Article

Camelid heat stress: 15 cases (2003–2011)

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Abstract — This case series describes novel findings associated with heat stress in 15 cases in South American camelids that had no pre-existing illnesses and which had clinical signs of illness after exposure to a warm environment. Novel findings include decreased packed cell volume and albumin concentration and mild spinal axonal degeneration. Heat stress should be considered in weak camelids with a history of hyperthermia.

Résumé — Stress thermique chez les camélidés : 15 cas (2003–2011). Cette série de cas décrit des constatations nouvelles associées au stress thermique dans 15 cas chez des camélidés d'Amérique du Sud qui n'avaient aucune maladie préexistante et qui ont présenté des signes de maladie après l'exposition à un environnement chaud. Les constatations nouvelles comprennent une valeur d'hématocrite réduite et une concentration d'albumine et une légère dégénération rachidienne axonale. Le stress thermique devrait être considéré chez les camélidés affaiblis ayant des antécédents d'hyperthermie.

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Introduction

Heat stress is characterized by systemic changes secondary to the inability to dissipate heat. The condition is common in South American camelids in locations with high environmental temperatures and humidity, frequently resulting in mortality (1). Evolutionary adaptation of camelids to temperatures less than 20°C has contributed to decreased ability to thermoregulate at higher temperatures (2). The integument and fiber of these species have developed to allow heat retention in cooler environments (1,3,4). A coarse outer coat and a finer undercoat prevent penetration of water through the coat and retain warmth (4).

Animals have a variety of adaptions to environmental heat. Camelids dissipate heat through thermal windows, which consist of areas of thinner skin and fiber and a large number of epitrichial sweat glands located at the ventral abdomen, axilla, and inguinal regions (1,3,4). Typically, animals regulate body temperatures via radiation, conduction, or convection and, in order to achieve cooling by these methods, the environmental temperature must be less than the animal's body temperature (1). High environmental temperatures and humidity negate the previous cooling methods by camelids, limiting unshorn animals to dissipate heat only through respiratory regulation and evaporative cooling (1). The thermal windows and respiratory mechanisms in camelids may not be adequate to alleviate heat, which may predispose unshorn animals to heat stress (3).

The objectives of this study were to describe environmental temperature and humidity, physical examination, clinical pathologic findings, common treatments, complications, and outcome associated with 15 cases of camelid heat stress. Current literature on camelid heat stress describes a syndrome of hemoconcentration, electrolyte imbalances, muscle necrosis, and decreased serum protein (2,5–7). However, there is a paucity of scientific evidence on this subject to document these findings other than 1 published case report (2). Conflicting literature on camelid heat stress indicates a need for evidence-based characterization of this condition.

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Materials and methods

Case selection

The study was conducted as a case series. Case definition included South American camelids > 6 months of age presented to Texas A&M University Veterinary Medical Teaching Hospital between January 2003 and June 2011. Camelids were included in the study only if they had no pre-existing illnesses and clinical signs of illness occurred after exposure to a warm environment.

Table 1. Clinicopathologic findings at admission for all 15 animals: Complete blood cell counts

Variable	Median	Range	Reference interval (6)
Red blood cell count (10^{12}/L)	8.9	5.9–12.3	10.5–17.2
Hemoglobin (g/L)	112	56.8–142	119–194
PCV (%)	21.3	10.9–30	27–45
Mean corpuscular volume (fL)	23.7	15.6–30.6	22.2–29.9
Mean corpuscular hemoglobin concentration (g/L)	491	458–577	393–468
Nucleated red blood cells (/mm^3)	1	0–12	0–2
White blood cells (10^9/L)	12.6	6.1–21.6	8–21
Segmented neutrophils (/mm^3)	10710	3965–19 872	4700–14 868
Band neutrophils (/mm^3)	0	0–1430	0–147
Lymphocytes (/mm^3)	648	0–2244	689–4848
Monocytes (/mm^3)	384	5–3408	0–1009
Eosinophils (/mm^3)	122	0–756	647–4867
Basophils (/mm^3)	0	0–79	0–298
Plasma protein (g/L)	54	43–73	51–79
Fibrinogen (µmol/L)	5.88	2.94–20.58	2.94–14.7

PCV — packed cell volume.

