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A novel hypokalaemic polymyopathy and subsequent unrelated nutritional thiamine deficiency in a young Burmese cat

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Abstract

Case summary An 8-month-old female spayed Burmese cat was referred for investigation of reduced appetite, reluctance to walk and jump and amaurosis. On serum biochemistry there was severe hypokalaemia and marked elevation of creatine kinase, suggestive of hypokalaemic polymyopathy. The neurological signs were consistent with thiamine deficiency. The cat was negative for the periodic hypokalaemic polymyopathy (PHP) of Burmese cats, and was ultimately diagnosed with a previously undescribed potassium wasting nephropathy requiring ongoing oral potassium supplementation. The response to treatment was excellent and the cat has remained clinically normal over a 12-month follow-up period.

Relevance and novel information PHP in Burmese cats has been well described, but all cases to date have been shown to be secondary to a genetic mutation in *WNK4*, resulting in potassium wasting into the urine. This is the first case report of another potassium wasting nephropathy in a young Burmese cat, with subsequent development of nutritional thiamine deficiency.

Keywords: Hypokalaemia; polymyopathy; thiamine deficiency; Burmese cat

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Case description

An 8-month-old female spayed Burmese cat was referred for a 2-week history of polyuria and polydipsia (PU/PD), progressive lethargy, reduced appetite and difficulty ambulating. The cat was reportedly small at the time of adoption when compared with its litter mates. It was routinely spayed 3 months prior to presentation, and was up to date with core vaccinations and ecto-/endoparasite prophylaxis. There was no outdoor access. No access to toxins and no history of trauma were reported; however, owing to hyporexia, its recent diet was essentially just raw prawns. At the time of presentation to our referral facility, the cat was receiving treatment with antibiotics (amoxycillin/clavulanate 16.6 mg/kg q12h PO [Noroclav; Norbrook]) owing to suspicion of a urinary tract infection, which was based on the identification of pyuria and bacteriuria by the referring general practitioner. No urine specific gravity (USG) had been recorded at the time.

On physical examination the cat's body condition score was 4/9, and there was a grade II/VI systolic heart murmur with a point of maximal intensity localised to the left side. On neurological examination the cat was mentally dull and had reduced pupillary light responses bilaterally, absent menace response and no ability to track objects visually. These findings could be suggestive of a lesion of the retina, optic tract, brainstem or visual cortex. The fundic examination was unremarkable.

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There was normal proprioception but profound weakness of all four limbs with reduced withdrawal reflexes, and ventroflexion of the neck. Using Doppler measurement on the right front leg with a size three cuff, the mean systolic blood pressure was 130 mmHg (normal range 125 ± 10.6).[1]

Haematology, serum biochemistry and electrolyte tests were performed and revealed a marked neutrophilia of 39.47 × 10^9/l (reference interval [RI] 1.48–10.29) with normal haematocrit and platelet count, severe hypokalaemia of 2.4 mmol/l (RI 3.5–5.8), a significant increase in creatine kinase of 1950 U/l (RI 0–314) and moderate azotaemia characterised by increased urea at 24.9 mmol/l (RI 5.7–12.9) with normal creatinine.

A feline immunodeficiency virus (FIV)/feline leukaemia virus (FeLV) test (IDEXX SNAP FIV/FeLV Combo test) was negative. Urinalysis obtained by cystocentesis showed suboptimally concentrated urine with a USG of 1.026, aciduria (pH 5), scant haematuria (presumed iatrogenic due to the sampling technique) and trace proteinuria. The sediment was inactive and urine bacterial culture was also negative at this time.

At this stage the most significant findings were considered to be the loss of vision, the generalised weakness and the 2-week history of poor appetite and PU/PD. The generalised weakness could be explained by the profound hypokalaemia. We considered the following broad categories of differential diagnoses for hypokalaemia in a cat: reduced intake due to hyporexia, gastrointestinal loss, renal loss (either through chronic kidney disease [CKD] or a specific potassium-wasting nephropathy), or hyperaldosteronism. The neurological signs were characterised by blindness, mental dullness and lower motor neuron tetraparesis. While the lower motor neuron signs could be explained by hypokalaemia and there may have been concurrent but unrelated central disease (eg, thiamine deficiency, cerebrovascular accident and neoplasia), we also considered multifocal systemic diseases affecting the brain and the neuromuscular unit, such as toxoplasmosis, feline infectious peritonitis (FIP) and lymphoma.

