Pregnancy toxemia and lipid mobilization syndrome in two alpaca (*Vicugna pacos*) at 6 and 10 months of gestation

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SUMMARY

Primary ketosis, or pregnancy toxemia, is an uncommon feature of pregnancy in camelids compared to small ruminant species. In severely debilitated females, induction of abortion or parturition should be considered to alleviate the syndrome. This case report describes the clinical findings and medical treatment approach of ketosis in two pregnant alpacas (*Vicugna pacos*) referred to the University Veterinary Teaching Hospital (OVUD) of the Department of Veterinary Medicine of the University of Perugia, Italy.

The first patient was a 7-years old female alpaca 6-months pregnant, 80 kg body weight and BCS 3.25, with a 5 days history of anorexia and regurgitation. At initial examination the body temperature was 38.6° C , with a glycaemia of 341 mg/dL. Ultrasound examination of the abdomen revealed no fetal heart activity. On the third day from admission the animal started to feed and the temperature decreased to 37.9° C. On the same day 100 µg of prostaglandin agonist (Estrumate®) were administered IM. On the fourth day of admission, appetite increased and abortion of a dead fetus was noticed. On fifth day of admission, temperature was 37.5° C, the alpaca showed good appetite and rumination, feces were normal and fetal membranes were expelled. Due to the improved general condition the alpaca was dismissed.

The second patient was a 3-year old female alpaca, 10-months pregnant, 65 kg body weight and BCS 3.0, which was referred with lethargy, anorexia and signs of colic. At presentation, glycaemia was 141 mg/dL and rumen activity was absent. Ultrasound examination revealed live and vital fetal parameters (heart rate; 110 bpm). A blood sample was taken and, once centrifuged, the serum appeared milky and triglycerides reached 1208 mg/dL. The general condition of the animal improved with fluid and supportive therapy. At day 4 of admission a morphologically normal, female cria was born; however, no suction reflex was present within the first 1.5 hours. The cria was bottle-feed with bovine frozen colostrum, but the general condition constantly declined; failure of passive transfer was noticed through biochemistry profile. Since no response to supportive therapy was achieved, the cria was euthanized at 36 hours of life. Dam's condition improved and, after expulsion of fetal membranes, the alpaca was dismissed.

Prognosis for camelids whit fat mobilization syndrome and pregnancy toxemia depends on the timing of diagnosis and intervention. In both reported cases, our approach showed good results in preserving the survival of the dams, while one fetus was diagnosed as already dead upon initial clinical exam, and the other one died within 48h from birth.

KEY WORDS

Pregnancy toxemia, hyperlipemia, induction of abortion, *Vicugna pacos*.

INTRODUCTION

Pregnancy toxemia is an uncommon disease of pregnancy in camelids, and is often secondary to other diseases. A case of primary ketosis was reported in a 3-year-old alpaca at the 11th month of pregnancy that presented a 2-week period of anorexia, lethargy, and weight loss together with ketonuria, hyperglycemia, hypokalemia, metabolic acidosis, and increased serum liver enzymes[1]. Conversely, in severely debilitated females, induction of abortion or parturition should be considered to alleviate the syndrome[2].

Insufficient energy intake during or at the end of pregnancy is usually responsible for increased body fat mobilization, liver lipidosis and ketonemia. Indirect evidence of a lipid disorder may be obtained by measuring liver function. Camelids with any of the following abnormalities such as γ-glutamyl transferase (GGT) greater than 60 IU/L, aspartate aminotransferase (AST) greater than 500 IU/L, sorbitol dehydrogenase (SDH) greater than 50 IU/L, NEFA greater than 1 mEq/L, beta-hydroxybutyrate (BHB) greater than 5 mg/dL, bile acids greater than 30 mg/dL should be considered at high risk. Direct evidence of hepatic lipidosis may be obtained by biopsy, but severely affected camelids occasionally die during or shortly after this procedure. At necropsy, gross lipidosis may be visible as well[3].