Information obtained included date of heat exposure, clinical signs, physical examination findings, results of clinicopathologic tests, treatment, clinical course, outcome, and necropsy results. Two animals included in the study were also presented in subsequent months for additional episodes of heat stress. The second admission for these animals was excluded to not skew categorical data.

Of 327 camelids that were presented between the selected dates, 15 camelids met the case definition. Criteria for selection included a rectal temperature greater than 39.4°C at admission or at the onset of clinical signs (recumbency or generalized weakness) plus 2 or more of the following 3 criteria: creatine kinase (CK) activity $>$ 476 U/L, sodium (Na) $<$ 148 mmol/L, and a diagnosis of heat stress. The CK value for case selection was determined as being 2 times greater than the upper end of the reference interval (6). The Na value for case selection was less than the lower end of the reference range (6).

Medical records review

The computerized medical record database was searched for cases that met the selection criteria. Complete blood cell count [CELL DYN® 3700 (after May, 2005), CELL DYN® 3500 (prior to May, 2005), Abbott Diagnostics, Lake Forest, Illinois, USA] and serum or heparinized plasma chemistry panel (Vitros-250 Analyzer; Ortho-Clinical Diagnostic, Rochester, New York, USA) data were reviewed. Microcentrifugation was used to manually determine packed cell volume (PCV). Manual differentials confirmed extreme white blood cell values.

Retrospective data of environmental parameters for the days owners first noticed clinical signs of heat stress were obtained from the National Oceanic and Atmospheric Administration through the Meteorological Assimilation Data Ingest System. The heat stress index (HSI) was calculated as humidity (%) + temperature (°F) (6,8).

Statistical analysis

Data were summarized using medians and ranges for continuous variables and tabulations for categorical variables. Data analysis was performed using S-Plus statistical software (Vitros-250 Analyzer; Ortho-Clinical Diagnostic).

Results

Historical and physical examination data

Of the 15 cases, 7 were llamas and 8 were alpacas. Of the llamas, 2 were intact males and 5 were intact females. Of the alpacas, 2 were intact females and 6 were intact males. The camelids in this case series were presented during the months of May to October, with the majority presenting in August (n = 8). The median age at presentation was 5 y (range: 0.5 to 13 y).

The median length of illness, recumbency or weakness without other obvious musculoskeletal or neurologic abnormalities, prior to presentation was 1 d (range: 0.5 to 10 d). Data for 8 of the 15 camelids was available for body temperature on the date the owner noted illness. The median body temperature reported was 41.8°C (range: 37.2°C to 42.7°C). The mean and maximum environmental temperatures and humidity on the day the owner first noted illness were obtained. The median mean environmental temperature was 28.8°C (range: 26.7°C to 31.6°C), the median maximum environmental temperature was 33.9°C (range: 31.1°C to 37.2°C), the median mean environmental humidity was 67% (range: 52.0% to 80.0%), and the median maximum environmental humidity was 89.0% (74.0% to 100.0%). Based on the environmental temperatures and humidity on the day of illness, the mean HSI was calculated to be 151 (range: 132 to 169). Based on maximum environmental temperatures and humidity, the calculated maximum HSI for those days was 182 (range: 162 to 199).

The median body temperature at presentation was 39.8°C (range: 36.1°C to 41.6°C). The median heart rate at presentation was 76 beats/min (range: 40 to 160 beats/min). The median respiratory rate at presentation was 40 breaths/min (range: 16 to 100 breaths/min). Scrotal edema was noted in 3 of the 8 males. Of the 7 females, 2 were pregnant. Eight animals were recumbent at admission. One camelid was sheared prior to the episode of heat stress. Two camelids had a history of heat stress. Four of the 15 animals were cooled prior to presentation. Of

Table 2. Clinicopathologic findings at admission for all 15 animals: Biochemical analysis

