Case Report Rapport de cas

Acute respiratory distress syndrome in an alpaca cria

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Abstract — A 7-hour-old alpaca was presented for lethargy and depression. The cria responded favorably to initial treatment but developed acute-onset dyspnea 48 hours later. Acute respiratory distress syndrome was diagnosed by thoracic imaging and blood gas analysis. The cria was successfully treated with corticosteroids and discharged from the hospital.

Résumé — Syndrome de détresse respiratoire aiguë chez un cria alpaga. Un alpaga âgé de 7 heures a été présenté en raison d'abattement et de dépression. Le cria a réagi favorablement au traitement initial mais a développé une dyspnée d'apparition aiguë 48 heures plus tard. Le syndrome de détresse respiratoire aiguë a été diagnostiqué par imagerie thoracique et gazométrie sanguine. Le cria a été traité avec succès à l'aide de corticostéroïdes et a reçu son congé.

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Introduction

Acute respiratory distress syndrome, referred to as ARDS, is the manifestation of an intra- or extra-pulmonary insult resulting in an overzealous inflammatory cascade in the lungs. Ultimately, interstitial pulmonary edema develops and is frequently fatal. The syndrome was first described in humans but has since been recognized in animals, particularly in companion animals and foals (1,2). Mortality rates vary from up to 60% in humans to almost 100% in small animal species (2). This syndrome has not been previously reported in a camelid species, but should be included on the list of differential diagnoses for crias with acute onset respiratory distress. Although the prognosis in other species is often guarded, treatment of alpaca crias can have a good outcome.

Case description

An approximately 7-hour-old 5.2-kg female intact Suri alpaca cria was presented to the Oklahoma State University Boren Veterinary Medical Teaching Hospital with the complaint of being hypothermic, lethargic, and unable to stand and nurse. By the owners' records the cria was at least 1 wk premature. The primiparous dam had delivered the cria unassisted and unobserved. Upon finding the cria, the owners determined that she was hypothermic (actual temperature not reported) and attempted to warm her with blankets, a heater, and warm water baths. Attempts were made to milk out the dam, but only 5 mL of colostrum were obtained and were fed to the cria along with 60 mL of milk replacer, which the cria suckled readily from a bottle. However, lethargy and inability to rise persisted and the cria was admitted to the hospital the following morning.

On presentation, the cria was obtunded and unable to maintain sternal recumbency. Rectal temperature was 36.7°C (98°F) [reference interval (RI): 37.8 to 38.9°C (100 to 102°F)], and the pulse was 104 beats/min (RI: 60 to 90 beats/min) with no detectable murmurs or arrhythmias. The respiratory rate was 60 breaths/min (RI: 10 to 30 breaths/min) with no auscultable abnormalities bilaterally, although mild nostril flaring was noted. Mucous membranes were hyperemic with a capillary refill time of < 2 s. The incisors were not erupted, and both ears were curled at the tips. Moderate scleral injection and mild hyphema were present bilaterally. A bilateral nasal oxygen cannula was immediately placed and oxygen administered at 2.5 L/min. A 20-gauge double lumen J-wire catheter was aseptically placed in the left jugular vein and blood was drawn for aerobic culture, complete blood (cell) count (CBC), and chemistry panel. The values from the CBC were within normal limits, and relevant abnormalities on the chemistry panel included hypoglycemia (1.1 mmol/L, RI: 4.2 to 9.8 mmol/L), increased alkaline phosphatase (770 U/L, RI: 0 to 610 U/L), hypoproteinemia (41 g/L, RI: 17 to 73 g/L) characterized by hypoalbuminemia (27 g/L, RI: 29 to 50 g/L), and increased creatine kinase (362 U/L, RI: 0 to 137 U/L).