In Australia, no commercial laboratories offer serum thiamine testing for cats with reliably established RIs; however, there are well-described characteristic findings on MRI, including bilaterally symmetrical foci of hyperintensity in the lateral geniculate nuclei, caudal colliculi, medial vestibular nuclei and cerebellar nodulus.[2] Ready MRI access was not available in this instance, so to investigate further a pre- and post-intravenous (IV) contrast CT scan was performed. The images were submitted for interpretation by a board-certified radiologist. The following abnormalities were identified on the kidneys: the kidneys were bilaterally at the lower limit of normal renal size, there was a right circumcaval ureter and subtle right renal subcapsular fluid (differentials suggested by the radiologist included FIP, nephritis and renal lymphoma). There were no structural changes of the gastrointestinal tract to explain excess potassium loss, and this was considered unlikely in the absence of any gastrointestinal clinical signs. There were also some likely incidental abnormalities identified: fusion of the thirteenth thoracic and first lumbar vertebrae with focal scoliosis but no apparent spinal cord compression, and a heterogeneously enhancing spleen with incomplete caval opacification (interpreted as likely associated with phase of contrast enhancement).

Considering the CT findings – and appreciating the limitations of this imaging modality – there were no abnormalities suggestive of multifocal systemic neurological disease such lymphoma or FIP, and there were no gross findings suggestive of gastrointestinal or metabolic illness such as gastrointestinal obstruction, adrenal gland tumour or portosystemic shunting.

The appearance of the kidneys and the anamnesis (Burmese cat) lead us to suspect periodic hypokalaemic polymyopathy (PHP) of Burmese cats,[3] other renal diseases such as acute-on-chronic kidney disease with tubular interstitial nephritis and subsequent hypokalaemia, and renal tubular acidosis (previously described in isolated case reports).[4,5] Considering the normal blood pressure and normal adrenal glands, hyperaldosteronism was considered less likely, which was further confirmed by a normal serum aldosterone level of 234 pmol/l (RI 194–388). Toxoplamosis was excluded on the basis of negative serum IgM and IgG titres (both <1:16).

In the meantime, the cat was treated empirically for thiamine deficiency and improved within 4 days. The generalised weakness improved with potassium supplementation. During hospitalisation, the cat received IV fluids (Compound Sodium Lactate [Hartmann's]; Baxter) with potassium chloride supplementation (40 mmol/l), oral potassium supplementation with potassium gluconate (0.5 mEq/kg PO q12h [Hypokal; Mavlab]), vitamin B complex (equivalent to 3 mg/kg thiamine SC q24h [B-Complex; Troy]) and empirical clindamycin (12.5 mg/kg PO q12h [Clinacin; Hypervet]) while awaiting the *Toxoplasma* titres.

Repeat haematology and biochemistry was performed prior to discharge and showed marked improvement of the inflammatory leukogram, with persistent – although improving – hypokalaemia (3.3 mmol/l) and markedly reduced creatinine kinase vs admission (451 U/l).

Further investigation into the renal disease included venous blood gases, which showed normal serum pH (7.35) with bicarbonate and partial pressure of carbon dioxide within the RIs. Concurrent urine pH was neutral (pH 7), thereby excluding renal tubular acidosis. Of particular note, the Orivet buccal swab PCR test for PHP was also negative.

The cat was discharged home with oral clindamycin and potassium gluconate (doses and frequency as above), in addition to oral vitamin B1 supplementation

Table 1 Urine fractional excretion of potassium

	Creatinine (μmol/l)	Potassium (mmol/l)
Urine	4290	49
Plasma	97	3.0

(16 mg/kg PO q12h) and instructions to feed good-quality kitten food.

The cat was clinically normal at its follow-up appointment 3 weeks later, and serum potassium was normal (3.5 mmol/l). Vitamin B1 supplementation was weaned over the following 2 weeks and clindamycin treatment ceased. Potassium gluconate supplementation continued, but the frequency was reduced to once daily, resulting in recurrent hypokalaemia. Subsequent urine cultures were negative.

Urine fractional excretion of potassium was then performed (Table 1). Urine potassium fractional excretion was therefore calculated as 37% (normal <4%). This was interpreted as an inappropriately high fractional excretion of potassium at the level of the kidney, especially in the face of hypokalaemia.

Potassium gluconate was henceforth prescribed ongoing (at a dosage of 0.3 mEq/kg PO q12h). A commercial adult renal food was also prescribed. This treatment resulted in normalisation of serum potassium at subsequent rechecks (between 3.5 and 4 mmol/l) and the cat was clinically normal at its 6-month and 1-year follow-up appointments.

The working diagnosis was a renal tubular defect resulting in chronic potassium wastage. This defect is not linked to the genetic disorder previously identified in Burmese cats, and questions remain about the origin of this defect: whether it was acquired and secondary to pyelonephritis, or congenital. The acute presentation, inflammatory leukogram and initial azotaemia would support an acquired cause; however, the persistence of hypokalaemia, despite correction of azotaemia and regaining normal urine concentrating ability, and concurrent congenital structural anomalies on CT scan would support a congenital defect.