Variable	Mean	Range	Reference interval (6)
Lactic acid (mmol/L)	1.03	0.72–6.60	NA
Glucose (mmol/L)	11.99	7.16–19.09	4.1–8.55
Blood urea nitrogen (mmol/L)	3.93	2.14–32.84	3.21–47.84
Creatinine (μmol/L)	167.96	97.24–786.76	123.76–282.88
Magnesium (mmol/L)	0.78	0.37–0.99	0.82–1.44
Calcium (mmol/L)	2.08	1.63–2.3	1.9–2.73
Phosphorus (mmol/L)	1.39	0.36–3.75	0.84–2.36
Total protein (g/L)	55	35–76	51–78
Albumin (g/L)	27	16–44	31–52
Globulin (g/L)	27	19–35	11–30
AST (U/L)	3563	404–15 375	127–420
CK (U/L)	5514	553–44 497	14–238
Alkaline phosphatase (U/L)	46	30–101	27–132
Gamma-glutamyl transpeptidase (U/L)	31	13–57	3–28
Total bilirubin (μmol/L)	1.71	1.71–8.55	2.22–2.57
Na (mmol/L)	139.5	118–151	148–158
Potassium (mmol/L)	3.6	2.6–4.4	3.6–6.2
Chloride (mmol/L)	109	84–122	98–120

AST — aspartate aminotransferase; CK — creatine kinase; Na — sodium; NA — not available.

these 4 animals, the median body temperature on day of illness was 41.6°C (range: 41°C to 42°C).

Clinicopathologic findings

Complete blood cell counts and biochemistry profiles were performed on all 15 camelids at admission (Tables 1, 2). Of the 15 animals, 10 had anisocytosis, 0 had polychromasia, and 3 had toxic changes. Platelets on 5 animals were clumped and therefore a platelet count was not available. Ten animals were estimated to have had adequate platelets. The serum albumin in the males with scrotal edema had a median of 20 g/L (range: 16 to 25 g/L) compared to the others having a median of 27 g/L (range: 19 to 44 g/L). Of the 8 recumbent camelids, the median CK was 7070 U/L (range: 652 to 44 497 U/L) and the median aspartate aminotransferase (AST) was 7500 U/L (range: 1654 to 15 375 U/L). The median CK of the 7 standing camelids was 3459 U/L (range: 377 to 9880 U/L) and the median AST was 750 U/L (range: 404 to 3613 U/L).

Treatments

Common treatments administered during hospitalization included intravenous fluids (n = 11) or colloidal support with plasma and hetastarch (n = 1). Other treatments included vitamin E (n = 6), dimethyl sulfoxide (n = 6), omeprazole (n = 4), flunixin meglumine (n = 4), thiamine (n = 4) and selenium (n = 3). Antimicrobials administered to 6 animals to treat suspected infections included procaine penicillin (n = 2), ceftiofur sodium (n = 3), oxytetracycline (n = 1), potassium penicillin (n = 1), enrofloxacin (n = 1), and florfenicol (n = 1). Of the 15 animals, 5 had clinical signs of pneumonia during hospitalization (coughing or tracheal rattle) and 1 had evidence of renal disease indicated by severely increased creatinine (786.76 μmol/L). Anthelmintics were administered to 9 animals. McMasters fecal analysis was performed on 5 animals and 4 had greater than 500 coccidia oocysts or strongyle eggs per gram.

Physical rehabilitation consisted of assistance in standing, instituting a routine of passive range of motion exercises, or encouraging mobility with a mobile sling device (n = 9). Hypothalamic dysregulation (2,9), which was characterized as hypothermia or hyperthermia in response to environmental temperatures without an identifiable systemic illness, was noted in 2 of the 7 discharged camelids with 1 camelid requiring 40 days to regain thermoregulation.

Outcome

Six animals were euthanized, 7 animals were discharged, and 2 animals died. Of the 7 discharged camelids, the median number of days recumbent was 1 (range: 0 to 12 d). Of the 8 non-survivors, the median number of days recumbent was 4.5 (range: 1 to 14 d). The median number of days of hospitalization was 6 (range: 0 to 45 d) for the discharged animals and 2.5 (range: 0.5 to 14 d) for the non-survivors.

Eight animals were necropsied. Six animals had grossly evident changes within skeletal muscles, which included pallor (n = 3), edema (n = 3), and hemorrhage (n = 1). Skeletal muscle was examined histologically in 7 of 8 cases and all 7 animals had skeletal muscle necrosis. Spinal cord was examined histologically in 5 animals and all had evidence of minimal to mild axonal degeneration, which included axonal swelling (spheroids) in 4 cases. Five cases included examination of the medulla oblongata, and 1 case had similar axonal changes as those described in the spinal cord. Other areas of the brain lacked significant changes.

