




Reversible positioning head tilt observed in 14 cats with hypokalaemic myopathy

Shinji Tamura¹, Yuya Nakamoto^{2,3} and Yumiko Tamura¹

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Abstract

Case series summary Positioning head tilt (PHT) is a dynamic neurological sign in which the head tilts to the opposite side to which it is moving. This sign is triggered in response to head movement and is thought to be due to the lack of inhibition of vestibular nuclei by the cerebellar nodulus and uvula (NU). The occurrence of PHT in animals has been suggested to be an indicator of NU dysfunction. Here, we describe the acute onset of PHT in 14 cats. All the cats were diagnosed with hypokalaemic myopathy caused by a range of pathologies. The PHT resolved along with other signs related to myopathy, such as cervical flexion and generalised weakness, after electrolyte correction in all cats.

Relevance and novel information Hypokalaemic myopathy was the likely cause of PHT in the present feline cases.

Keywords: Positioning head tilt; hypokalaemic myopathy; hypokalaemia; reversible

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Introduction

Positioning head tilt (PHT) is a neurological sign that was first reported in 2016.¹ Animals exhibiting this sign can turn freely in any direction at will. The head is in a level position when the animal looks forward; however, the head tilts to the opposite side when the animal turns its head. As a result, the side of tilting changes every time the animal turns its head.^{1,2} The cerebellum is responsible for the automatic maintenance of normal head position. Signals from the vestibular system are transmitted to the vestibulocerebellar module (the flocculonodular lobe, the paraflocculus and the fastigial nucleus) when the head is moved.^{3–8} Vestibular nuclear projections to the spinal cord are situated in the vestibulospinal tracts. The fibres terminate on interneurons that facilitate ipsilateral extensor and decussate to inhibit contralateral extensor muscle activity. The vestibulospinal tracts facilitate spinal reflexes, especially those involved in maintaining posture and the antigravity/extensor muscles. Turning the head to the left causes a shift in the distribution of body mass to the left. This shift in mass is supported by increased extension on the left side, which is reflexively induced by both myotatic and vestibular reflexes. This also reduces extension on the right side, and thereby minimises weight

transfer to the left. The cerebellar nodulus and uvula (NU; lobules of the cerebellar vermis IX and X, respectively) coordinate this system by inhibition of stimulation of vestibular nuclei to maintain a level head position in response to head movement.¹ This inhibition is impaired in animals with NU dysfunction and, consequently, PHT occurs. Thus, PHT can be used to ascertain lesion localisation.¹ To date, PHT has been reported in three dogs with NU hypoplasia,¹ in dogs with five different types of lysosomal storage disease⁹ and in a dog with gliomatosis cerebri affecting NU.^{10–12}

Hypokalaemic myopathy is a relatively common myopathy in cats associated with low extracellular potassium concentration. It often occurs in cats with chronic kidney

¹Tamura Animal Clinic, Hiroshima, Japan

²Neuro Vets Animal Neurology Clinic, Kyoto, Japan

³Veterinary Surgery, Graduate School of Life and Environmental Science, Osaka Metropolitan University, Sakai, Japan

Corresponding author:

Shinji Tamura PhD, DVM, Tamura Animal Clinic, 7-16, Yoshimien, Saeki-ku, Hiroshima, 731-5132, Japan.

Email: cqx03426@ms8.megaegg.ne.jp



disease (CKD), hyperthyroidism, dietary potassium deficiency, hyperaldosteronism, fluid over-administration, chronic vomiting/diarrhoea and overuse of potassium-wasting diuretics. Diagnosis is based upon signalment, historical and clinical findings, resolution of clinical signs with potassium supplementation and supportive evidence of myopathy from electromyogram (EMG) analysis and muscle biopsy.^{13,14} A hereditary condition in Burmese kittens is also suspected to cause potassium-losing nephropathy with periodic hypokalaemia and signs of myopathy.^{15,16} Hypokalaemia leads to hyperpolarisation of the sarcolemma resting membrane potential, making it refractory to depolarisation and subsequent contraction. Feline hypokalaemic myopathy is a generalised polymyopathy, which is often associated with observed cervical flexion. In general, the prognosis associated with feline hypokalaemic myopathy is good if potassium concentrations are supplemented and the primary cause of the hypokalaemia is treated.^{13,14}

The current report describes reversible PHT observed in 14 cats with hypokalaemic myopathy. A potential mechanism for the PHT observed in these cats is described and discussed.