General assessment of renal function, protein and electrolyte concentrations are recommended, especially in camelids on IV fluids. Refractometers may not provide accurate estimates of blood protein in camelids with severe hyperlipemia.

This case report describes the clinical findings and medical approach to ketosis in a 6-months and a 10-months pregnant alpacas (*Vicugna pacos*) reared in two different farms.

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First case

The first patient was a 7-years old female alpaca 80 kg body weight, BCS of 3.00, 6-months pregnant. She was referred at 9.30 PM to the University Veterinary Teaching Hospital (OVUD) of the Department of Veterinary Medicine of the University of Perugia, Italy, with a 5 days history of anorexia and regurgitation. In the days previous to the admission, the alpaca underwent medical treatment for gastric ulcer with Sucralfate®, antibiotic therapy (Baytril® 5 mg/kg) and intravenous fluid-therapy (Ringer Lactate), as established by the veterinary practitioner in charge of the farm.

On presentation at the OVUD, the patient was lethargic and in sternal recumbence; body temperature was 38.6° C, heart rate was 80 bpm and respiratory rate was 48 breaths per minute. Mucous membranes were normal, slight de-hydration was present, together with complete C1 compartment stasis. Venous blood sample from oral mucosa revealed glucose concentration of 341 mg/dL through field glucometer. The patient received an IM injection of 40 IU of human insulin (Humulin®), but the response was unsatisfactory: the animal was still hyperglycemic at the following control, which was carried out one hour later (241 mg/dL). The animal received 3 L of Ringer Lactate through intravenous infusion overnight for stabilization. For the following days, the treatment protocol consisted in the administration of Sucralfate® at the dose of 0.5 gr per OS four times a day and IV fluid therapy with Ringer Lactate (2 L per day).

The day after admission, body temperature was 38.9° C. An ultrasound examination of the abdomen was performed through a machine equipped with a 3-8 MHz convex transducer (MyLab 30 Gold, Esaote, Genova, Italy). Fetal annexes, amniotic and allantois fluids were normal but fetal heart activity was absent. Thus, fetal death was confirmed. Other abdominal viscera appeared normal. Venous blood sample was obtained from the jugular vein for a complete biochemistry profile (Table 1). A diagnosis of ketosis and lipid metabolism imbalance was proposed.

Table 1 - Biochemistry profile of the first adult female pregnant alpaca referred to the OVUD.

Biochemistry profile	Value	Reference limits[4,5]
Cholesterol (mg/dL)	63.0	15.5 - 88.9
Triglycerides (mg/dL)	126.0	10.62 - 45.14
BHB (mmol/L)	0.93	< 0.48
NEFA (mmol/L)	0.82	< 0.8
BUN (mg/dL)	86.0	21.62 - 60.66
Creatinine (mg/dL)	2.53	1.0 - 2.4
Glucose (mg/dL)	161.0	90.0 - 149.0
Total proteins (g/dL)	6.3	5.7 - 7.2
Albumin (g/dL)	3.15	2.9 - 4.3
Calcium (mg/dL)	8.4	4.2 - 9.0
Phosphorous (mg/dL)	2.3	4.5 - 7.3
AST (IU/L)	575.0	137.0 - 391.0
ALP (IU/L)	297.0	32.0 - 167.0
GGT (IU/L)	20.0	13.0 - 50.0
CPK (IU/L)	928.0	56.0 - 662.0
LDH (IU/L)	1612.0	10.0 - 695.0

Moderate response to the insulin was seen, since glycaemia was 161 mg/dL, and insulin administration was interrupted, but the animal was still anorectic. The treatment plan was refined by adding a non-steroidal antinflammatory drug (Rimadyl® 4 mg/kg SC) and 2 gr of yeasts per OS diluted in warm water. The second day of admission the general condition slightly worsened: temperature increased to 39.1° C, hyperglycemia recurred and therapy was changed to 60 IU of insulin (Caninsulin®) IM, due to the major sensitivity of camelids to canine insulin[6®]. Slow IV infusion of 500 mL of glucose 5% solution was started, together with 5 mL IV of vitamin-B complex (Dobetin-B1® 10 mg/kg). Four hours later, glycaemia was within normal range.