Major problems identified initially included obtunded mentation, hypothermia, tachycardia, tachypnea, scleral injection, hyphema, and hypoglycemia. Differentials for these findings included birthing trauma, dysmaturity, perinatal asphyxia,

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neonatal maladjustment syndrome, septicemia, and congenital malformation. Based on the initial case assessment, 6 mL of 50% dextrose was administered as a bolus followed by a balanced polyionic electrolyte solution (Normosol-R; Hospira, Lake Forest, Illinois, USA) with 15 mEq potassium chloride and 50% dextrose added to make a 5% solution, administered at 50 mL/kg body weight (BW) per day. A warming blanket (Bair hugger; Arizant, Eden Prairie, Minnesota, USA) was placed over the cria until her temperature rose into the normal range. Ceftiofur sodium (Naxcel; Pfizer Animal Health, New York, New York, USA) was administered at 5 mg/kg BW, IV, q12h due to clinical evidence of septicemia, and omeprazole (Omeprazole Na; Premier Pharmacy Labs, Weeki Wachee, Florida, USA) was given at 0.5 mg/kg BW, IV, q24h. Flunixin meglumine (Banamine; Schering-Plough Animal Health, Union, New Jersey, USA) was given at 0.3 mg/kg BW, IV, q8h for the anti-endotoxic effects [dose extrapolated from data from another species, as there is no published dose for a camelid species in the literature (3)]. Based on the owners' history of complete failure of passive transfer, and the dam's continued lack of colostrum production, along with previous administration of milk replacer that may have resulted in reduced IgG absorptive capacity of the small intestine, 250 mL of llama plasma (Triple J Farms; Kent Laboratories, Bellingham, Washington, USA) was administered IV over 3 h.

The cria responded favorably to initial treatment, and within 3 h was bright and alert and able to maintain sternal recumbency on its own. Every 2 h the cria was offered 50 mL of alpaca milk replacer, which she suckled readily from a bottle. The umbilical stalk was dipped in 0.5% chlorhexidine diacetate solution. Physical parameters were monitored hourly along with indirect mean arterial pressure, blood glucose, urine output, and SpO_2 via pulse oximeter. During the course of the day the cria was intermittently mildly tachycardic and tachypneic and continued to flare its nostrils on inspiration but maintained an SpO_2 near 100%. An arterial blood gas revealed a pO_2 of 431 mmHg and a pCO_2 of 46.9 mmHg with a pH of 7.39 while on nasal oxygen.

The physical parameters were stable by the following day, although the cria was unable to maintain blood glucose in the normal range without supplementation. The hyphema had resolved bilaterally and was thus attributed to traumatic origin but scleral injection was still present. Because of previously reported differences in the clinical presentation of septic crias compared with neonatal ruminant species (4) and the additional risk factors of documented prematurity and initial failure of passive transfer, another CBC was performed. This revealed a leukopenia ($4.1 \times 10^3/\mu L$, RI: 4.9 to $11.0 \times 10^3/\mu L$) characterized by a neutropenia (neutrophils 2993/μL, RI: 4600 to 16 000/μL, bands 205/μL, RI: 0 to 350/μL). Sepsis was suspected despite a preliminary negative blood culture. Antibiotics were changed to amikacin sulfate (AmiJect D; Butler Animal Health Supply, Dublin, Ohio, USA) at 22 mg/kg BW, IV, q24h and potassium penicillin (Pfizerpen; Pfizer Animal Health, New York, New York, USA) at 40 000 IU/kg BW, IV, q6h and another 250 mL of llama plasma was administered IV for immune support and colloidal effects.

On day 3 of the cria's hospitalization, both heart rate and respiratory rate began trending upward. The respiratory rate remained consistently in the 80s with a minor abdominal component. SpO_2 displayed a downward trend, as it started at 98% in the morning but decreased to 87% by mid-afternoon. Increased large airway sounds were auscultable diffusely bilaterally, particularly in the caudodorsal lung fields with loss of small airway sounds. The cria also appeared more depressed and lethargic than it had the previous day and became hyporexic. Thoracic radiographs were taken and demonstrated diffuse interstitial pulmonary infiltrates in all lung lobes, with several small multifocal areas of alveolar pulmonary infiltrate in the dorsal caudal lung lobes and air bronchograms in the caudoventral lung lobes. All pulmonary vessels that could be seen appeared within normal limits. Arterial blood gas sampled 20 min after removal of nasal oxygen revealed a pO_2 of 39 mmHg, pCO_2 of 51.8 mmHg, and pH of 7.38, interpreted as hypoxemia with a mild compensated respiratory acidosis.

The cria's clinical condition deteriorated following these diagnostic procedures. Two hours after being placed back on nasal oxygen it was unable to raise its head and inspiratory effort and nostril flare were notably worsened compared with earlier in the day. Acute respiratory distress syndrome was diagnosed based on the following criteria: acute onset of tachypnea and dyspnea with hypoxemia; risk factors including documented prematurity with clinical and laboratory evidence of sepsis, indication of trauma, and multiple transfusions; characteristic radiographic findings; PaO_2/FiO_2 of < 200 mmHg; lack of clinical responsiveness to supplemental oxygen; and absence of cardiac abnormalities. Prednisolone sodium succinate (Solu-Delta-Cortef; Pfizer Animal Health) was administered at 5 mg/kg BW, IV due to the cria's rapidly deteriorating clinical condition.