Case series description

Cases and data collection

A 5-year-old neutered male domestic shorthair cat (case 1) was presented to Neuro Vets Animal Neurology Clinic with a history of head tilt and cervical flexion. A general physical examination revealed no abnormalities. A skin turgor test revealed <5% dehydration. On neurological examination, cervical flexion and PHT was clearly observed (Figure 1a; see also Video 1 in the supplementary material). Complete blood count results were within the normal reference intervals. Serum biochemistry revealed azotaemia and hypokalaemia (see file in the supplementary materials). Creatine kinase activity was not examined. Thoracic and abdominal radiographs revealed no abnormalities. Brain MRI (Figure 2) and cerebrospinal fluid analysis on the day of presentation revealed no abnormalities. Temporalis, Masseter, trapezius, clavicular cervicis, posterior sternal, longissimus (cervicis and thoracis), triceps brachii, biceps brachii, extensor carpi radialis, quadriceps femoris, tibialis anterior, gastrocnemius and interdigital muscle were evaluated by EMG. EMG revealed fibrillation potentials and positive sharp waves in the constituent muscles of the whole body, especially in the cervical muscles (Figure 3). Based on these findings, a diagnosis of kidney failure with hypokalaemic myopathy was made. An intravenous infusion of 0.9% saline supplemented with potassium (40mmol/l) was administered; after this treatment, no further signs of weakness suggestive of myopathy or PHT were observed.

To further investigate the relationship of PHT and hypokalaemic myopathy, the authors sought cats with

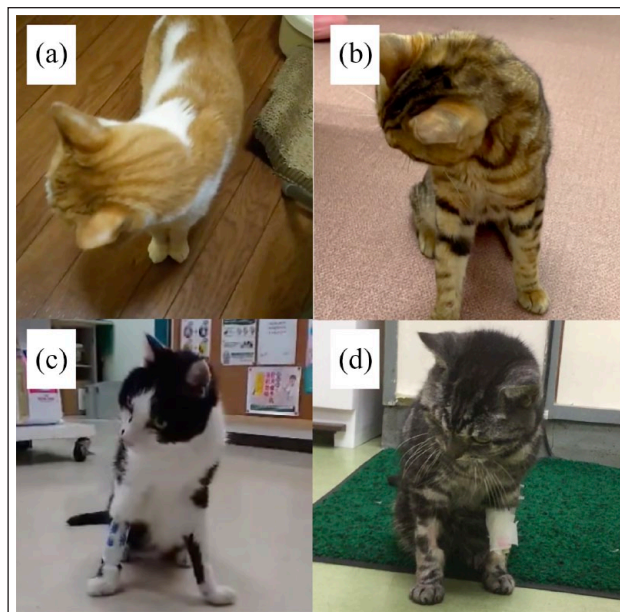


Figure 1 (a–d) Still images captured from videos of cases 1, 7, 10 and 11, respectively. The head is seen tilting to the left when the head of the cats turned to the right; positioning head tilt is observed clearly in cases 1 and 7 and mildly in cases 10 and 11

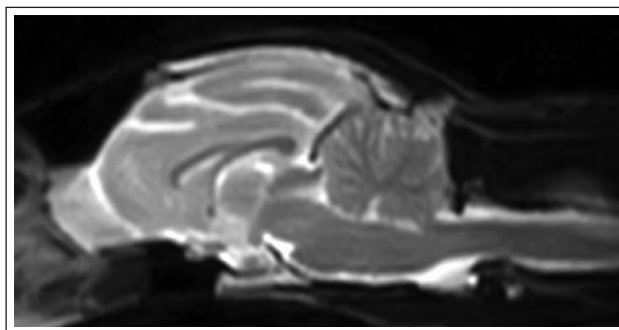


Figure 2 Mid-sagittal brain T2-weighted magnetic resonance image of case 1. No abnormality is evident