On third day of admission the animal started to feed, temperature decreased to 37.9° C, even if no abortion occurred. Thus, 100 μg of prostaglandin F2 (Estrumate®) was administered IM. Vital parameters were monitored at 30-min interval. After prostaglandin injection heart rate immediately increased to 60 bpm while respiratory rate raised to 39 breaths per minute, then normalization occurred one hour later.

On fourth day of admission, appetite increased and abortion was noticed. The animal was kept in the hospital in order to verify expulsion of fetal membranes, thus two IM injections of 20 IU of oxytocin (Pitocina®) at an interval of 12 hours were given.

On fifth day of admission, temperature was 37.5° C, the alpaca showed good appetite and rumination, feces were normal and fetal membranes were expelled. Due to the improved condition of the animal and to the normalization of glycaemia, the female alpaca was dismissed.

Second case

The second patient was a 3-year old female alpaca, 65 kg body weight with a BCS of 3.0, at the 10th month of pregnancy, which was referred to the OVUD at evening time, with a history of lethargy, anorexia and colic symptoms. The veterinary practitioner in charge of the farm already started a therapy based on rumen-stimulatory drug (Zoocolagogo®) and Sucralfate® three times a day. At presentation at the OVUD the animal was slightly lethargic, body temperature was 37.9° C, heart rate was 56 bpm and breath rate was 48 per minute. A peripheral venous blood drop was obtained and used for glucose stick (glycaemia: 141 mg/dL). Rumen activity was almost absent.

Ultrasound examination of the abdomen revealed a live and vital fetus, with heart rate of 110 bpm and spontaneous movements. No abnormalities were identified in the other abdominal organs. An IV fluid therapy was started with 1 L Ringer Lactate and 0.5 L NaCl 0.9% overnight.

The day following admission, fluid therapy was maintained and associated to vitamin-B complex (Dobetin-B1®, 6 mL IV and Metabolase®, 8 mL IM). Blood cell count and biochemistry profile were obtained (Tables 2 and 3). Once centrifuged, serum appeared milky, as shown in Figure 1. General condition of the animal improved and the alpaca started to feed and drink, to ruminate and to eliminate urine and feces.

At day 4 after admission a presumably premature female cria of 5.5 kg weight was born. The cria was morphologically normal, assumed standing position within 2 hours, but no suction reflex was present within the first 1.5 hours. A venous catheter was placed into the right jugular vein for hydration. When the owners provided bovine frozen colostrum, 2 hours later, the cria started spontaneously to suckle milk from the bottle. Every

Table 2 - Blood cell count of the second adult female pregnant alpaca referred to the OVUD.

Blood cell count	Value	Reference limits[4,5]
WBC (10^3/µL)	11.59	5.7 - 32.9
RBC(10^3/µL)	11.83	9.1 - 13.8
Hgb (g/dL)	13.9	10.4 - 17.0
Htc (%)	23.9	24 - 36
MCV (fL)	20.2	21.8 - 28.9
MCH (pg)	11.7	10.6 - 12.7
MCHC (g/dL)	58.2	39.3 - 46.8
Plt (10^3/µL)	439	200 - 600

Table 3 - Biochemistry profile of the second adult female pregnant alpaca referred to the OVUD.