One animal had marked renal tubular necrosis with intratubular myoglobin casts. Lung changes included severe bronchopneumonia with intralesional bacteria (n = 2), neutrophilic bronchiolitis (n = 1), and mild edema (n = 4). One animal had severe ulcerative esophagitis from presumed aspiration and proliferative gastritis from probable chronic ostertagiasis. Other necropsy findings included pleural effusion (n = 4), abdominal effusion (n = 3), pericardial effusion (n = 2), dependent subcutaneous edema (n = 3), and petechiae on the costal pleura (n = 1). The two animals that died in hospital both had pathologic findings of pulmonary disease: neutrophilic bronchiolitis (n = 1) and bronchopneumonia with intralesional bacteria (n = 1). None of

the survivors had pleural, peritoneal, or pericardial effusion. Of the 3 animals that had third space losses, the serum albumin values were 25, 29, and 31 g/L.

Discussion

Heat stress can be a primary disease in healthy animals or secondary in animals that are predisposed by other factors, including parasitism, lameness, weaning, obesity, inadequate nutrition, decreased shade, high ambient temperature, and high humidity (2,9,10). In addition to hyponatremia and increased muscle enzymes (> 2 times the upper limit of normal), other findings in these camelids included anemia, hypoproteinemia, mild spinal axonal degeneration, and skeletal muscle necrosis.

Heat stress is commonly diagnosed in unshorn South American camelids in the southern United States and other regions of high heat or humidity during the mid-summer to fall months. Environmental evaluation through calculation of a HSI was performed. Non-essential handling should be avoided when the HSI is 120 to 150 (6,8). In this study, the onset of clinical signs was during days of high environmental stress (mean HSI of 151).

Shearing may have the beneficial effect of decreasing body temperature and allowing additional evaporative cooling, and unshorn camelids have a higher predisposition to heat stress (1,3,10). In this study, only 1 of the 15 camelids was sheared; however, shearing occurred 4 mo prior to onset of clinical signs, and the coat was moderately long at presentation, which likely contributed to decreased effective cooling.

Hemoconcentration, generally determined by an increased PCV, is reported to occur with heat stress (3,7,10), but was not observed in these camelids. It is possible that hemoconcentration occurred in the early stages of heat stress, and the cases presented in this study reflect a more chronic process with a decreased PCV, red blood cell concentration, and hemoglobin concentration. In ruminants with heat stress, hemoglobin concentrations and packed cell volumes have been shown to decrease, likely secondary to decreased hematopoiesis, hemodilution, or hemolysis (11). Anemia in camelids may be secondary to increased body water or parasitism with *Haemonchus contortus* (1). No evidence of regeneration, anisocytosis, or reticulocytosis, was observed. Thus the reason for the anemia is unknown. None of these animals were administered oral or intravenous fluids prior to presentation.

Creatine kinase and AST activities were increased, secondary to muscle injury or necrosis. Rhabdomyolysis in conjunction with dehydration can lead to acute renal failure through myoglobinuric nephrosis, as evident in 1 case with a creatinine of 786.76 μmol/L and a CK of 16 000 U/L. This animal had been recumbent for 10 d prior to presentation and was euthanized shortly after presentation. In addition, direct thermal injury has been proposed as a mechanism for myocyte and renal damage and is seen in other mammals that have suffered heat stress/stroke (12,13).

Camelids differ from dogs and humans in that hyponatremia is common with heat stress (1,5,10,13). Sodium has been described as being significantly decreased in unsheared alpacas compared with sheared alpacas when exposed to high environmental temperatures (1). This is thought to be secondary to increased body water (11), decreased aldosterone production (11), parasitism, or increased hydrosis. Increased body water is an adaptive mechanism to promote heat dissipation in ruminants and may lead to scrotal edema (11). Further studies are warranted to determine the cause of the consistent hyponatremia.

Causes for hypoalbuminemia include systemic vasculitis, increased body water (11), protein-losing nephropathy, severe hepatic disease, haemonchosis, or increased gastrointestinal permeability. There was no clinical or pathologic evidence of vasculitis, increased gastrointestinal permeability, hepatic or primary renal disease; therefore, these etiologies are less likely. Increased environmental temperatures increase the production of catabolic hormones, glucocorticoids, and catecholamines, and may lead to decreased feed nitrogen intake, further promoting a decreased albumin (11). Third space losses were noted in some of the camelids; however, these camelids did not have severe hypoproteinemia.