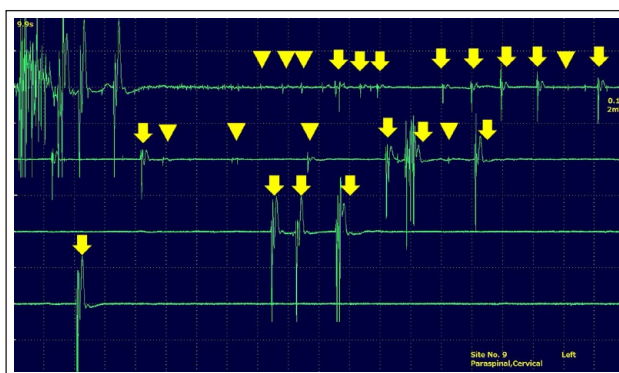


Figure 3 Needle electromyogram of the cervical left paraspinous muscle. Fibrillation potential (arrowheads) and fasciculation potential (arrows) are found in the muscle

hypokalaemic myopathy using social networking sites (Facebook) and personal emails. The authors obtained videos and clinical information of cats that fulfilled our search criteria. The inclusion criteria were as follows: a cat with hypokalaemia; myopathic signs, such as characteristic posture with cervical flexion and generalised weakness consistent with myopathy; and resolution of weakness after potassium correction. Clinical data included breed, sex, age of onset, diet at onset, complete blood count, blood chemistry and other clinical examination results. MRI, EMG and biopsy were not performed in primary care clinics.

In total, data on 14 feline cases, including case 1, were obtained; the breed, age, sex, cause of hypokalaemic myopathy, serum potassium concentration and serum creatine kinase level data are summarised in Table 1. Other blood chemistry data and haematological data on which a clinical diagnosis was based are summarised in the supplementary material. Twelve domestic shorthair cats, a Munchkin and a Scottish Fold, were included. Nine males, eight of which were castrated, and five spayed females were included in the investigation. The age of one cat was uncertain; the median age at the time of diagnosis for the remainder was 12 years (range 3–20 years).

The most common cause of hypokalaemic myopathy was CKD ($n = 8$); other causes were severe diarrhoea ($n = 2$), anorexia caused by feline viral rhinotracheitis ($n = 1$) and suspected primary aldosteronism ($n = 1$); in two cats, the cause was not diagnosed. Three different instruments were used to measure serum potassium concentration (reference ranges: 2.9–4.5, 3.4–4.6 and 3.5–5.8 mmol/l, respectively) and cases with measurements below the lower limit of the reference range were diagnosed as hypokalaemia. The median serum potassium concentration was 2.45 mmol/l (range 1.6–3.0 mmol/l). Serum creatine kinase activity was measured in 11 cases; the median was 720 U/l (range 215–>2000 U/l). In nine cases, activity exceeded the upper reference limit of the measuring instrument. In all 14 cases, myopathic signs such as cervical flexion and generalised weakness resolved after potassium correction.

Evaluation of videos

Most of the cases did not move spontaneously at the time of diagnosis of hypokalaemic myopathy but adopted a recumbent or prone position. In these cases, videos were taken and immediately evaluated when potassium correction enabled them to support themselves on all four

Table 1 Data on breed, age, sex, cause of hypokalaemic myopathy, serum potassium concentration, serum creatine kinase level, degree of cervical flexion, degree of positioning head tilt and outcome of 14 feline cases

Case	Breed	Age (years)	Sex	Diet at onset	Cause of HM	K (mmol/l)	CK (U/l)	Degree of CF	Degree of PHT	Outcome
1	DSH	5	MC	CCF	CKD	2.4	NE	Clearly	Clearly	PHT disappeared
2	Munchkin	5	MC	PD for LUTD	CKD	2.5	NE	Clearly	Clearly	PHT disappeared
3	DSH	3	MC	PD for liver disease	Unknown	2.6	>2000	Clearly	Clearly	PHT disappeared
4	DSH	14	FS	CCF	CKD	3	672	Clearly	Clearly	PHT disappeared
5	DSH	9	FS	CCF	CKD	2.4	267	Clearly	Clearly	PHT disappeared
6	DSH	16	FS	PD for renal disease	Anorexia (FVR)	2.1	839	Clearly	Clearly	PHT disappeared
7	DSH	Unknown	M	Unknown (stray cat)	Severe diarrhoea	1.6	1770	Clearly	Clearly	PHT disappeared
8	DSH	8	MC	PD for allergic dermatitis	CKD	2.2	720	Clearly	Clearly	PHT disappeared
9	Scottish Fold	12	MC	CCF	Suspected PA	2.9	>2000	Clearly	Clearly	PHT disappeared
10	DSH	14	MC	PD for gastrointestinal disease	Severe diarrhoea	1.8	NE	Mild	Mild	PHT disappeared
11	DSH	18	MC	CCF	CKD	3	574	Mild	Mild	PHT disappeared
12	DSH	18	FS	PD for renal disease	CKD	2.8	215	Mild	Mild	PHT disappeared
13	DSH	11	MC	PD for LUTD	Unknown	2.8	966	Mild	Mild	PHT disappeared
14	DSH	20	FS	Jerky, boiled chicken, cheese for cats	CKD	2	536	Mild	Mild	PHT disappeared

