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Successful treatment of atypical hypoadrenocorticism in a cat presenting with hypoglycaemic seizures

Emily Madden and Briannan-Kym Deguara

Abstract

Case summary A 4-year-old male castrated Ragdoll cat presented for generalised seizures. The cat displayed hyporexia, lethargy and hiding behaviour 24–48 h before presentation. The cat had a chronic history of daily vomiting and tachypnoea for 12 months. Severe hypoglycaemia was noted at 1.8 mmol/l (reference interval 4.11–8.84) on initial presentation. The hypoglycaemia persisted despite multiple glucose boluses, resulting in the cat being treated with a glucose and glucagon continuous rate infusion. The cat underwent extensive diagnostic evaluation during hospitalisation, consisting of serial venous blood gas assessment, haematology and biochemistry analysis, urinalysis, serum insulin assay, resting cortisol, adrenocorticotropic hormone (ACTH) stimulation test, abdominal and thoracic imaging, and airway culture. A resting cortisol level of <14 nmol/l was obtained on day 2 of hospitalisation with a follow-up ACTH-stimulation test reporting a baseline cortisol of <28 nmol/l and a 1 h post-ACTH cortisol of 7 nmol/l, supporting a diagnosis of hypoadrenocorticism. The cat was successfully treated with glucocorticoid therapy and discharged home 8 days after initial presentation.

Relevance and novel information There are limited cases of feline hypoadrenocorticism present in the literature, most of which describe cats with both glucocorticoid and mineralocorticoid deficiency. Only two previous case reports of feline atypical hypoadrenocorticism exist. Only one of these case reports describes hypoglycaemia with signs of neuroglycopaenia on initial presentation. To the author's knowledge, this is the first successfully treated case of atypical hypoadrenocorticism presenting with hypoglycaemic seizures in a cat, demonstrating successful long-term management.

Keywords: Addison's; hypoadrenocorticism; hypoglycaemia; adrenal gland; neuroglycopaenia; seizures

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Case description

A 4-year-old male castrated Ragdoll cat was presented for generalised seizures. The cat had been hyporexic, lethargic and displaying hiding behaviour for 24–48 h before presentation. The cat had a 12-month history of daily vomiting and tachypnoea with resting respiratory rates in the range of 60–80 bpm. The cat had no previous history of seizures, no toxin access and was up to date with routine vaccinations.

On presentation, the cat was in lateral recumbency, unable to ambulate with head tremors. A physical examination revealed hypothermia (below a detectable thermometer level), bradycardia (heart rate 140 bpm) and weak femoral pulses. The cat was 5–7% dehydrated and had a body condition score of 3/9 with generalised muscle condition loss. In-house haematology was unremarkable. The in-house biochemistry analysis revealed an alanine aminotransferase (ALT) elevation of 185 U/l (reference interval [RI] 12–130) and a blood glucose level of 1.8 mmol/l (RI 4.11–8.84). Electrolytes were within the RI

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on presentation. Three-view thoracic radiographs were performed, revealing a diffuse bronchointerstitial pattern, suspected initially to be secondary to post-seizure non-cardiogenic pulmonary oedema. Abdominal ultrasound revealed prominent small intestinal layering, with prominent ileocaecocolic lymph nodes measuring up to 0.31 × 0.78 cm, with hyperechoic surrounding mesentery. Both adrenal glands measured 0.19 cm in maximal height. Blood was also submitted to an external laboratory, with haematology revealing a neutrophilia of 9.8×10^9/l (RI 2.1–9.1), lymphocytosis of 7.2×10^9/l (RI 1.6–7.0) and eosinophilia of 2.15×10^9/l (RI <1.41). External biochemistry analysis revealed a blood glucose level of 2.4 mmol/l (RI 3.9–8.3), bilirubin of 5 µmol/l (RI 0–4), ALT of 136 U/l (RI 1–80), total protein of 47 g/l (RI 61–83), albumin of 23 g/l (RI 28–40), globulin of 24 g/l (RI 29–50), creatine kinase of 1530 U/l (RI 0–444) and cholesterol of 1.9 mmol/l (RI 2.4–5.2). All other parameters, including total thyroxine (TT4), were within the RI.

The cat was treated initially with a 0.5 ml/kg 50% glucose intravenous (IV) bolus, followed by a glucose constant rate infusion (CRI), IV fluid therapy (Hartmann's), amoxicillin 25 mg/kg IV, maropitant 1 mg/kg IV and chlorpheniramine 0.5 mg/kg IV. A single glucagon 50 µg/kg bolus was administered, followed by a glucagon CRI at 10 µg/kg/min. At this time, the main differential diagnoses included insulinoma, another insulin-secreting tumour and sepsis; however, hypoadrenocorticism, hepatic insufficiency and toxicity could not be excluded. The cat was placed in an oxygen cage because of persistent tachypnoea with mild increase in respiratory effort.