The initial clinical signs observed in camelids with heat stress are a decreased appetite, reluctance to rise, inability to kush, and lethargy (10). The forelimbs may be weaker than the hind limbs (7), and a progressive generalized weakness is typically noted, as in the camelids in this study. Scrotal edema is also a common clinical sign (2,3,9,10) and was noted in 3 males. This may be secondary to a prolonged hypoalbuminemia or increased body water. Physical examinations generally identify tachycardia, tachypnea, and an increased rectal temperature initially, although normothermia is often observed by the time of admission (7,10).

It has been suggested that hyperthermia in camelids can lead to inadequate thermal regulation (3,7,10). Suspected hypothalamic dysfunction was noted in 2 animals in this study during hospitalization, 1 of which required 40 d to thermoregulate appropriately. In this case, hyperthermia was noted during exposure to increased environmental temperatures and was not responsive to anti-inflammatory drugs. The alpaca was hospitalized with gradually increasing exposure to environmental temperatures until adequate thermoregulation was achieved.

The most consistent postmortem findings in these camelids were skeletal muscle necrosis and mild spinal axonal degeneration. Two animals had bronchopneumonia and 1 had bronchiolitis, which may have predisposed these animals to decreased respiratory cooling. These animals had clinical signs of lower respiratory disease at admission. The other 2 animals with clinical signs of respiratory disease were discharged alive.

In dogs with hyperthermia, disseminated intravascular coagulopathy and acute renal failure are risk factors for death (12). Central nervous system changes in dogs consist of hyperemia and edema of the meninges and brain (13).

The pathophysiology of heat stroke in humans is complex. Hyperthermia leads to splanchnic hypoperfusion, which in turn leads to intestinal mucosal injury, hyperpermeability, and the leakage of endotoxins into the systemic circulation, triggering a cytokine cascade that results in vascular endothelial damage and microthrombosis (14). The pathologic findings in heat stroke in humans and dogs include hemorrhage and necrosis in multiple organs and neuronal degeneration (15,16).

The pathologic findings in these camelids were much less severe than those described in canine and human heat stroke. Hemorrhage is the predominant gross finding in dogs and humans, but hemorrhage was limited in these camelids. Platelet aggregation may be a feature of heat stress as heat directly activates platelets in humans and 5 of the camelids had clumped platelets on blood smears (17). Of the 5 with clumped platelets, 1 died and 2 were euthanized. The multi-organ necrosis reported in canine and human cases was also not evident. One animal had renal tubular necrosis, but this finding can likely be attributed to myoglobinuria. Myonecrosis appears to be one lesion that is consistent in all 3 species. The mortality rate in humans and dogs with heat stroke is near 50% (12,14), similar to the findings herein.

Mild spinal axonal degeneration was noted in all 5 cases in which the spinal cord was examined. This lesion has not been described in other species with heat stroke, but few studies have included spinal cord examination. Migration of *Parelaphostrongylus tenuis* is a well-recognized cause of spinal axonal degeneration in camelids and cannot be excluded in these cases. However, given the lack of inflammation in all spinal cord sections examined, a heat-related mechanism may be the etiology. Many of these cases had clinical signs of progressive weakness, characterized by the ability to stand at presentation and progression to recumbency. Therefore, a neurologic component cannot be ruled out in addition to an apparent myopathy.

One limitation of this study is that the sample size was small due to the stringent selection criteria used to exclude other disease. This could bias some of the results. Also, established reference intervals for biochemical analyses are not available at our laboratory, and therefore published parameters were used.

In conclusion, we found that the pathology in the camelids with heat stress was much less severe than with humans or dogs, although the exact pathophysiology for this remains unclear. Myonecrosis appears to be a common finding in all 3 species. Why hyponatremia and hypoalbuminemia are common in South American camelids is unclear, but these seem to be common biochemical abnormalities in camelids with heat stress. More research is needed to evaluate risk factors for morbidity and mortality, allowing prognostication of this condition.

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