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CASE REPORT

Companion or pet animals

Hyperthermia in a Chow Chow under general anaesthesia for magnetic resonance imaging

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Abstract

A 5-year 7-month-old, entire, male Chow Chow presented with paraparesis and ataxia due to a previously diagnosed T11–T12 spinal diverticulum. Due to the progression of clinical signs, magnetic resonance imaging was indicated to reassess the lesion. Preoperative rectal temperature was unable to be assessed due to temperament; however, it was likely the patient would be hyperthermic as it had been hyperthermic (40.6°C) under general anaesthesia 4 months earlier. Consequently, measures were taken to attempt to reduce body temperature before general anaesthesia. While under general anaesthesia for imaging, the patient was confirmed to be markedly hyperthermic. This report details the management of a patient with hyperthermia under general anaesthesia. The patient was gradually cooled before recovery from anaesthesia. Once recovered from anaesthesia and normothermic, the patient was discharged home the same day. Follow-up confirmed no adverse effects.

BACKGROUND

Body temperature is a vital sign that is strictly regulated to allow normal physiological function in the body, for example, maintenance of coagulation pathways and immune function.[1–3] Fluctuations in body temperature may have detrimental physiological effects that ultimately can have adverse effects on patient outcome.[1] Hypothermia, for example, may impair immune function and inhibit numerous inflammatory responses.[3] Hyperthermia may increase metabolic demand and cardiovascular workload, making it more dangerous than a similar degree of hypothermia.[1] Furthermore, hyperthermia affects coagulation leading to a prothrombotic state, which, in extremes, may lead to consumption coagulopathy resulting in simultaneous intravascular thrombotic obstruction and uncontrolled bleeding.[2]

While under general anaesthesia (GA), a change in body temperature is common with hypothermia being much more likely to occur than hyperthermia.[1]

Increase in body temperature may be categorised as controlled or uncontrolled. A controlled increase occurs when pyrogens act on the hypothalamus to increase the temperature set point, whereas an uncontrolled increase may occur due to drugs impairing the thermoregulatory response mechanisms or by extreme exposure to heat from an environmental source.[4]

Hyperthermia may be defined as core temperature exceeding normal values. In dogs, the normal reference range (ref) is considered to be 37.6°C–39.3°C; this is different from pyrexia, which is a regulated increase in core body temperature secondary to the effects of pyrogens on the hypothalamus, increasing the temperature set point.[1,5,6]

CASE PRESENTATION

A 5-year 7-month-old, entire, male Chow Chow, with body mass 28.2 kg, presented for investigation of ongoing paraparesis and ataxia. Magnetic resonance imaging (MRI) 4 months previously had diagnosed a T11–T12 spinal diverticulum, which was elected to be medically managed with an anti-inflammatory glucocorticoid course. Initially, the patient was prescribed prednisolone (0.5 mg/kg, Prednicare, Animalcare) orally (PO) once daily for 7 days, tapering to 0.35 mg/kg PO once daily until re-presentation due to there being no significant improvement in clinical signs. The patient required GA for computer tomography (CT) and repeat MRI.

Review of the previous anaesthesia record highlighted an increased temperature during MRI, with the highest recorded temperature of 40.6°C, which reduced to 40.4°C by the end of anaesthesia and was recorded as 39.8°C in the immediate recovery period. At initial presentation, 4 months previously, on pre-anaesthetic examination the patient was panting and had a heart rate of 124 beats per minute. As with the reported case pre-anaesthetic temperature was not taken due to patient temperament. Anaesthesia protocol for initial MRI included

premedication with medetomidine (0.01 mg/kg, Medetor, Virbac), methadone (0.2 mg/kg, Comfortan, Dechra) administered intramuscularly (IM), induction with propofol (2 mg/kg, PropoFlo, Abbott) intravenously (IV) and anaesthesia maintained with isoflurane (IsoFlo, Abbott) vaporised in 100% oxygen. Other than hyperthermia, the only complication to report would be mild hypercapnia as end tidal carbon dioxide ($ETCO_2$) was 48–58 mmHg (6.4–7.7 kPa); however, no intervention was made.

