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Short-term severe polyuria responsive to vasopressin after hypoglycaemia and hypotension in a domestic shorthair cat

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Abstract

Case summary An 8-month-old male neutered domestic shorthair cat presented for acute vomiting. Abdominal ultrasound examination revealed a jejunal foreign body, which was removed via enterotomy. Preoperatively, the patient was hypoglycaemic and, intraoperatively, a dopamine infusion was required to maintain a mean arterial pressure >60 mmHg. Despite glucose supplementation, the cat remained severely hypoglycaemic on recovery. Within 24 h postoperatively, despite euglycaemia and normalisation of the cardiovascular status, the patient developed progressive polyuria (up to 14 ml/kg/h). This was associated with neurological signs suggestive of diffuse brain disease, and absence of azotaemia or signs of overhydration. During the first 4 days of hospitalisation, any attempts to decrease intravenous fluid therapy were associated with hypotension, weight loss and clinical dehydration. Urine specific gravity (USG) during this time was in the range of 1.005–1.010 and failed to increase during fluid challenges. A presumptive diagnosis of central diabetes insipidus was made, and desmopressin (1 µg/cat SC) was administered on day 5 of hospitalisation. Consequently, the cat's urinary output decreased and his weight increased within 4 h. The patient required a total of four doses of desmopressin during hospitalisation, but no further doses since discharge. Urinary output on discharge was 3 ml/kg/h. Three months later, the cat's neurological signs and polyuria had completely resolved, and the USG was >1.050.

Relevance and novel information In this case, a presumptive diagnosis of central diabetes insipidus was supported by clinical progression, neurological signs and the response to desmopressin. To our knowledge, this is the first report of reversible diabetes insipidus after diffuse brain injury secondary to hypotension and hypoglycaemia.

Keywords: Polyuria; hypoglycaemia; central diabetes insipidus

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Introduction

Diabetes insipidus is a syndrome characterised by polyuria and compensatory polydipsia[1] due to a deficient production, secretion or response to antidiuretic hormone (ADH). Feline central diabetes insipidus (CDI) is rare and is characterised by a complete or partial deficiency of ADH[1] secondary to trauma, neoplasia or congenital cysts.[1–6] The syndrome is caused by a lack of production of vasopressin in the supraoptic and paraventricular hypothalamic nuclei. Patients presenting with CDI usually have low urine osmolarity,

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hyposthenuria, increased serum osmolarity,[7,8] hypernatraemia and polyuria.[9]

Case description

An 8-month-old male neutered domestic shorthair cat presented to his primary veterinary practice for evaluation of acute vomiting, dehydration and lethargy. Initial blood work revealed metabolic alkalosis, hypoglycaemia, hypokalaemia and borderline hyponatraemia. A right lateral abdominal radiograph revealed mild small intestinal distension. As a result of abnormal mentation and persistent hypovolaemia, the cat was referred to our institution.

On presentation (day 1), the patient was recumbent and severely obtunded. On physical examination, he had pale and dry mucous membranes, prolonged skin tenting (Table 1), tachycardia (heart rate 230 beats/min), poor peripheral pulses and tachypnoea (respiratory rate 46 beats/min). He was normothermic (rectal temperature 38.4°C) and normotensive (mean blood pressure [BP] 95 mmHg). Thoracic auscultation was unremarkable and abdominal palpation revealed moderate abdominal pain. Body condition score was 3/9 and his weight on initial presentation was 2.98 kg. The cat's historical weight at his primary veterinary practice was 3.3 kg.

Point-of-care venous blood gas, electrolyte and metabolite analysis (EPOC; Woodley Trial Solutions) showed hypochloraemic metabolic alkalosis, hyperlactataemia, moderate azotaemia and hypoglycaemia (Table 1). Serum biochemistry and haematology tests were performed after initial stabilisation and were largely unremarkable.

Initial stabilisation included administration of three isotonic crystalloid fluid boluses (20 ml/kg IV, Aqupharm 11; Animalcare) and two dextrose boluses (1 g/kg IV, Glucose 50%; Hameln). Perfusion parameters improved and glucose normalised after initial resuscitation, but mentation remained abnormal with severe obtundation. Additional treatment is outlined in Table 2.