Within hours of corticosteroid administration the cria's clinical appearance was markedly improved. Although its respiratory rate remained higher than the previous day, SpO_2 began displaying an upward trend and the nostril flare was less apparent. The cria became more responsive to environmental stimuli, and was once again able to raise its head. However, hyporexia persisted and partial parenteral nutrition (PPN) was initiated with 8.5% amino acids added to 50% dextrose in a 1:1.25 ratio at one-quarter of the calculated daily caloric requirement. The fluid rate was decreased by the same amount per hour as the PPN in order to keep the total volume of fluids administered per hour at a maintenance rate to avoid increased pulmonary capillary pressures and excess extravascular lung water. The next day the respiratory rate remained increased although small airway sounds could occasionally be ausculted; crackles were detected diffusely and bilaterally. Thoracic ultrasonography was performed and revealed mild right-sided cranioventral lung lobe atelectasis as well as bilaterally diffuse finely grained hyperechoic images immediately deep to the pulmonary pleura with reduction of reverberation artifact, consistent with pulmonary edema. Cardiac ultrasound findings were within normal limits. Prednisolone sodium succinate was again administered IV but at a tapered dose (one-tenth of the dose given the previous day).

Mild clinical improvement was appreciable daily, and 2 days later an arterial blood gas analysis off nasal oxygen revealed a pO_2 of 47 mmHg, pCO_2 of 47.6 mmHg, and pH of 7.41, indicating gradual improvement of the hypoxemia. Therapy was continued as previously described although corticosteroids were discontinued after the second dose because of a concern over immunosuppression in a neonate with probable sepsis. Ketoprofen (Ketofen; Fort Dodge Animal Health, Fort Dodge, Iowa, USA) was administered instead at 2.2 mg/kg BW, IV, q24h as it has been shown in horses to have similar anti-inflammatory properties as other nonsteroidals but with less potential for nephrotoxicity and gastric mucosal ulceration (5). Parenteral vitamin E and selenium were administered once subcutaneously (Bo-Se; Schering-Plough Animal Health, Union, New Jersey, USA) for their antioxidant properties.

Six days after the initial radiographic study, repeat thoracic radiographs revealed a decrease in the unstructured interstitial pattern within the caudodorsal lungs. Air bronchograms were again noted in the same regions but were less pronounced. The cria's heart rate returned to the normal range over the next few days; a favorable prognostic indicator (6). Overall, the crias's condition appeared to be slowly improving. The patient remained hospitalized until pO_2 normalized and abnormal clinical signs completely resolved. Twenty days after she was admitted an arterial blood gas revealed a pO_2 of 80 mmHg, pCO_2 of 44.2 mmHg, and pH of 7.40 on room air. Supplemental oxygen was gradually discontinued as were other treatments. At 29 days of age the cria was discharged from the hospital.

Discussion

An acute respiratory distress syndrome was first reported in adult humans in 1967 (7,8). The term adult respiratory distress syndrome (ARDS) was coined to describe the signs of tachypnea, hypoxemia, panlobular infiltrates on thoracic radiographs, and loss of lung compliance (9). The syndrome was later referred to as acute respiratory distress syndrome (ARDS) (10,11), and a similar syndrome resembling that of ARDS in humans has since been recognized in animals, primarily in dogs, cats, and foals (1,2). This is the first report that the authors are aware of in which ARDS was diagnosed in a camelid species.