At re-presentation, on pre-anaesthetic examination the patient was evidently stressed with a heart rate of 128 beats per minute and panting so an accurate respiratory rate (*f*R) was difficult to ascertain. Oral mucous membranes were pigmented, as is normal for the breed, therefore capillary refill time was difficult to assess. Due to temperament and demeanour, temperature was not measured or recorded as part of the pre-anaesthetic examination. As the patient had a history of hyperthermia, before pre-anaesthetic medication fans were directed at the kennel and the air conditioning was turned on to the coolest setting in the kennel area in an attempt to avoid increasing body temperature.

Pre-anaesthetic medication consisted of medetomidine (0.01 mg/kg, Medetor, Virbac), acepromazine (0.01 mg/kg, ACP, Elanco) and butorphanol (0.2 mg/kg, Dolorex, MSD Animal Health) administered IM into the epaxial muscles of the neck. Sedation was negligible, so a further 0.01 mg/kg medetomidine was administered IM 20 minutes later, which provided mild but adequate sedation to allow cannulation of the right cephalic vein with a 20-gauge intravenous catheter. An additional dose of medetomidine (0.005 mg/kg) was administered IV, which achieved a good level of sedation. Anaesthesia was induced with alfaxalone (Alfaxan, Jurox) to effect, a total dose of 1 mg/kg IV was administered. The trachea was intubated with a cuffed 10.5-mm internal diameter endotracheal tube. The endotracheal tube was connected to a small animal circle breathing system, and anaesthesia was maintained with isoflurane vaporised in 100% oxygen with a fresh gas flow of 4 L/min.

The patient was positioned in dorsal recumbency on a cushioned MRI table, and a torso coil (dStream Torso Coil, Philips) was fitted to enhance image quality. Physiological monitoring was via multiparameter monitor (Philips Expression IP5) and included percentage arterial haemoglobin oxygen saturation (SpO_2), $ETCO_2$ tension, end tidal isoflurane concentration (ETiso), non-invasive arterial blood pressure, via oscillometry and oesophageal temperature. In addition, the patient was administered Hartmann's solution (Aqupharm 11, Animalcare), which had been stored at room temperature, IV at a rate of 4 ml/kg/h.

Immediately after placement of the oesophageal temperature probe, the patient's temperature was recorded at 41.3°C. The fan system in MRI was increased to maximum and a heat and moisture exchanger (HME) was removed and replaced with a capnograph connector. Ice cold packs (approximately 0°C), wrapped in tissue paper to protect the patient's skin, were placed around the head and inguinal region. Surgical spirit was sprayed on all footpads in an attempt to cool the patient. The MRI scan was initiated while active cooling was in progress and oesophageal temperature was monitored. Temperature decreased to 41.2°C and 20 minutes later, additional ice packs were used and surgical spirit re-applied to the footpads. After a further 15 minutes, the patient's temperature was 41.1°C at which point the decision was made to abandon the MRI scan and actively cool the patient. The patient was spontaneously ventilating throughout this time; $ETCO_2$ was between 56 and 62 mmHg (7.5–8.3 kPa), ETiso was 1.1%–1.4%, SpO_2 was 98%–100%, mean arterial blood pressure was 82–89 mmHg, HR was 41–58 beats per minute and *f*R was 11–13 breaths per minute.

LEARNING POINTS/TAKE HOME MESSAGES

- It is important to monitor the patients' body temperature before and during anaesthesia, particularly in stressed patients with dense coats.
- If hyperthermia is noted, discontinue active warming of patient. If this is unrewarding, begin active cooling of the patient.
- If patient has been hyperthermic (>41°C) intraoperatively, consider checking for adverse effects, for example, monitoring urine output and checking serum biochemistry in case of acute kidney injury.
- In cases of sudden, marked increase in end tidal carbon dioxide concurrent with increased temperature, suspect malignant hyperthermia and take appropriate action.

TREATMENT

The patient was removed from the MRI scanner room and moved to a separate prep room. Isoflurane anaesthesia was discontinued, and GA was instead maintained with a propofol infusion (Propofol-Lipuro, Virbac) at 0.1–0.2 mg/kg/min. The breathing system was exchanged from a small animal circle to a parallel lack and fresh gas flow was maintained at 4 L/min to prevent rebreathing of carbon dioxide and increase elimination of isoflurane while the patient continued to spontaneously ventilate. Ice packs were placed in the axillary and inguinal regions and attempts were made to reduce ambient temperature, with air conditioning and fans directed at the patient.