After suspicion of a jejunal foreign body during abdominal ultrasound examination, an exploratory laparotomy was performed and a toy mouse was retrieved via enterotomy. Intraoperatively, the patient was persistently borderline hypotensive, requiring a dopamine continuous rate infusion to maintain a mean BP of 60 mmHg. Dopamine infusion was later discontinued at extubation when there was a consistent oscillometric BP of 100 mmHg.

On recovery in the intensive care unit, the patient again became cardiovascularly unstable with very poor femoral pulses, persistent hypotension (Doppler BP of 43 mmHg) and hypothermia (temperature 35.3°C). He was found to be severely hypoglycaemic and hyperlactataemic (Table 1). Heart rate and respiratory rate were 178 bpm and 36 bpm, respectively. This was suspected to

Table 1 pH, electrolytes, lactate, weight, creatinine, urea, PCV, TS and blood glucose data for the first 5 days of hospitalisation

	RI	Day 1 before surgery	Day 1 postoperatively	Day 2	Day 3 before fluid challenge	Day 3 after fluid challenge*	Day 4	Day 5
Creatinine (µmol/l)	88–195	295	213	72	71	58	44	<27
Urea (mmol/l)	5.4–12.1	20.6	21.3	7.2	5.6	6.5	2.9	3.2
BUN (mg/dl)	15–34	58	60	20	16	18	8	9
Lactate (mmol/l)	0.50–2.70	9.65	5.80	2.62	3.82	2.44	1.34	2.08
pH	7.35–7.40	7.411	7.28	7.432	7.62	7.438	7.44	7.40
Manual PCV (%)	25–45	54	50	46	35	37	35	37
Blood glucose (mmol/l)	5.5–10.27	2.1	1.3	6.4	6.3	5.6	10.6	10.6
Ionised calcium (mmol/l)	1.20–1.32	1.00	1.07	1.12	0.90	1.08	1.05	1.12
Potassium (mmol/l)	2.9–4.2	3.5	2.5	3.3	3.2	2.7	3.0	3.4
Sodium (mmol/l)	147–162	144	143	148	145	150	147	151
Chloride (mmol/l)	112–125	104	103	113	115	113	118	117
Estimated dehydration (%)	<0	12	10	5	0	5	0	0
Calculated osmolarity (mOsm/l)	280–300[3]	315	308	309.6	301.9	312.1	307.5	315.8

*On day 3, an attempt to reduce the fluid therapy rate was made (fluid challenge). The values displayed in the column 'Day 3 after fluid challenge' were taken after two fluid boluses of 5 ml/kg each of Hartmann's solution were administered

BUN = blood urea nitrogen; PCV = packed cell volume; RI = reference interval; TS = total solids; USG = urine specific gravity

