipsia or adipsia is a rare disorder that has been sporadically described in cats as a result of head trauma, hydrocephalus, holoprosencephaly or intracranial neoplasia.^{14,16,17,26–29} In the case presented here, CDI was also diagnosed. Adipsic CDI results from damage to or destruction of areas in the brain responsible for thirst perception, water-seeking behavior, osmoregulation and ADH secretion, such as the organum vasculosum of the lamina terminalis and subfornical organ.²⁹ If their disease is severe enough, patients may present with signs

characteristic of hypernatremia such as obtundation, vomiting and lethargy.³⁰ In this case, the patient presented with neurologic signs that were suspected to be secondary to severe hypernatremia. Severe hypernatremia and hyperosmolar states can result in encephalopathy with a range of central nervous signs, including paroxysmal episodes and anisocoria as observed in this case.^{31,32}

Pituitary cystic lesions, such as Rathke's cleft cyst, are encountered incidentally in up to 20% of humans during routine autopsies, and rarely cause clinical signs,³³ but are infrequently reported in dogs and cats.³⁴ Clinical syndromes associated with these malformations include dwarfism and aggressive behavior in dogs, and syndrome of inappropriate ADH secretion in one cat.^{35–38} This is the first report of a pituitary cyst resulting in adipsic CDI in the veterinary literature.

Therapy of adipsic CDI requires administration of free water, in this case initially through IV fluids then long term through a feeding tube, and CDI management with desmopressin acetate.²⁶ Prognosis of people and dogs with adipsic hypernatremia is good with appropriate therapy, and in this case, the cat is clinically well 4 years post-diagnosis.^{29,34}

Conclusions

This report describes the successful long-term management of a cat with adipsic CDI owing to a pituitary cyst and severe secondary hypernatremia, which has never been reported in the literature. While management can be challenging and costly with this constellation of clinical signs, the prognosis is good, so prompt diagnosis and treatment should be recommended.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval This work involved the use of non-experimental animals only (including owned or unowned animals and data from prospective or retrospective studies). Established internationally recognised high standards ('best practice') of individual veterinary clinical patient care were followed. Ethical approval from a committee was therefore not specifically required for publication in *JFMS Open Reports*.

Informed consent Informed consent (either verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (either experimental or non-experimental animals) for the procedure(s) undertaken (either prospective or retrospective studies). For any animals or humans individually identifiable within this publication, informed consent (either verbal or written) for their use in the publication was obtained from the people involved.