Once the patient was changed to being on a propofol infusion, $ETCO_2$ decreased to 48–56 mmHg (6.4–7.5 kPa), and consequently, the patient continued to spontaneously ventilate without intervention. Given that the patient demonstrated only mild hypercapnia ($ETCO_2$ 45–59 mmHg) during spontaneous ventilation, the decision was made not to intervene and allow permissive hypercapnia. Mild permissive hypercapnia is not considered to be physiologically detrimental and may even have favourable effects on circulation.[7]

At this point, a venous blood sample was taken (EPOC, Siemens), which demonstrated a hyperlactataemia of 4 mmol/L (ref: <2 mmol/L) and a respiratory acidosis, pH 7.24 (ref: 7.35–7.45), $PaCO_2$ 67 mmHg (8.9 kPa) (ref: 35–45 mmHg, 4.7–6.0 kPa). An intravenous bolus of Hartmann's solution was administered at a rate of 10 ml/kg over 10 minutes. The end of the fluid drip line, just before it connected to the cannula, was wrapped around an ice pack. Respiratory acidosis would have occurred during anaesthesia most likely due to the respiratory depressant effects of isoflurane initially

followed by propofol.[8,9] As hypoventilation was considered the cause of the respiratory acidosis and the hyperlactataemia had been treated with fluid boluses, once the patient was recovered from anaesthesia, no further blood gases were taken. We were concerned further blood samples would be stressful for our patient and potentially lead to an increase in body temperature. Renal parameters were within normal limits as follows: urea 4.8 mmol/L (ref: 3.6–9.3 mmol/L) and creatinine 78 μmol/L (ref: 44–115 μmol/L). Renal parameters were not checked after anaesthesia, but at follow-up telephone consultation, the patient had no clinical signs of renal disease, such as polyuria/polydipsia. Furthermore, we were concerned about the patient re-attending the hospital for repeat blood sampling, which could result in a further hyperthermic event.

Twenty minutes after leaving MRI, the patient's rectal temperature was 41.0°C. Further interventions were made, including bladder lavage with saline, which had been stored in a fridge kept at 0°C–4°C. Bladder catheterisation was performed aseptically, with an 8-Fr 600-mm dog urinary catheter (Portex) and the bladder emptied. Following emptying, 500 ml of cool saline was instilled into the bladder, left in situ for 5 minutes, then removed and repeated three times. Immediately following this, rectal temperature reduced to 39.9°C.

Following this initial stabilisation of hyperthermia, the decision was made to proceed with a CT scan in order to rule in or out any vertebral malformations that may be contributing towards the patients underlying neurological condition while the patient remained under GA. Following the CT scan, the propofol infusion was discontinued and the patient recovered from anaesthesia. Paracetamol (10 mg/kg, Perflagan, BMS Pharmaceuticals) was administered IV and a further IV bolus of Hartmann's solution (10 mg/kg) was administered over 10 minutes. To hasten recovery from anaesthesia, atipamezole (0.025 mg/kg, Revertor, Virbac) was administered IV. During the recovery period, rectal temperature continued to decrease from 39.4°C to 39.1°C; however, 30 minutes following atipamezole administration, the patient remained intubated. Atipamezole (0.05 mg/kg) was administered IM and patient was suitably extubated within 10 minutes, in total, 45 minutes after cessation of propofol infusion. Vital parameters in recovery, following extubation, were HR 60 beats per minute, *f*R 30 breaths per minute and rectal temperature of 38.5°C.

OUTCOME AND FOLLOW-UP

Following recovery, the patient demonstrated mild twitching for approximately 10–15 minutes and significant ataxia; however, this was likely a combination of effects of the propofol infusion as well as the underlying condition. Evidence suggests patients recovering from propofol anaesthesia can display neurological signs such as muscle tremors/twitching, which resolve without medical intervention.[10] The patient was discharged home later that day.

Follow-up via telephone conversation 2 weeks later confirmed that the patient was bright, alert and responsive with normal appetite and coping well with mobility issues. A telephone update 4 months later detailed the owners were now considering surgical intervention as a treatment option and opted to seek a second opinion.