CCF = commercial cat food; CF = cervical flexion; CK = serum creatine kinase level; CKD = chronic kidney disease; DSH = domestic shorthair; FS = spayed female; FVR = feline viral rhinotracheitis; HM = hypokalaemic myopathy; K = serum potassium concentration; LUTD = lower urinary tract disease; M = male; MC = castrated male; NE = not examined; PA = primary aldosteronism; PD = prescription diet; PHT = positioning head tilt

limbs. Cervical flexion was clear in nine cases and was mildly present in five cases. PHT was clear in nine cases and mildly present in five cases and corresponded to the observations of cervical flexion. The degree of cervical flexion and PHT and outcome after treatment are summarised in Table 1. The extent of PHT in cats with hypokalaemic myopathy is presented in Figure 1, and in Videos 1–4 in the supplementary material.

PHT after potassium correction

In all cats, PHT resolved along with other signs related to myopathy, such as cervical flexion and generalised weakness, after electrolyte correction.

Discussion

Typical clinical signs, such as cervical flexion and generalised weakness, clinical pathologic data and response to treatment indicate a diagnosis of hypokalaemic myopathy caused by multiple pathologies in the present feline cases. Myopathy of any aetiology, anorexia and non-muscle pathology may also cause creatine kinase elevation. Creatine kinase elevation is considered an indication of muscle damage but significant pathologic changes in muscle have not been reported in cats with hypokalaemic myopathy.¹⁴ Serum creatine kinase activity in two cases did not exceed the reference range of the measuring instrument. However, elevated creatine kinase levels are not observed in all cases of hypokalaemic myopathy.¹³

In all the cases reported here, PHT and other signs related to hypokalaemic myopathy resolved after recovery from hypokalaemia. No NU abnormalities (where a lesion would cause PHT^{1,2}) were detected by MRI in case 1. The clinical outcomes in the present cases suggested that PHT was related to hypokalaemic myopathy and was reversible. Mild PHT is present in cats described in the supplementary videos of a review article on hereditary hypokalaemia in Burmese kittens (see Video 3 in Malik et al)¹⁶ and a cat with hypokalaemic myopathy in a previous publication (see Video 5–68 in De Lahunta et al).¹⁷ Weakness in the cervical muscles in these cats, and in cases 10–14 in the present study, is thought to be milder than that of cases 1–9. Mild PHT in cats with mild weakness and clear PHT in cats with severe weakness indicates that the sign is related to myopathy. There is no information on PHT in the two references cited above^{16,17} as a possible mechanism of PHT had not been postulated and the abnormal head positioning was not reported.

The mechanism of the PHT in the present feline cases is unclear. Most metabolic disorders, such as hypokalaemia, would be expected to cause generalised (and likely bilateral) abnormality. With regard to pathways related to PHT,^{1,2} we suggest that PHT in the present feline cases with hypokalaemic myopathy could be explained by the following hypothesis. In order to maintain the equilibrium of the head when it is moving, the vestibular nuclei

contract the oblique and rectus capitis muscles bilaterally through the vestibulospinal tract based on the information of movement from the vestibular apparatus.^{1,2} The function of the NU is to inhibit the reflexive excitation of the vestibular nuclei and to initiate appropriate muscle contraction. In order to achieve this function, the NU needs information on how much to inhibit the excitation of the vestibular nuclei. Actual head position is detected by the proprioceptive receptor (muscle spindle) of the obliquus and rectus capitis muscles. The muscle spindles of these muscles transmit information on the changes in lengths of the cervical muscles (ie, the actual tilt of the head) to the NU through the spinocuneocerebellar tract.^{3–8} Thus, the degree of inhibition of the vestibular nuclei to maintain the equilibrium of the head when it is moving is determined by a comparison of information on head movements from the right and left vestibular apparatus with information on the actual head tilt from the muscle spindles of the oblique and rectus capitis muscles. Therefore, if the muscle spindles malfunction, information on the changes in cervical muscle length is not sent to the NU; consequently, the NU judges that muscle tension is insufficient and does not produce the output to inhibit the vestibular nucleus.