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References

- Nelson RW. **Water metabolism and diabetes insipidus**. In: Feldman E, Nelson R, Feldman E, et al (eds). *Canine and feline endocrinology*. 4th ed. St Louis, MO: Elsevier, 2014, pp 1–36.
- Winterbotham J and Mason KV. **Congenital diabetes insipidus in a kitten**. *J Small Anim Pract* 1983; 24: 569–573.
- Smith J and Elwood C. **Traumatic partial hypopituitarism in a cat**. *J Small Anim Pract* 2004; 45: 405–409.
- Simpson CJ, Mansfield CS, Milne ME, et al. **Central diabetes insipidus in a cat with central nervous system B cell lymphoma**. *J Feline Med Surg* 2011; 13: 787–792.
- Rogers W, Valdez H, Anderson B, et al. **Partial deficiency of antidiuretic hormone in a cat**. *J Am Vet Med Assoc* 1977; 170: 545–547.
- Aroch I, Mazaki-Tovi M, Shemesh O, et al. **Central diabetes insipidus in five cats: clinical presentation, diagnosis and oral desmopressin therapy**. *J Feline Med Surg* 2005; 7: 333–339.
- Court M and Watson A. **Idiopathic neurogenic diabetes insipidus in a cat**. *Aust Vet J* 1983; 60: 245–247.
- Burnie A and Dunn J. **A case of central diabetes insipidus in the cat: diagnosis and treatment**. *J Small Anim Pract* 1982; 23: 237–241.
- Kanemitsu N, Kawauchi A, Nishida M, et al. **Familial central diabetes insipidus detected by nocturnal enuresis**. *Pediatr Nephrol* 2002; 17: 1063–1065.
- Bellis T, Daly M and Davidson B. **Central diabetes insipidus following cardiopulmonary arrest in a dog**. *J Vet Emerg Crit Care* 2015; 25: 745–750.
- Ezzat S, Asa SL, Couldwell WT, et al. **The prevalence of pituitary adenomas: a systematic review**. *Cancer* 2004; 101: 613–619.
- Polledo L, Grinwis GCM, Graham P, et al. **Pathological findings in the pituitary glands of dogs and cats**. *Vet Pathol* 2018; 55: 880–888.
- Feldman EC, Nelson RW, Reusch C, et al. *Canine and feline endocrinology*. 4th ed. St Louis, MO: Elsevier Saunders, 2014.
- Dow SW, Fettman MJ, LeCouteur RA, et al. **Hypodipsic hypernatremia and associated myopathy in a hydrocephalic cat with transient hypopituitarism**. *J Am Vet Med Assoc* 1987; 191: 217–221.
- Croton C, Purcell S, Schoep A, et al. **Successful treatment of transient central diabetes insipidus following traumatic brain injury in a dog**. *Case Rep Vet Met* 2019; 2019: 3563675. DOI: 10.1155/2019/3563675.
- Miller RL, Bell R, Matiassek K, et al. **Neuroendocrine pituitary macroadenoma of a cat presenting with primary adipsia and hypernatraemia**. *JFMS Open Rep* 2015; 1. DOI: 10.1177/2055116915589838.
- Shimbo G, Tagawa M, Yanagawa M, et al. **MRI of lobar holoprosencephaly in a cat with hypodipsic hypernatraemia**. *JFMS Open Rep* 2018; 4. DOI: 10.1177/2055116918801602.
- Djermane A, Elmaleh M, Simon D, et al. **Central diabetes insipidus in infancy with or without hypothalamic adipsic hypernatremia syndrome: early identification and outcome**. *J Clin Endocrinol Metab* 2016; 101: 635–643.
- Modawi I, Barger GR and Rossi NF. **Central diabetes insipidus and adipsia due to astrocytoma: diagnosis and management**. *CEN Case Rep* 2013; 2: 11–16.
- Schaff-Blass E, Robertson GL and Rosenfield RL. **Chronic hypernatremia from a congenital defect in osmoregulation of thirst and vasopressin**. *J Pediatr* 1983; 102: 703–708.
- Sherlock M, Agha A, Crowley R, et al. **Adipsic diabetes insipidus following pituitary surgery for a macroprolactinoma**. *Pituitary* 2006; 9: 59–64.
- Smith D, Finucane F, Phillips J, et al. **Abnormal regulation of thirst and vasopressin secretion following surgery for craniopharyngioma**. *Clin Endocrinol* 2004; 61: 273–279.
- Zhang Y, Wang D, Feng Y, et al. **Juvenile-onset gout and adipsic diabetes insipidus: a case report and literature review**. *J Int Med Res* 2018; 46: 4829–4836.
- Dugger DT, Mellema MS, Hopper K, et al. **Comparative accuracy of several published formulae for the estimation of serum osmolality in cats**. *J Small Anim Pract* 2013; 54: 184–189.
- Epstein S. **Urinary electrolyte concentrations**. In: Ettinger SJ, Feldman EC and Cote E (eds). *Textbook of veterinary internal medicine*. St Louis, MO: Elsevier, 2017, pp 289–291.
- Bach J and Claus K. **Primary hypodipsia in a cat with severe hypernatremia**. *J Feline Med Surg* 2014; 16: 240–242.
- Morrison JA and Fales-Williams A. **Hypernatremia associated with intracranial B-cell lymphoma in a cat**. *Vet Clin Pathol* 2006; 35: 362–365.
- Weingart A, Gruber A, Kershaw O, et al. **Disturbances of water metabolism in two dogs and one cat with central nervous system disorders**. *Schweiz Arch Tierheilkd* 2013; 155: 463–469.
- Jeffery ND, Watson PJ, Abramson C, et al. **Brain malformations associated with primary adipsia identified using magnetic resonance imaging**. *Vet Rec* 2003; 152: 436–438.
- Ueda Y, Hopper K and Epstein SE. **Incidence, severity and prognosis associated with hypernatremia in dogs and cats**. *J Vet Intern Med* 2015; 29: 794–800.
- Barr JM, Khan SA, McCullough SM, et al. **Hypernatremia secondary to homemade play dough ingestion in dogs: a review of 14 cases from 1998 to 2001**. *J Vet Emerg Crit Care* 2004; 14: 196–202.
- Hardy RM. **Hypernatremia**. *Vet Clin North Am Small Anim Pract* 1989; 19: 231–240.
- Zada G, Ditty B, McNatt SA, et al. **Surgical treatment of Rathke cleft cysts in children**. *Neurosurgery* 2009; 64: 1132–1138.
- MacKillop E. **Magnetic resonance imaging of intracranial malformations in dogs and cats**. *Vet Radiol Ultrasound* 2011; 52: S42–S51.
- Hasegawa D, Uchida K, Kobayashi M, et al. **Imaging diagnosis – Rathke’s cleft cyst**. *Vet Radiol Ultrasound* 2009; 50: 298–300.
- Hamann F, Kooistra H, Mol J, et al. **Pituitary function and morphology in two German Shepherd dogs with congenital dwarfism**. *Vet Rec* 1999; 144: 644–646.
- Alexander J. **Anomaly of craniopharyngeal duct and hypophysis**. *Can Vet J* 1962; 3: 83.
- DeMonaco SM, Koch MW and Southard TL. **Syndrome of inappropriate antidiuretic hormone secretion in a cat with a putative Rathke’s cleft cyst**. *J Feline Med Surg* 2014; 16: 1010–1015.