Discussion

This case had a unique clinical presentation involving concurrent hypokalaemic polymyopathy and thiamine deficiency. After discussions with the owner, our hypothesis is that the cat first developed profound hypokalaemia and muscle pain, resulting in poor appetite, and the owner offered raw prawns as the only food option the cat would accept. Raw seafood has been well documented to contain high levels of thiaminase, the enzyme that breaks down vitamin B1.[6] Clinical signs of thiamine deficiency may include various neurological disturbances such as loss of vision, ataxia, mydriasis, vestibular signs and seizures.[2] Thiamine deficiency is notably difficult to test for owing to the lack of established serum RIs in companion animal medicine; however, the rapid return of vision and resolution of neurological signs when vitamin B1 was supplemented essentially confirmed the diagnosis. Once the cat was established on a commercial feline diet there were no further episodes of any clinical signs attributable to thiamine deficiency.

Feline hypokalaemic polymyopathy is a well-recognised disorder, first described in 1980.[7] The majority of cases of severe hypokalaemia are attributable to disorders affecting the renal tubules. In this case, we considered PHP[3] – a disease characterised by a genetic mutation in *WNK4*, resulting in excessive potassium wasting into the urine, acute-on-chronic kidney disease with tubular interstitial nephritis, renal tubular acidosis or an as-yet-undescribed tubular defect in cats.

As mentioned, hyperaldosteronism was ruled out, and renal tubular acidosis was excluded on the basis of normal serum pH and normochloraemia.

CKD was considered given the presence of renal azotaemia and borderline small kidneys. Hypokalaemia occurs in 20–30% of cats with CKD. The pathophysiology of hypokalaemia in CKD is thought to be multifactorial and related to decreased dietary intake, reduced functional nephrons for reabsorption, increased distal delivery of sodium and water within the nephron, and activation of the renin–angiotensin–aldosterone system.[8] Seldom does the hypokalaemia caused by CKD become marked enough to result in clinical signs of polymyopathy. In general terms, muscle weakness is exhibited when serum potassium is <3.0 mEq/l, and overt signs of muscle damage and rhabdomyolysis are seen when serum potassium is <2.0 mEq/l.[9] Because of the persistent isothenuria at follow-up appointments, this cat was categorised as International Renal Interest Society stage 1, but in isolation this is not expected to cause such marked potassium wasting, or at least this is not commonly reported and perhaps warrants closer attention.

The two remaining differentials included chronic tubular interstitial nephritis with permanent renal tubular damage, or a congenital renal tubular defect (as yet unidentified). When considering the CT findings, the cat was born with several congenital malformations, which raises suspicion for a congenital defect. However, the CT scan also identified right renal subcapsular fluid, and differentials provided by the interpreting radiologist included FIP, lymphoma or nephritis. FIP and lymphoma were excluded on the basis of the excellent response to treatment and lack of disease progression; at the time of writing the cat was clinically normal at >2 years post-diagnosis with only enteral potassium supplementation. Concurrent pyelonephritis at the time of presentation is plausible, and could explain the marked inflammatory

leukogram and azotaemia, particularly given that pyuria and bacteriuria had been identified by the referring veterinarian prior to presentation. Differentiating between these two diseases would be challenging. Renal biopsy could be considered; however, morbidity of the procedure, difficulty in interpreting the findings and limited alternative treatment options make this difficult to justify in a clinically well cat.

This case highlights the importance of avoiding pattern recognition in the approach to a case. Since the discovery of the *WNK4* mutation, young Burmese cats with hypokalaemic polymyopathy are often presumed to have PHP. The PCR test can identify carriers and homozygous individuals, and, to date, false positives or negatives have not been documented. The current recommendation is to screen Burmese breeding cats with the PCR test in an attempt to eliminate the disease.[3] This cat's presentation raises the questions of whether the genetic mutation in *WNK4* is the only factor contributing to periodic hypokalaemia in this breed, and also whether closer follow-up is required in the aftermath of conditions such as pyelonephritis.

Conclusions

This case is an interesting demonstration of two very separate, yet related, disease entities, and serves as an important reminder that one disease process does not always explain all the observed clinical signs and laboratory abnormalities. It highlights the importance of meticulous history taking, with particular attention to diet and habits of the pet in the home environment. In addition, profound hypokalaemia in a young Burmese cat should not always be assumed to be genetic in origin and should prompt further investigation into an underlying cause.

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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) 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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