A 2 year 3 month old FN French Bulldog was presented due to acute collapse and seizure while out on a walk. On arrival the patient was recumbent, unconscious and was actively seizuring. The dog had been previously healthy with no prior history of neurological signs. Seizure activity ceased following administration of 0.5mg/kg diazepam intravenously. On examination the dog was stuporous with a weak gag reflex. Mucous membranes were hyperaemic. Heart rate was 180bpm. Peripheral pulses were synchronous but weak. Systolic blood pressure (measured using Doppler) was 55mmHg. Oxygen saturation measured using pulse oximetry was 91% and increased to 94% with administration of flow-by oxygen. Temperature was 42.5°C and a large volume of melaena was passed during examination.
1) Outline your initial management of this case

An intravenous catheter was placed and following administration of diazepam and cessation of seizuring, a bolus of 20ml/kg of Hartmanns solution was administered over 10 minutes. Active cooling was instituted and the patient was intubated (a combination of fentanyl and midazolam was administered to facilitate intubation). Oxygen was initially provided at a FiO2 of 100% and the oxygen saturation increased to 98%. Blood was collected for a minimum database. A further 20ml/kg of crystalloid was administered following which the heart rate reduced to 100bpm and the blood pressure had increased to 110mmHg. Active cooling was continued until the temperature had reduced to 39.5°C.

2) Differential diagnoses & further diagnostic testing

The problem list and differential diagnoses for this dog included:

- Seizure
  - Intracranial causes
    - Idiopathic
    - Congenital
    - Infectious –bacterial (*Pasteurella, Staphylococcus, Nocardia*), fungal (*Aspergillus, Blastomyces, Coccidioides*), parasitic (*Dirofilaria*), protozoal (*Toxoplasma, Neospora*), rickettsial (*Ehrlichia, Anaplasma*), viral (canine distemper virus)
    - Inflammatory or immune-mediated (meningoencephalitis)
    - Trauma
    - Vascular
      - Haemorrhage (*Angiostrongylus, coagulopathy*)
      - Thromboembolism
  - Extracranial causes
    - Metabolic (hypoglycaemia, hypernatraemia, hyponatremia, hypocalcaemia, hepatic encephalopathy, renal encephalopathy)
    - Nutritional (thiamine deficiency)
    - Drugs/toxins (baclofen, blue-green algae, ethylene glycol, metaldehyde)

- Hyperthermia
Infection
Immune-mediated disease
Neoplasia
Tissue damage
Impaired heat loss
Increased muscular activity
Pathological hyperthermia
Drugs/toxins

• Melaena
  o Ingestion of blood
    ▪ Nasal/oropharyngeal/respiratory disease
  o Gastrointestinal disease
    ▪ Inflammatory or immune-mediated
    ▪ Ulceration
    ▪ Ischaemia
    ▪ Neoplasia
  o Extra-gastrointestinal disease
    ▪ Hypoadrenocorticism
    ▪ Liver disease
    ▪ Disseminated mastocytosis
    ▪ Vasculitis
    ▪ Coagulopathy
      • Drugs/toxins
      • Congenital/hereditary disorder (factor deficiency, von Willebrand’s disease)
      • DIC
      • Thrombocytopenia
      • Platelet function disorder

• Hypoxaemia
  o Reduced inspired oxygen
  o Hypoventilation
  o V/Q mismatch (pneumonia, pulmonary haemorrhage, pulmonary oedema)
  o Cardiovascular (anatomic shunt)
  o Reduced venous oxygen content
    ▪ Low cardiac output/shock
    ▪ High oxygen extraction (ie seizures)
    ▪ Haemoglobin abnormalities

Diagnostic tests performed:

It was not known in this patient whether the hyperthermia was a cause or a consequence of the seizure, particularly as there was no prior history of neurological signs. Therefore initial diagnostics were directed at ruling out extracranial causes of seizure. Minimum database was unremarkable except for a blood lactate of 8.1mmol/L (normal < 2mmol/L). This was suspected to result from a combination of hypoperfusion and seizure activity. Venous blood gas analysis revealed a moderate metabolic acidosis, likely a lactic acidosis. Electrolytes (including ionised calcium) were within normal limits. No free pleural or abdominal fluid was identified on point-of-care ultrasound. ECG revealed a
sinus tachycardia. Blood smear examination revealed a small number of nucleated red blood cells. In the absence of significant regeneration, breed predisposition and unremarkable medical history these were suspected to result from heatstroke. A manual platelet estimate revealed a mild thrombocytopenia (approx. 120 x10^9/L), likely not severe enough to cause intracranial haemorrhage or spontaneous gastrointestinal bleeding alone. PT and aPTT were measured to rule out coagulopathy. PT was within normal range and aPTT was mildly increased. An Angiostrongylus snap test was negative.

Haematology revealed a mild stress leukogram and confirmed the mild thrombocytopenia. Serum biochemistry showed a mild azotaemia and moderate increase in ALT and total bilirubin. Azotaemia was subsequently confirmed to be pre-renal based on a urine specific gravity of >1.050. The increase in ALT and total bilirubin were considered most likely due to hepatic hypoxia but primary hepatic or post-hepatic causes could not be ruled out at this stage. Creatine kinase was markedly increased (suspected due to skeletal muscle injury). Basal cortisol was moderately increased, ruling out hypoadrenocorticism. Urinalysis and urine sediment examination were unremarkable. A faecal sample was collected and submitted for parasitology and culture to rule out an infectious cause of melaena. A Parvovirus snap test was negative. Thoracic radiographs and abdominal ultrasound were unremarkable.