On day 2, repeat venous blood gas analysis revealed hypokalaemia of 3.1 mmol/l (RI 3.9–5.3), hyperchloraemia of 121 mmol/l (RI 110–120) and hypoglycaemia of 2.5 mmol/l (RI 4.0–8.0). Urinalysis was unremarkable. A thoracic and abdominal CT scan was performed, which revealed thickened bronchial walls with multiple bronchi containing soft tissue/fluid. These findings were considered most consistent with a diagnosis of feline lower airway disease with feline asthma as the primary differential; however, an infectious or parasitic aetiology also could not be excluded. Neoplasia and oedema were considered less likely. Additional abnormalities detected on CT were deemed non-specific for a definitive diagnosis. An endotracheal swab submitted for bacterial culture did not yield any growth. A resting cortisol test was performed, returning a result of <14 nmol/l (RI 30–100). Serum insulin was also assessed and returned a result of <2 µU/l, representing an appropriate response to hypoglycaemia, making hyperinsulinaemia an unlikely cause for the cat's hypoglycaemia. An ACTH-stimulation test was performed on day 3, which returned a baseline cortisol level of <28 nmol/l. Tetracosactide (5 µg/kg IV) was administered and 1 h later a cortisol level of 7 nmol/l was documented, supporting a diagnosis of hypoadrenocorticism. A validated feline cortisol assay was used (Vetnostics Pathology).

The cat was commenced on dexamethasone at an initial dose of 0.2 mg/kg IV on the first day, with subsequent daily dosing of 0.1 mg/kg IV q24h. At this time, antimicrobials were discontinued. IV fluids supplemented with 5% glucose, maropitant and glucagon CRI continued. On day 4, the glucagon and glucose CRI were discontinued and the cat maintained euglycaemia. The cat was successfully weaned off oxygen supplementation on day 5. Repeat daily venous blood gas assessments revealed persistent hypokalaemia despite supplementation with potassium gluconate (Hypokal, 78 mEq PO q12h) and a good appetite, resulting in an additional 2 days of hospitalisation. This is suspected to have been secondary to IV fluid therapy. On day 6, the cat was commenced on a 5-day course of fenbendazole 50 mg/kg PO q24h, in case the airway disease was parasitic in origin. The cat was clinically stable and discharged home on day 8 with oral prednisolone (1 mg PO q12h), Hypokal 78 mEq PO q12h and fenbendazole 50 mg/kg PO q24h for 5 days.

The cat presented for a revisit on days 12, 26 and 150, at which time the cat was clinically well at home.

Two weeks after discharge, resolution of vomiting, dyselectrolytaemia and tachypnoea was documented. Repeat thoracic radiographs were unremarkable. The cat was commenced on a fluticasone 125 µg inhaler 1 puff q24h for suspected feline asthma. Prednisolone was tapered to 0.11 mg/kg PO q12h. Potassium supplementation was discontinued. Weekly vomiting episodes were reported by the owner at 5 months; however, the cat was otherwise clinically well on daily prednisolone 0.1 mg/kg PO q24h. Repeated haematology and biochemistry were within normal limits.

Discussion

Hypoadrenocorticism, or Addison's disease, is an uncommon canine and rare feline endocrine disorder with only approximately 40 reported feline cases in the literature.[1–3] Often referred to as 'the great pretender', canine Addisonian patients may present with a wide variety of clinical signs, ranging from vague signs of lethargy, waxing waning gastrointestinal signs, weakness and weight loss to more severe signs of hypovolaemic shock associated with acute hypoadrenocortical crisis.[2,4] Diagnostic findings in these patients are also highly variable, the most common of which include hyperkalaemia, hyponatraemia, azotaemia, mild normocytic, normochromic anaemia, hypercalcaemia, hypoglycaemia and lack of a stress leukogram most often characterised by a lymphocytosis.[4] Although feline cases are less well-documented, clinical presentation appears similar to canine patients.[1,5]

Primary hypoadrenocorticism most commonly arises as a result of immune-mediated destruction of the adrenal cortex, usually resulting in a deficiency of glucocorticoids and mineralocorticoids.[2,5,6] Other aetiologies have been implicated in some cats, including neoplastic infiltration of the adrenal glands[7] and external trauma.[8,9] Less commonly, secondary hypoadrenocorticism may occur as a result of deficiency in ACTH production from the anterior pituitary[6] or reduced corticotropin-releasing hormone (CRH) secretion from the hypothalamus.[10] Endogenous ACTH level was not performed in this case; however, it may have provided insight into the origin of the hypocortisolism and should be considered in future cases.