DISCUSSION

Thermoregulation

Mammals maintain normal body temperature by producing heat via vasoconstriction, shivering and dissipate excess metabolic heat to the environment via evaporation and conduction.[11,12] The majority of mammals maintain desired body temperature via peripheral vasodilation and the evaporation of sweat.[11,12] Dogs lack extensive sweat glands and rely on other methods of heat dissipation. Evaporation of water from moist mucous membranes of the respiratory tract dissipates excess metabolic heat in dogs, which is as effective as sweating for thermoregulation; however, less efficient.[12] To maximise water evaporation and heat dissipation, the amount of air flowing over the oral and nasal mucosa must be increased. Panting is an active process; dogs use very low tidal volumes at a rapid rate to increase air flow across moist mucosal surfaces. However, this further increases metabolic rate and heat production, which can be an issue particularly in brachycephalic breeds.[12] Hyperthermic patients under GA may hyperventilate in an attempt to reduce their body temperature; however, as panting requires air movement over moist mucosal surfaces, this method is ineffective when the trachea is intubated.[13]

Well-insulated breeds, such as Chow Chows and St. Bernards, may struggle to maintain normal core body temperature, making them more prone to hyperthermia, especially in a warm, stressful environment.[4] Chow Chows have a double coat consisting of primary and secondary hair.[14] Primary hair, also known as 'guard hair', protects against snow and are even able to shed water.[15] In winter, the secondary hair, also known as the undercoat, lies close to the skin trapping a layer of air close to the body.[15,16] This air is warmed by body heat until it reaches ideal body temperature, which is maintained in cold climates.[16] In summer, the undercoat is shed. Without this, cool air can circulate through the guard hair, allowing the skin to be cooled.[15] On reflection, this case was seen during the summer, so we may assume the secondary hairs were sparser at this time. However, due to positioning of the patient in the MRI and the addition of a coil, it is unlikely sufficient airflow was able to circulate through the guard hair to allow a normal body temperature to be maintained.

Differentiating hyperthermia versus pyrexia

Hyperthermia is the result of heat being produced being in excess of heat loss via radiation, evaporation, convection and conduction.[4] Hyperthermia is categorised as having a core body temperature of >41°C and occurs when normal core temperature cannot be maintained via thermoregulatory response mechanisms.[17] Pyrexia is an increase in the thermoregulatory set point secondary to a systemic inflammatory response initiated by exogenous pyrogens such as infectious agents and immune complexes.[18] Pyrexia needs to be distinguished from hyperthermia. Due to normal thermoregulation mechanisms being overwhelmed in hyperthermia cases, temperature levels encountered during hyperthermia are usually higher than those with pyrexia.[18] The temperature in this case is thought to be due to hyperthermia, as the recorded body temperature was in excess of 41°C, likely due to patient being

unable to dissipate heat effectively or as a result of excessive metabolic heat production.

Contributing factors

Breed and temperament

The breed and temperament of the patient likely predisposed them to hyperthermia. First, as a Chow Chow, the double coat may have reduced heat dissipation. The patient was stressed on presentation and stress has been proven to increase body temperature.[19] Animal studies have demonstrated that exposing mice or rats to stressors such as changing their environment, removing cage-mates or addition of an intruder increases core body temperature (T_c).[19] Acute psychological stress, as this is termed, has been demonstrated to increase T_c by up to 2°C within 30 minutes when laboratory animals were exposed to dominant animals within their environment.[19] Similarly, studies have reported that T_c is higher in humans before emotional events than T_c after these events.[19] This increase in body temperature may have increased the temperature of the air trapped between the secondary hair and the body wall leading to a higher than normal temperature and reducing heat dissipation via convection. Furthermore, there was no indication from the history or from the clinical signs the patient presented with that would suggest the patient would be pyrexic.