3) Treatment and monitoring

Anaesthesia was maintained using a constant rate infusion of midazolam, fentanyl and propofol. Active cooling was performed using application of cool water and fans and was stopped once the patient’s temperature reached 39.5°C to avoid hypothermia. Volume resuscitation was continued until normalisation of cardiovascular parameters.

Once cardiovascular status was considered stable and normoxaemia with normal end-tidal carbon dioxide was maintained without need for ventilation, the FiO2 was progressively decreased, the propofol infusion stopped and the midazolam/fentanyl infusion was also weaned. On return of swallowing the patient was extubated. Close monitoring was continued and the dog regained consciousness with a normal gag reflex over the following 2 hours.

Particular concerns in this patient included ongoing or recurrent seizure activity due to underlying neurological disease or cerebral oedema resulting from heatstroke. Serial neurological assessment was performed and the modified Glasgow Coma scale used to help with monitoring. The degree of hyperthermia also raised concern for sequelae such as hypoglycaemia, gastrointestinal damage, acute kidney injury, hepatopathy and coagulopathy. A urinary catheter was placed to allow monitoring of urine output. ‘Ins’ and ‘outs’ were calculated and matched. Urine specific gravity was also monitored and daily urine sediment examination performed. It has been suggested that glomerular and tubular injury occurs to some extent in most if not all heatstroke patients but may not be apparent on routine serological testing. Fractional excretion of sodium has been proposed as a cost-effective, readily available marker of tubular function in heatstroke patients but was not performed in this case. Serial monitoring of cardiovascular parameters, electrolytes, blood glucose, bodyweight, coagulation parameters, platelet count and acid-base status was performed. It is recommended that monitoring for DIC should be continued for at least 24-48 hours (including platelet count, PT/aPTT and D-dimers. Respiratory rate and effort were also closely monitored as non-cardiogenic pulmonary oedema can result from seizures and from heatstroke. Continuous ECG monitoring was performed as a significant number of heatstroke patients develop arrhythmias.
Hypoglycaemia was documented following volume resuscitation and was treated with an initial bolus of diluted 50% dextrose followed by a 5% glucose constant rate infusion. Subsequent mild hypokalaemia was also managed with intravenous supplementation. Due to the hypoglycaemia and concern over development of sepsis due to gastrointestinal bacterial translocation, treatment with intravenous amoxicillin/clavulanate was instituted. Omeprazole was also administered. Azotaemia resolved following rehydration. Mild hypoalbminaemia was also documented and as the patient was inappetant a nasogastric tube was placed to allow enteral feeding. The patient’s demeanour improved over the following 48 hours and the dog began to eat small amounts. Fluid therapy was slowly weaned. The patient made a full recovery and was discharged from the hospital after 4 days. No further seizures have been documented.

Discussion

In people, heatstroke has been defined as “a form of hyperthermia (>40°C) associated with a systemic inflammatory response leading to a syndrome of multi-organ dysfunction in which encephalopathy predominates”. Strong similarities have been found with the syndrome in dogs where temperature exceeds 41°C and reported mortality rates range from 40-64%. The most common cause is exposure to high external temperatures but an exertional form is also described. During heatstroke hyperthermia is detected by thermoreceptors and by the hypothalamus. Radiation and convection are the main mechanisms of heat loss. Panting, central vasoconstriction and peripheral vasodilation are compensatory mechanisms which aim to maximise them. However a number of factors can impair an individual’s ability to dissipate heat. These include factors such as upper airway abnormalities, obesity, certain medications and underlying medical disorders. Further compensatory mechanisms include an acute phase response involving endothelial cells, leukocytes and production of cytokines. Heat shock proteins are also produced.

If body temperature continues to increase, organ injury may result due to direct thermal cytotoxicity and ischaemia which results from distributive hypoperfusion and microthrombosis. The most commonly affected organs are the central nervous system, kidneys, liver, heart, lungs and coagulation system. Multiple organ dysfunction can ensue and the clinical course of heatstroke has many parallels with that seen in SIRS or sepsis patients. Potential sequelae include acute lung injury/acute respiratory distress syndrome, acute kidney injury, rhabdomyolysis and disseminated intravascular coagulation. The most prevalent lesions at post mortem include haemorrhagic diathesis, microthrombosis and coagulative necrosis.

Although heatstroke patients are classically hyperthermic on presentation, normo- or hypothermia is also possible. During active cooling ice packs or excessively cold water should be avoided as they may cause peripheral vasoconstriction and shunting of blood to the core. Gastric lavage or cold water enema were an additional option in this anaesthetised patient but both safety and efficacy of these techniques have been questioned.

Due to the presence of neurological signs concurrent with hypoperfusion and normal serum sodium, a better choice for volume resuscitation in this case may have been hypertonic saline. Neurological abnormalities are common in heatstroke patients and the presence of seizures or altered mental status is a poor prognostic indicator although CNS lesions are not thought to be a cause of death and the canine brain appears to be relatively resistant to direct hyperthermic damage. Other negative prognostic indicators reported include persistent hypoglycaemia (<2.6mmol/L), increased serum creatinine (>132.6μmol/L) at 24 hours of hospitalisation, coagulation abnormalities, petechiation, DIC,
delayed treatment (>90 minutes), ventricular arrhythmias, increasing age, hypotension and obesity. The number of nucleated red blood cells may also be associated with outcome. A scoring system incorporating many of these factors has been proposed but may have limited use in predicting outcome in individuals.

References