Table 2 Fluid therapy, CRI and medications during hospitalisation*

Day of hospitalisation	IV fluid therapy	IV fluid therapy supplementation	IV CRIs	Other medications
Day 1 preoperatively	Hartmann's 4 ml/kg/h	Potassium chloride 40 mmol/l, 2.5% dextrose		Methadone 0.2 mg/kg IV q4h
Day 1 postoperatively	Hartmann's 4 ml/kg/h	Potassium chloride 40 mmol/l, 2.5% dextrose	Metoclopramide 0.5 mg/kg q24h, noradrenaline 0.2 mg/kg/min	Methadone 0.2 mg/kg IV q4h, maropitant 1 mg/kg IV q24h, cefuroxime 20 mg/kg IV q8h
Day 2	NaCl 0.9% 7 ml/kg/h Hartmann's 1 ml/kg/h	Potassium chloride 40 mmol/l, 2.5% dextrose	Metoclopramide 1 mg/kg q24h, noradrenaline 0.2 µg/kg/min	Buprenorphine 20 µg/kg IV q6h, maropitant 1 mg/kg IV q24h, cefuroxime 20 mg/kg IV q8h
Day 3	NaCl 0.9% 2 ml/kg/h NaCl 0.9% 8 ml/kg/h	Potassium chloride 40 mmol/l	Metoclopramide 1 mg/kg q24h	Buprenorphine 20 µg/kg IV q6h, maropitant 1 mg/kg IV q24h, potentiated amoxicillin 20 mg/kg IV q8h
Day 4	NaCl 0.9% 5 ml/kg/h Hartmann's 7 ml/kg/h	Potassium chloride 40 mmol/l	Metoclopramide 1 mg/kg q24h, magnesium 0.3 mEq/kg q24h	Potentiated amoxicillin 20 mg/kg IV q8h, buprenorphine 20 µg/kg IV q6h
Day 5	NaCl 0.9% 5–2 ml/kg/h† Hartmann's 8–5 ml/kg/h‡	Potassium chloride 40 mmol/l	Metoclopramide 1 mg/kg q24h, magnesium 0.3 mEq/kg q24h	Potentiated amoxicillin 20 mg/kg IV q8h, desmopressin 1 µg/cat SC
Day 6	NaCl 0.9% 4 ml/kg/h Hartmann's 2 ml/kg/h	Potassium chloride 40 mmol/l		Potentiated amoxicillin 20 mg/kg IV q8h
Day 7	NaCl 0.9% 4 ml/kg/h Hartmann's 1 ml/kg/h	Potassium chloride 40 mmol/l		Potentiated amoxicillin 20 mg/kg IV q8h, desmopressin 1 µg/cat SC
Day 8	NaCl 0.9% 3 ml/kg/h Hartmann's 1 ml/kg/h	Potassium chloride 40 mmol/l		Potentiated amoxicillin 20 mg/kg IV q8h, desmopressin 1 µg/cat SC
Day 9	NaCl 0.9% 2 ml/kg/h Hartmann's 2 ml/kg/h			Potentiated amoxicillin 20 mg/kg IV q8h, desmopressin 1 µg/cat SC
Day 10	NaCl 0.9% 2 ml/kg/h Hartmann's 2 ml/kg/h			Potentiated amoxicillin 20 mg/kg IV q8h
Day 11	Hartmann's 2 ml/kg/h			Potentiated amoxicillin 20 mg/kg PO q12h
Day 12	Hartmann's 2 ml/kg/h			Potentiated amoxicillin 20 mg/kg PO
Day 13				Potentiated amoxicillin 20 mg/kg PO

*Buprenorphine (Vetergesic; Ceva), cefuroxime (Zinacef; GlaxoSmithKline), magnesium (Magniject 25% w/v Solution; Norbrook), maropitant (Cerenia; Zoetis), methadone (Comfortan; Dechra), metoclopramide (Emeprid; Ceva), noradrenaline (Noradrenaline; Hospira), potassium chloride (Potassium Chloride; MercuryPharma), potentiated amoxicillin IV (Augmentin; GlaxoSmithKline), potentiated amoxicillin PO (Synulox Palatable Tablets; Zoetis) CRI = continuous rate infusion; IV = intravenous; SC = subcutaneous

†Fluid therapy was reduced from 5 ml/kg/h to 2 ml/kg/h

‡Fluid therapy was reduced from 8 ml/kg/h to 5 ml/kg/h

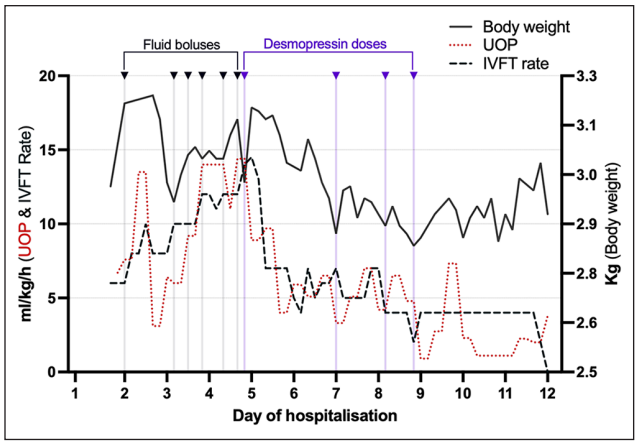

Figure 1 Body weight, fluid therapy rate and average urine output measurement during the 13 days of hospitalisation. These data have been recorded starting from the postoperative period until the first dose of desmopressin was given

be due to systemic inflammatory response syndrome. Point-of-care ultrasound showed no free fluid in the chest or abdomen, and no other sources of infection were found. On neurological examination, the patient was stuporous, recumbent, with mild extensor rigidity of the front and hind limbs and deep pain present in all four limbs. He had absent pupillary light reflex (PLR), mydriatic pupils and absent menace response bilaterally. Auricular reflex and facial symmetry were normal.