Anaesthetic drugs

Anaesthetic agents may alter body temperature via their mechanisms of action while also impairing the body's autonomic responses to temperature derangement.[1] For example, isoflurane has been demonstrated to impair thermoregulatory vasoconstriction in paediatric patients.[1] Medetomidine, an α_2-adrenoreceptor agonist, was administered both IM and IV to provide sedation before induction. Action of α_2-agonists at peripheral α_2-adrenoreceptors leads to an increase in systemic vascular resistance (SVR).[20] As vasoconstriction results in decreased blood flow to the skin surface, this leads to a reduction in conductive and convective heat loss, which could have contributed to hyperthermia in this case.[21] Acepromazine, a phenothiazine, was also administered. Acepromazine antagonises α_1-adrenergic receptors, resulting in vasodilation and decreased SVR.[22] Vasodilation leads to transfer of heat from the central compartment to the periphery and ultimately the skin surface, where heat is lost via convection.[21] Volatile anaesthetic agents, such as isoflurane, which were initially used for maintenance of anaesthesia, also cause vasodilation and may contribute to heat loss via similar mechanisms.[23] Additionally, while under GA, behavioural responses to an increase in core body temperature, such as panting or moving to lie on a cold surface, are eliminated.[1,24]

Diagnostic procedures

During MRI, most of the radiofrequency power transmitted for imaging is transformed into heat, due to resistive losses, which can lead to an increase in body temperature.[25] The degree of increase in tissue temperature is dependent on multiple factors, including the ability of the patients' thermoregulatory system to cope with thermal challenge, duration of exposure, as well as ambient temperature within the MRI scanning room.[25] If thermoregulatory mechanisms are overwhelmed, as they were in this case, this can lead to accumulation of heat within tissues and an increase in overall tissue temperature.[25] Heat from MRI did not cause hyperthermia in this case, as the patient was hyperthermic before starting the MRI scans. It may have contributed to body temperature not decreasing despite active cooling of the patient while in the MRI scanner.

Inadequate fluid intake

Inadequate fluid intake due to stress or unavailability can aggravate hyperthermia, which could have been a contributing factor in this case.[4] The patient had been in transit to the hospital that day and had reduced access to drinking water. Additionally, the patient was panting, as noted on pre-clinical examination, which will have contributed to further water loss via evaporation of water from the respiratory tract.[12]

Temperature management

Unfortunately, due to temperament, temperature was not taken preoperatively; however, in hindsight this would have been useful to assess if the patient was already hyperthermic on presentation. Ideally rectal temperature should have been taken following pre-anaesthetic medication once the patient was sedated; however, the effect of the initial premedication was minimal. Consequently, it was not possible to check rectal temperature. Medetomidine (0.005 mg/kg, IV) was administered, with a moderate effect, followed a few minutes later by induction of anaesthesia. First oesophageal temperature probe recording (41.3°C) was within 5 minutes of induction. On reflection, if hyperthermia had been confirmed before induction of anaesthesia, it is unlikely the patient would have been anaesthetised.

Iatrogenic hyperthermia

Most commonly, a patient's core temperature will decrease during anaesthesia due to depression of the thermoregulatory centre, reduced metabolic rate, muscle inactivity and in some cases, drug-induced peripheral vasodilation.[26] All these factors contribute to redistribution of heat by increasing the temperature gradient between the core and peripheral tissues.[27] It is important to take preventive measures to minimise heat loss as hypothermia can have pronounced effect on drug metabolism, cardiac function and recovery times.[26] Prewarming patients before anaesthesia to raise the temperature of the periphery thereby decreasing the temperature gradient between the core and peripheral tissues has been proven to be effective in delaying hypothermia in humans and rats.[27,28] In some patients, iatrogenic hyperthermia can occur during anaesthesia.[4] The use of low-flow anaesthesia and HMEs may lead to the temperature of inspired gases to increase.[4] HMEs are a passive form of maintaining heat and moisture by storing

heat and moisture from exhaled gases; however, in a case of hyperthermia, a HME can contribute to a patient's inability to dissipate heat from the respiratory tract via evaporation.[29] One study by Hofmeister et al. found that use of a HME did not contribute to maintenance of body temperature in dogs undergoing GA for orthopaedic procedures; however, HMEs should be removed in cases of hyperthermia to encourage heat loss from the respiratory tract, which will contribute to cooling the patient.[29,30] In addition to low-flow anaesthesia, the chemical reaction between soda lime and carbon dioxide in a circle rebreathing system will generate heat, thus warming gas mixture within the breathing system.[4] Using a non-rebreathing system or increasing the fresh gas flow when using a rebreathing system will increase elimination of warm gases and may contribute to heat loss.[4]

If these initial steps do not have the desired effect, initiation of active cooling is advised.