Muscle spindles are highly specialised stretch receptors distributed throughout the skeletal muscles. These spindle-shaped receptors are made of several small skeletal muscle fibres often referred to as intrafusal fibres. For the central nervous system to recognise sensory stimuli, sensory receptors must convert a stimulus into neural activity.¹⁸ It has been reported that reduction and eventual disappearance of the dynamic overshoot of receptor potential occurs in isolated frog muscle spindles in a potassium-free solution.^{19,20} Dysfunction of muscle spindles in the obliquus and rectus capitis muscles bilaterally, as well as that of the general skeletal muscle fibres, is believed to be characteristic of hypokalaemia (ie, hypokalaemic myopathy). As a result, information on cervical muscle tension is not sent to the NU and, by the above mechanism, the heads of these cats tilt towards the opposite side of their movement. Proprioceptive system deficit owing to muscle spindle dysfunction partially consistent with this hypothesis is suggested in a large number of human muscular dystrophy patients. They have symptoms such as postural instability, sudden falls and poor manual dexterity.^{21–24}

We considered, but rejected, other possible causes for PHT in the present cases. Cerebellar abnormalities, including malformation, degenerative diseases, encephalitis and tumours affecting the NU, were ruled out because of the acute onset of PHT and its disappearance after potassium correction. Cerebellovascular diseases were excluded because there were no other cerebellar signs seen. Cerebellar trauma was ruled out based on the clinical history of the cats. There were no cases of

suspected diet-induced thiamine deficiency, although one cat had an unknown dietary history, and all patients improved without thiamine supplementation. Although uremic polyneuropathy in humans is described in the literature, haemodialysis and transplantation are required to reduce the prevalence and severity of peripheral neuropathy in these patients.²⁵ Therefore, uremic neuropathy was excluded.

Although the anaemia, hypokalaemia, megacolon and diarrhoea observed in the present cases have not been reported to cause cerebellar disorders or neuropathy in humans and animals, we cannot rule out that NU dysfunction or a bilateral spinocerebellar dysfunction caused by an unknown mechanism related to them could be present in the current cases.

The limitations of this study include the small number of cases analysed and the lack of muscle pathological evaluation, including that of intrafusal fibres. A detailed observation of the clinical signs and course in a larger number of cases with similar characteristics to those of the present study is warranted. However, it may be difficult to detect pathological changes in muscle biopsy specimens. Previous studies identified no abnormalities or only mild abnormalities in the muscles of cats with hypokalaemic myopathy.^{3,4,14} In addition, it is ethically problematic to perform an invasive biopsy requiring anaesthesia on cases diagnosed with hypokalaemic myopathy based upon signalment, historical and clinical findings and resolution of clinical signs with potassium supplementation to validate the conclusions of this study. The possibility cannot be ruled out that weakness of the cervical muscles alone may be the cause of the inability to maintain head equilibrium when the head is turned to the side. Behavioural posturing of the head to increase the visual field of view can also cause head tilt in cats with weakness.

The mechanism of weakness/myopathy in association with hypokalaemia is not yet fully understood. It is unclear whether PHT would be expected to be a clinical feature of other cases of generalised myopathy. Proprioceptive system deficit owing to muscle spindle dysfunction is suggested in human muscular dystrophy patients.^{21–24} This suggests that PHT may also be seen in dogs and cats with muscular dystrophy. To verify whether PHT is also observed in other muscle diseases, such as muscular dystrophy and myasthenia gravis, more specific observations are warranted.

Conclusions

This is the fourth study describing this clinical neurological abnormality and there is still very limited published information about this neurological sign. Although PHT has been reported to reflect lesions localised in the NU, hypokalaemic myopathy was suspected as the cause of

PHT in the present feline cases. The recognition of these clinical signs and the proposed mechanism for PHT may alert veterinary clinicians to the presence of hypokalaemic myopathy in cats, as well as help neurophysiologists acquire further understanding of the mechanism of equilibration of the head. Further observations and investigation may help in determining more precisely the mechanism for PHT in cats with hypokalaemic myopathy.

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Supplementary material The following files are available online:

Video 1: Case 1.

Video 2: Case 7.

Video 3: Case 10.

Video 4: Case 11.

File 1: Summary of blood chemistry data and haematological data.

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Ethical approval The work described in this manuscript involved 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*. 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) for all procedure(s) undertaken (prospective or retrospective studies). For any animals or people individually identifiable within this publication, informed consent (either verbal or written) for their use in the publication was obtained from the people involved.

ORCID iD Shinji Tamura  <https://orcid.org/0000-0002-1005-2598>

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