Postoperative management included several isotonic crystalloid IV boluses (total of 40 ml/kg over 4 h) and a dextrose IV bolus (0.5 g/kg). Because of persistent hypoperfusion and hypotension, the cat was started on a noradrenaline infusion and received two colloid boluses (Voluven; Fresenius Kabi), for a total of 5 ml/kg. Further treatments can be found in Table 2.

Relevant hospitalisation data, including indirect urinary output (UOP), daily blood results and fluid therapy, are summarised in Tables 1 and 2 and Figure 1.

On day 2, it was noticed that the patient's UOP had increased to 8 ml/kg/h and several fluid boluses were needed to avoid hypotension and recurrence of weight loss indicative of dehydration (Table 1). Venous blood gas analysis revealed a persistent hypochloraemic metabolic alkalosis; therefore, the patient was started on NaCl 0.9% (Aqupharm 1; Animalcare). At this time, the USG was reported to be in the range of 1005–1010. A full neurological examination by a specialist neurologist was first performed approximately 18 h postoperatively and revealed a recumbent and non-ambulatory patient, obtunded mentation, absent bilateral PLRs, with mydriatic pupils and absent menace response, resulting in suspected blindness. Moreover, the cat had absent proprioception on the front limbs with normal proprioception on the hind limbs. When supported, he presented voluntary movement in all four limbs. Neurological examination was suggestive of diffuse brain disease. Differential diagnoses included hypoglycaemia, hypoxia or ischaemia.

On day 3, an attempt to decrease the IV fluid rate was made, which resulted in the development of hypotension, acute weight loss and worsening mentation within 2 h (Figure 1), requiring further fluid boluses. After this, the fluid rate was increased to correct and prevent further dehydration, hypotension and weight loss. Moreover, more fluid boluses were needed owing to intermittent hypotension and weight loss (Figure 1). A similar episode occurred on day 4.

On day 4, the patient's mentation improved: he was now quiet, alert and responsive. He started to walk, albeit with a very ataxic gait, and had improved proprioception on the front limbs. He was still suspected to be bilaterally blind, as his PLRs were still reduced, his menace response was absent and his pupils were mydriatic. He continued to be hyposthenuric (USG 1005–1010).

Because of the presence of persistent neurological abnormalities, polyuria and hyposthenuria, CDI was suspected. On day 5, the patient was given a low dose of desmopressin (4 µg/ml, DDAVP Injection; Ferring Pharmaceuticals) (Table 2) for both therapeutic and diagnostic purposes. Within 2 h of DDAVP administration, the urine output was significantly reduced (Figure 1). In addition, urine osmolarity was measured (371 mOsm/kg) along with serum osmolality (314 mOsm/kg, reference interval [RI] 299–327).

Administration of desmopressin at the same dosage was repeated on days 7, 8 and 9 of hospitalisation for a total of four doses. After the last administration, the UOP reduced to 2.3 ml/kg/h. At this stage, the patient was bright, alert and walked with a normal gait, but remained blind. The patient was discharged on day 13 of hospitalisation and did not require further administration of DDAVP after discharge. Re-examination 3 months later revealed complete resolution of neurological signs, normal serum biochemistry and normal urinalysis with adequate urine concentrating ability (USG >1050).

Discussion

CDI is characterised by inappropriate polyuria followed by compensatory polydipsia.[1] This is rarely reported in cats,[1–3,5,6] and is normally associated with trauma,[1,6] congenital conditions[3] or neoplasia.[5] In this case, CDI was suspected as a result of the severity of the polyuria, the response to IV fluid therapy and persistent neurological signs. The neurological signs were thought to be secondary to a diffuse brain injury, given their bilateral symmetrical nature. Because of concerns over the patient's safety, the doctors elected not to perform further imaging.