Active cooling

Methods of active cooling used in this case included spraying alcohol on the foot pads and using ice packs to increase heat loss via conduction; however, care must be taken to avoid direct contact between ice packs and the skin.[4] Application of ice packs to the skin may cause local vasoconstriction, which may mitigate heat transfer via the skin surface. In human studies, the use of chemical cold packs with a temperature of 13°C was not associated with vasoconstriction in non-haired skin areas, therefore cool packs rather than ice packs would be recommended.[31]

Other non-invasive methods would be placing a fan near the patient to dissipate heat via convection; evidence on how effective this is in dogs is limited. In this case, the inbuilt fan system in MRI was on maximum flow, an additional free-standing fan would have been impractical for safety reasons. A fan was placed near the patient before induction of anaesthesia and after the patient was removed from the MRI scanning room. Administration of cold intravenous fluids may also help with cooling, this can be achieved by wrapping the IV fluid line around an ice pack; however, the evidence for how effective this is at reducing body temperature in dogs is limited.[4] Cold intravenous saline has been shown to reduce body temperature in paediatric patients with acute brain injury. When mean volume of 18 ml/kg was given as an infusion over 10–15 minutes, body temperature reduced on average by 1.7°C.[32]

Clipping the coat, especially in thick-coated breeds, could increase heat loss via conduction. Other options were instigated first in this case as drastic clipping could be aesthetically unfavourable and unexpected by the owners; however, this method was in the plan should more aggressive active cooling be required. Administration of cold water over the body surface should be avoided as this can lead to vasoconstriction of superficial blood vessels hindering heat loss.[4] Similarly, the application of wet towels should be avoided as although they may initially cool the skin, they may also lead to local vasoconstriction. Additionally, they can act as a barrier trapping heat between the towel and patient's body surface.[33]

Use of cool fluids to lavage body cavities can contribute to reducing body temperature via conduction. For a patient undergoing abdominal surgery, lavage of the exposed abdominal cavity with cool fluids would be a suitable option.[4] A recent study in human medicine compares different methods to actively cool patients under GA. Gastric lavage involved instilling 500 ml of chilled sterile water via an orogastric tube and allowing the water to sit for 5 minutes before aspiration, leading to a reduction in body temperature of 1.5°C. Bladder lavage was performed in a similar way using a urethral catheter to instil 300 ml of Ringer's solution chilled to 4°C–8°C into the bladder, allowing it to sit for 5 minutes before aspiration, leading to a reduction in body temperature of 0.8°C. Both these methods were repeated every 10 minutes for 40 minutes. This study concluded that bladder lavage provides less heat transfer; due to the bladder's small surface area and relatively low blood flow; however, no adverse effects were reported. Conversely, while gastric lavage appears to be the superior method of cooling, only 30% of volume instilled was able to be re-aspirated, abdominal cramping and severe diarrhoea were reported during the recovery period, which needs to be taken into consideration if using this method of active cooling.[34] Colonic lavage could also be considered as it has a larger surface area than the bladder and a relatively greater blood supply.[34]

Malignant hyperthermia

In any patient under GA, where there is a rapid increase in body temperature unresponsive to active cooling measures, malignant hyperthermia (MH) should be considered.[4] MH is a rare yet life-threatening hyperthermic reaction, which occurs when a patient is exposed to certain pharmacological agents.[6] MH is caused by a mutation of the ryanodine receptor type 1 (RyR1) gene responsible for encoding calcium release channels in the sarcoplasmic reticulum of skeletal muscle.[35,36] Mutation of the RyR1 gene results in excess calcium release into the myoplasm causing a hypermetabolic state.[35] This hypermetabolic state occurs in response to inhalational anaesthetic agents, such as halothane and isoflurane, and the depolarising neuromuscular blocker, succinylcholine.[37]