Since the 1980s, consensus groups have developed definitions for acute lung injury (ALI) and ARDS in human and veterinary medicine (8,10,11). In 2007 the definition of veterinary ARDS included 4 required criteria: acute onset of tachypnea; known risk factors including infection, sepsis, trauma, and multiple transfusions; evidence of pulmonary capillary leak without increased pulmonary capillary pressure, demonstrable by bilateral/diffuse infiltrates on thoracic radiographs; and evidence of inefficient gas exchange, demonstrable by hypoxemia with a PaO_2/FiO_2 ratio of $\leq$ 200 mmHg (8). A fifth criterion that was highly recommended was evidence of diffuse pulmonary inflammation (8). A related clinical syndrome with different etiology is now referred to as neonatal equine respiratory distress syndrome (NERDS) and is believed to be similar to infant respiratory distress syndrome (IRDS), also known as RDS or hyaline membrane disease (8). This syndrome (RDS) is believed to be a primary surfactant deficiency similar to that seen in human neonates, and has been described in lambs, calves, and foals (12). Respiratory distress syndrome was considered unlikely in this case based on the delayed onset ($>$ 60 h postpartum) and continual worsening of clinical signs. Respiratory distress syndrome usually begins within 10 to 15 min following parturition, and clinical signs reach a peak after approximately 1 h (12). Additionally, many equine neonatologists agree that primary surfactant deficiency rarely plays a role in acute respiratory distress in foals (1), although it is widely recognized that surfactant dysfunction is a component of the underlying pathophysiology in ARDS patients (13).

Acute respiratory distress syndrome is not a disease entity but rather the end result of either intra- or extra-pulmonary pathologic processes resulting in diffuse alveolar damage. Common predisposing intrapulmonary insults include pneumonia, aspiration of gastric contents, and pulmonary contusion. Extrapulmonary diseases predisposing to ARDS include infection, sepsis, systemic inflammatory response syndrome, trauma, and multiple transfusions (8,14,15). The initial insult results in an inflammatory response intended to eradicate infection and repair tissue damage (14,15). In some individuals the immune response becomes self-destructive and results in leukocyte adhesion to the pulmonary vasculature followed by release of cytokines, vasoactive substances, and reactive oxygen and nitrogen species that ultimately lead to interstitial pulmonary edema (14,16).

Differential diagnosis for ARDS has historically included upper airway obstruction, pneumothorax, pleuropneumonia, pleural effusion, aspiration pneumonia, pneumonia of bacterial or viral origin, and congenital cardiac anomalies (14). Upper airway obstruction was ruled out by the absence of stridor and strong bilateral nasal airflow (14). Pneumothorax, pleural effusion, and congenital cardiac abnormalities were ruled out based on auscultation, and radiographic and ultrasonographic imaging. Pleuropneumonia, aspiration pneumonia, and pneumonia of infectious origin could not be completely ruled out but may occur concurrently with ARDS (14). Clinical signs of pneumonia including pyrexia, coughing, nasal discharge, and harsh crackles and wheezes on auscultation were not observed in this cria. However, the 4 required criteria recently described by the Dorothy Russell Havemeyer Consensus Workshop on ALI/ARDS in Veterinary Medicine as being essential to a diagnosis of ARDS were all met. Additional diagnostics to confirm the fifth described criterion could have included a transtracheal wash or bronchoalveolar lavage to document cytologic evidence of pulmonary inflammation but this procedure was considered too risky in this compromised neonate (8).

Treatment of ARDS is aimed at improving oxygenation, therapy for the primary disease process, attenuating the inflammatory response and providing supportive care (14). Oxygen insufflation at 2.5 L/min was considered adequate in a patient this size; ideally a second arterial blood gas with the patient on supplemental oxygen would document the expected minimal improvement in a case of ARDS. The stress of obtaining a blood gas in a compromised patient and the detrimental effects that may be the result of such a procedure must be considered. Antibiotics, anti-inflammatories, parenteral nutritional and fluid support, and antioxidants were also used in this case.

Corticosteroids have been a cornerstone of ARDS treatment in both human and veterinary patients, and one report in foals showed that only those treated with corticosteroids survived (17). However, a more recent review of the human literature found that evidence supporting the administration of low- to moderate-dose corticosteroids in the treatment of early ARDS (defined as < 7 days' duration) was controversial (18).

Additional treatments that have recently been reviewed in the veterinary literature include mechanical ventilation, inhalation of nitric oxide, or administration of surfactant (1). Lack of controlled studies in addition to economic constraints precluded the use of these therapeutic options in this case.

For crias presented with acute onset of respiratory distress, ARDS should be included on the list of differential diagnoses. This syndrome can have a favorable outcome, despite historically high mortality rates reported in other animal species. Complete history and physical examination, diagnostic imaging, and arterial blood gas analysis may be used to attempt to differentiate ARDS from other insults to the respiratory system. Treatment of ARDS in camelids appears to be similar to that described in other species.

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