We hypothesise that the patient suffered from a reversible brain injury secondary to perioperative hypotension and hypoglycaemia. This was supported by persistent altered mentation and neurological signs. As a neurological examination was not performed until day 2 of hospitalisation, the relationship between the hypotension, hypoglycaemia and onset of neurological signs could not be precisely established. Although other causes of CDI (such as trauma, neoplasia or sepsis) could not be excluded, these appeared less likely given the patient's history and clinical progression. It should be noted that although ischaemia is a reported cause of pituitary dysfunction in human medicine,[10,11] similar reports do not exist in veterinary medicine.

In this case, the cause of the hypoglycaemia is difficult to establish. In fact, reported causes such as sepsis (which influences ADH response through various pathways[12]), impaired liver function or neoplasia[13] could not be identified.

Usually, CDI manifests with hyposthenuric urine (USG <1006), increased serum osmolality (>330 mOsm/kg), polyuria (>50 ml/kg/day) and a serum sodium level >165 mmol/l.[14] Diagnostic criteria for CDI have yet to be identified in cats, and a diagnosis of CDI largely relies on human and canine studies. For this patient, the polyuria fitted the above diagnostic criteria; however, the USG was only intermittently below the RI. This could be due to plasma osmolarity and USG being normally higher in cats[15,16] compared with dogs,[16] or to a lack of data regarding these variables in cats with CDI. On the other hand, a partial CDI resulting in a higher USG (range 1008–1010) in the presence of polyuria is reported[8] and similar may have applied in this patient.

CDI is usually accompanied by hypernatraemia, which was never reported in this patient. However, the careful monitoring and adjustment of fluid therapy rate may have prevented the patient from developing hypernatraemia via supplementation of sufficient amounts of free water.[4,17] Attempts to reduce IV fluid therapy and perform a 'fluid challenge' were made during the first 3 days of hospitalisation. However, these attempts failed owing to marked weight loss and the development of hypoperfusion.

The initial azotaemia in the presence of isosthenuria, inappropriately high UOP and dehydration (Table 1 and Figure 1) raised concerns for acute kidney injury. However, after fluid resuscitation and rehydration, urea and creatinine normalised within 24 h while the polyuria persisted. Although an intrinsic renal injury could not be completely excluded, it appears less likely to be the sole primary cause of this patient's polyuria.

Renal concentrating ability[14] was demonstrated by measuring urine osmolarity and calculating the urine: plasma osmolarity ratio. In addition to the clinical response to DDAVP, this supported the presumptive CDI diagnosis. However, interpretation of urine osmolality is difficult owing to the wide RIs provided in literature.[15] Moreover, this value was measured after DDAVP was administered, making its interpretation even more challenging.

The presence of positive fluid balance could also have explained the polyuria. However, the patient's usual weight (3.3 kg) was never matched during hospitalisation and no clinical evidence of fluid overload was noticed at any point during hospitalisation.[18] Moreover, the weight loss (>5%) and hypotension noticed when attempting to reduce the fluid rate on day 3 are typical findings in cases of CDI.[14]

DDAVP is the elective treatment for diabetes insipidus[2,18,19] and is usually administered subcutaneously, into the conjunctival sac or orally.[2,3,5,6] The DDAVP test performed on day 5 supports the claim of CDI, as the patient's UOP decreased after administration and was correlated with a normal serum osmolality[2,3,5] (Table 1).

Conclusions

In this case, a presumptive diagnosis of CDI in the absence of hypernatraemia was reached by exclusion and supported by a response to DDAVP administration. To our knowledge, diabetes insipidus after persistent hypotension and hypoglycaemia is not reported in veterinary patients, proving this to be a challenging case to diagnose and treat.

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Ethical approval The work described in this manuscript involves the use of non-experimental (owned or unowned) animals. Established internationally recognised high standards ('best practice') of veterinary clinical care for the individual patient were always followed and/or this work involved the use of cadavers. Ethical approval from a committee was therefore not specifically required for publication in *JFMS Open Reports*. Although not required, where ethical approval was still obtained, it is stated in the manuscript.

Informed consent Informed consent (verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (experimental or non-experimental animals, including cadavers, tissues and samples) for all procedure(s) undertaken (prospective or retrospective

studies). For any animals or people individually identifiable within this publication, informed consent (verbal or written) for their use in the publication was obtained from the people involved.

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