The following clinical features are reported with MH: increase in $ETCO_2$, increase in body temperature, increases in heart rate from baseline and muscle rigidity.[6] Treatment of MH includes discontinuation of volatile anaesthetic agents and instead maintaining anaesthesia with intravenous agents such as a propofol infusion or recovering the patient from anaesthesia.[4,6] As the patient in this case was hyperthermic (41.3°C) from the onset of anaesthesia and there was no further increase in temperature, MH was considered unlikely. When body temperature did not decrease despite initiation of active cooling measures, interventions were administered in the event of this being a rare case of MH. Following termination of MRI, isoflurane was discontinued, and anaesthesia maintained with a propofol infusion at 0.1–0.2 mg/kg/min. It is also recommended that the patient should be hyperventilated with 100% oxygen, ideally using a non-rebreathing circuit, to increase elimination of the trigger agent and eliminate CO_2 as well as maximise oxygen delivery to tissues.[6] The breathing system was exchanged from a rebreathing system (circle) to a non-rebreathing system (Parallel Lack). A fresh high gas flow was used to prevent rebreathing of expired carbon dioxide and to increase elimination of isoflurane. Also, as fresh gas flow increases, the patient is exposed to cooler

gases, which encourages heat loss from the respiratory tract via convection.[38]

As part of the treatment of MH, dantrolene, a direct acting skeletal muscle relaxant, should be administered at 4–5 mg/kg.[4,39] Dantrolene blocks calcium release from the intracellular sarcoplasmic reticulum, consequently muscle contraction is decreased without an effect on the action potential patterns of the neuromuscular junction.[39] It was not available to be used in this case, as it is not kept in stock in the hospital.

If this patient re-presented for surgical management of its subarachnoid cyst, it may be worth considering genetic testing for MH as part of the preoperative assessment. Canine MH is an autosomal dominant inherited condition caused by a mutation in the RyR1 gene encoding skeletal muscle calcium release channel.[36] Genetic testing is available for canine MH in the United Kingdom (Laboklin, UK).[40] If genetic testing was not an option, given the patients history, it may be prudent to avoid inhalational anaesthetic agents if MH cannot be completely excluded.

Paracetamol

As well as active cooling, paracetamol was administered intravenously. Anti-pyretic drugs, such as paracetamol, act on the hypothalamus, reducing the temperature set point promoting vasodilation to enhance heat loss via conduction.[18] In human studies, it has been demonstrated that paracetamol reduces the level of prostaglandin E_2 in the hypothalamus by inhibiting the enzyme cyclooxygenase; however, this specific mechanism of action has not been fully evaluated in dogs.[41,42] Administration of paracetamol in this case would have been ineffective, as the temperature set point is not elevated in hyperthermia.[4,18] Paracetamol was administered to this patient, as pyrexia could not be completely ruled out as a cause of increased body temperature. On reflection this was not necessary.

Measurement of body temperature

Both oesophageal and rectal temperatures were recorded in this case depending on if the patient was anaesthetised or recovering from anaesthesia. Oesophageal temperature measurements are affected by cooling of the trachea by cold inspired gases as well as inappropriate probe positioning. Rectal temperature varies depending on local blood flow to the rectal wall, placement of temperature probe and presence of faeces.[43] The temperature of the oesophagus responds more rapidly to changes in blood temperature as the probe is closer to the great vessels of the heart compared with rectal temperature.[44] When cooling a hyperthermic patient, rectal temperature will be slower to respond to a reduction in blood temperature. For this reason, active cooling should be terminated once rectal temperature reaches 39.4°C.[45]

Hyperlactataemia

Hyperlactataemia is defined as a lactate measurement of >2 mmol/L as in this case (4 mmol/L).[46] Hyperlactataemia can be categorised as type A and type B, although fundamentally they both occur due to cell mitochondria being unable to process the high levels of pyruvate within the cell.[47] Type A occurs due to tissue hypoperfusion and hypoxia, which may occur in all shock states (hypovolaemic, cardiogenic, obstructive, septic) as well as a result of seizures and regional ischaemia.[47] Type B occurs when there is no tissue hypoperfusion or hypoxia, for example, in cases of excessive exercise, liver disease and diabetic ketoacidosis.[47]

During exercise, muscle temperature increases, which studies have shown to increase glycolytic activity.[48,49] Glycolysis breaks down glucose into two pyruvate molecules, which are then converted to acetyl CoA by pyruvate dehydrogenase before entering the Krebs cycle.[50–52] When there is increased metabolic activity, production of pyruvate exceeds the catalytic activity of pyruvate dehydrogenase, consequently leading to an increase in lactate production even in aerobic conditions.[50,53] Applying this to the case, an excessive increase in body temperature could have contributed to an increase in lactate production within the muscles similar to type B hyperlactataemia seen during excessive exercise.[47–49]

Conversely, glycolysis in anaerobic conditions results in pyruvate being converted to lactate by lactate dehydrogenase more commonly seen in type A hyperlactataemia.[47,52]

Type A hyperlactataemia due to hypovolaemia and consequent tissue hypoperfusion were assumed in this case and treated with a crystalloid fluid bolus. Evaporative heat losses from panting and inadequate fluid intake were considered contributing factors.[54] On reflection, type B hyperlactataemia was conceivably more likely.