Historically, hypoadrenocorticism has been referred to as 'typical' in cases where the patient displays glucocorticoid deficiency in addition to mineralocorticoid deficiency typified by the presence of hyponatraemia and/or hyperkalaemia, or 'atypical' in cases where the patient displays glucocorticoid deficiency in the absence of the electrolyte derangements classically seen with mineralocorticoid deficiency.[4] More recently, the Agreeing Language in Veterinary Endocrinology (ALIVE) project developed by the European Society for Veterinary Endocrinology (ESVE) has suggested alternative nomenclature for the different subtypes of hypoadrenocorticism.[11] The ALIVE project proposes the term 'hyponatraemic and/or hyperkalaemic primary hypoadrenocorticism' rather than the previous term 'typical', and 'eunatraemic, eukalaemic primary or secondary hypoadrenocorticism' rather than the previous term 'atypical'.[11] This nomenclature, however, does have limitations in its inability to distinguish cases that have electrolyte concentrations within the RI despite mineralocorticoid deficiency.[4] It also does not distinguish cases that have glucocorticoid deficiency alone but that have electrolyte derangements for other reasons.[4] In the present case, the cat did not display typical electrolyte imbalances consistent with mineralocorticoid deficiency, presenting with normal electrolytes and developing hypokalaemia and hypernatraemia during hospitalisation.

Hypoglycaemia has been reported to occur in up to 30% of dogs with hypoadrenocorticism and is thought to occur secondarily to glucocorticoid deficiency.[10] The cat in this case was administered broad spectrum antimicrobials early in the treatment course, owing to concern for sepsis; however, the cat was ultimately unable to maintain euglycaemia until it was treated with corticosteroids. Cortisol is integral in the regulation of blood glucose concentrations because of its role in hepatic gluconeogenesis and glycogenesis, in addition to stimulation of lipolysis and protein catabolism and reduction of peripheral glucose utilisation.[4] Hypoglycaemia has been documented in both typical[12] and atypical[13–15] cases of hypoadrenocorticism in canine patients, occurring in up to one-third of the patients in one study.[16] Symptomatic neuroglycopaenia, however, appears less common, with only 3/14 (21%) hypoglycaemic dogs in one study[16] and 3/37 (8%) hypoglycaemic dogs in another study[17] developing severe weakness and generalised seizures secondary to neuroglycopaenia. Two case reports have also documented canine patients presenting with hypoglycaemic seizures attributable to hypoadrenocorticism.[12,14] Hypoglycaemia appears comparatively rare in feline hypoadrenocorticism patients, with four documented cases in the literature.[7,18,19] One cat presented with hypoglycaemic seizures due to adrenal insufficiency secondary to lymphocytic panhypophysitis;[19] however, in the other cases, patients displayed no signs of neuroglycopaenia on presentation.[7,18] The limited number of cases of feline hypoadrenocorticism present in the literature primarily describes patients with both glucocorticoid and mineralocorticoid deficiency, with only two previous case reports of feline atypical hypoadrenocorticism.[19,20] One of these patients was normoglycaemic on presentation.[20] The other was severely hypoglycaemic and presented with signs of neuroglycopaenia similar to the present case; however, that patient was euthanased 24 h after initiating therapy with dexamethasone.[19]

Comorbidities were noted in this case, including chronic vomiting, which improved with corticosteroid treatment but did not resolve and concurrent feline asthma. Therefore, it is possible that there was some overlap in reported vomiting and possible coughing. Another underlying condition contributing to the vomiting, such as a chronic enteropathy, could not be excluded.

Lymphocytosis and eosinophilia were identified on presentation. This is consistent with a lack of stress leukogram, commonly seen in Addisonian canine patients.[10] In patients with normal adrenal function, increased cortisol leads to lymphopaenia due to transient sequestration of lymphocytes in the lymph nodes and bone marrow, with reduced circulation in lymph and blood.[10] This does not occur in patients with glucocorticoid deficiency.[10] In a review of 48 feline patients with hypoadrenocorticism, only 6/48 cats had lymphocytosis and 4/48 cats lacked a stress leukogram on presentation.[1]

The cat had moderate ALT elevation on presentation, which was presumed to be a hypoxic hepatic injury secondary to seizure activity. In a review of 48 feline patients with hypoadrenocorticism, only six cats had elevated ALT on presentation.[1] Although the ALT elevation had resolved at the last follow-up, a concurrent hepatopathy could not be excluded in the current case. In addition, hypocholesterolaemia and hypoalbuminaemia were documented, which appear commonly in dogs with hypoadrenocorticism.[10] It is speculated that hypocholesterolaemia in cases of hypoadrenocorticism may be due to the essential role of glucocorticoids in fat absorption,[10] whereas the proposed mechanisms of hypoalbuminaemia include anorexia, gastrointestinal

mucosal ulceration leading to haemorrhage, protein-losing enteropathy and reduced albumin synthesis due to hepatopathy.[10]

Conclusions

To the authors' knowledge, this is the first successfully treated case of atypical hypoadrenocorticism presenting with hypoglycaemic seizures in a cat. Hypoadrenocorticism should be considered a differential diagnosis in young cats presenting with hypoglycaemia with or without clinical signs of neuroglycopaenia. A favourable outcome can be seen in cats with atypical hypoadrenocorticism undergoing treatment.

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Ethical approval The work described in this manuscript involved the use of non-experimental (owned or unowned) animals. Established internationally recognized 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). No animals or people are identifiable within this publication, and therefore additional informed consent for publication was not required.

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