Consequences of hyperthermia

If left untreated, hyperthermia can have adverse effects on the brain, heart, liver and kidneys. Hyperthermia may result in impaired enzyme function, denaturation, coagulopathies and cell death. Mild hyperthermia is considered as temperatures below 40°C and may not require treatment, however when temperatures exceed 42°C, oxygen delivery requirements can no longer be met and cell damage starts to occur.[4] Acute kidney injury (AKI) can occur following hyperthermia.[55] Pathogenesis of heat stroke-induced AKIs are multifactorial but likely due to decreased perfusion from dehydration and hypovolaemia, rhabdomyolysis-associated myoglobinuria, direct thermal injury and systemic inflammatory response syndrome (SIRS).[55,56] Heatstroke-induced AKIs are often subclinical at presentation, but can be diagnosed by an increase in renal biomarkers.[23,24]

Hyperthermia may also lead to acid–base imbalance, with metabolic acidosis being the predominant change in 81% of cases, followed by respiratory alkalosis in 55% of cases. Based on a study of 109 patients presenting for heatstroke, prevalence of metabolic acidosis was significantly associated with the degree of hyperthermia, for example, 63%, 95% and 100% at 41°C, 42°C and 43°C, respectively.[57]

Severe hyperthermia may lead to disseminated intravascular coagulopathy and SIRS, which ultimately leads to multiple-organ failure and death. In a case series detailing three dogs undergoing postmortem examination following heatstroke caused by exposure to high environmental temperatures, the most common pathological findings included congestion, haemorrhage and thrombosis of multiple organs. All three cases had died within 6 hours of initial exposure to extreme temperature, emphasising how important it is to

rapidly control hyperthermia once identified to avoid these fatal changes occurring.[17]

Reflections

On reflection, as the patient had been hyperthermic during a previous MRI 4 months earlier, there are a few ways this case could be approached differently. First, it demonstrates the importance of trying to ascertain rectal temperature as part of the pre-anaesthetic clinical examination. If the patient was recognised to have a raised body temperature at this stage, investigations may have been postponed until a later date.

As the patient was evidently stressed on arrival at the hospital, it may have been worth considering administration of sedatives or anxiolytics at home. Trazodone, a serotonin antagonist and reuptake inhibitor, has been used as an anxiolytic and antidepressant in humans.[58] In dogs, trazodone has been used to facilitate calming of patients in postsurgical confinement as well as prompting low-stress handling during veterinary visits in anxious dogs.[58] Trazodone administered 90 minutes before attendance at a veterinary clinic reduces stress associated with handling and examination, which would have been of benefit in this case.[58] Dexmedetomidine oromucosal gel (Sileo, Zoetis) is licensed for the treatment of anxiety associated with noise phobias, it has also been shown to be effective in reducing fear and anxiety in dogs during veterinary visits.[59] Gabapentin has been investigated as an anxiolytic in dogs, it is effective in reducing fear responses in dogs exposed to thunderstorms; however, ataxia was observed as an adverse effect.[60] As the patient in this case report was already presenting with ataxia, there is a risk that gabapentin administration before admission may have affected neurological examination. Managing stressed patients by prescribing anxiolytics for administration before attendance may reduce stress, which is known to exacerbate hyperthermia.[19]

We elected to keep this patient anaesthetised during active cooling as the patient's temperament when conscious may have hindered this process. The patient was recovered once rectal temperature stabilised at 39.9°C.

In conclusion, this case highlights the importance of monitoring core body temperature of patients under GA and management of hyperthermia.

CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

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ETHICS STATEMENT

No ethical approval was required as this is a retrospective description of a case, which was not experimental.

AUTHOR CONTRIBUTIONS

Katherine Robson managed the clinical case during anaesthesia. Heather Jones researched the subject and wrote the manuscript with the support and supervision of Katherine Robson.

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