Biochemistry profile	Value	Reference limits[4,5]
Cholesterol (mg/dL)	169.0	15.5 - 88.9
Triglycerides (mg/dL)	1208.0	10.62 - 45.14
BHB (mmol/L)	0.55	< 0.48
NEFA (mmol/L)	1.07	< 0.8
BUN (mg/dL)	30.0	21.62 - 60.66
Creatinine (mg/dL)	1.67	1.0 - 2.4
Glucose (mg/dL)	113.0	90.0 - 149.0
Total proteins (g/dL)	8.0	5.7 - 7.2
Calcium (mg/dL)	8.9	4.2 - 9.0
Phosphorous (mg/dL)	7.9	4.5 - 7.3
Sodium (mEq/L)	154.0	144.0 - 155.0
Potassium (mEq/L)	3.6	4.0 - 5.7
Chloride (mEq/L)	118.0	97.0 - 111.0

two hours, the cria was bottle-fed with 60 mL of colostrum. The day after, due to the lack of elimination of the meconium, 2.25 gr of pediatric glycerol diluted in 60 mL of warmed soap water was used as an enema, with success.

The general condition of the cria started to decline. A biochemistry, hemogasanalysis and hematocrit profile of the cria were obtained (Tables 4 and 5), which confirmed hypo-proteinemia and failure of passive transfer of immunity. A venous blood collection (100 mL) was performed from the jugular vein of the dam for haemo-transfusion. Whole blood was transferred

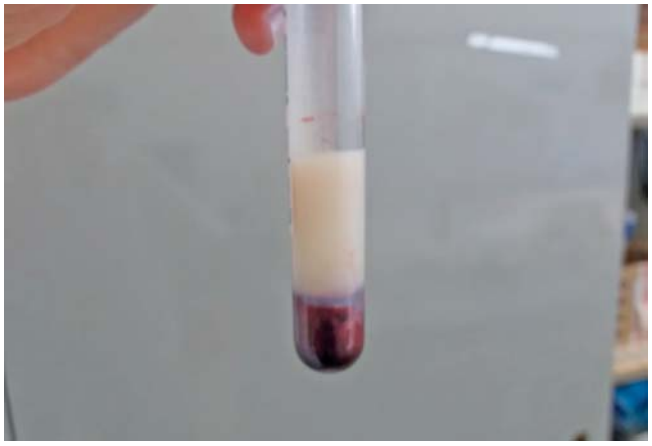

Figure 1 - Milky and dense aspect of the blood serum of the second female pregnant alpaca referred to the OVUD.

Table 4 - Blood cell count of the neonate alpaca cria.

Blood cell count	Value	Reference limits[4,5]
WBC (10^3/µL)	2.30	5.7 - 32.9
RBC(10^3/µL)	10.31	9.1 - 13.8
Hgb (g/dL)	10.9	10.4 - 17.0
Htc (%)	21.5	24 - 36
MCV (fL)	20.9	21.8 - 28.9
MCH (pg)	10.6	10.6 - 12.7
MCHC (g/dL)	50.7	39.3 - 46.8
Plt (10^3/µL)	430	200 - 600
Neutrophils (%)	87.9	49 - 65
Lymphocytes (%)	10.4	21 - 25
Monocytes (%)	1.7	0 - 5
Eosinophils (%)	0.0	6 - 22
Basophils (%)	0.0	0 - 0.5

Table 5 - Biochemistry profile and haemogas analysis of the neonate alpaca cria.

Biochemistry profile and hemogasanalysis	Value	Reference limits[4,5]
BUN (mg/dL)	43	21.62 - 60.66
Creatinine (mg/dL)	2.26	1.0 - 2.4
Glucose (mg/dL)	121	90.0 - 149.0
Total proteins (g/dL)	4.4	5.7 - 7.2
Albumin (g/dL)	3.14	2.9 - 4.3
Calcium (mg/dL)	10.4	4.2 - 9.0
AST (IU/L)	101.0	137.0 - 391.0
ALP (IU/L)	549.0	32.0 - 167.0
GGT (IU/L)	54.0	13.0 - 50.0
CPK (IU/L)	35.0	56.0 - 662.0
LDH (IU/L)	1083.0	10.0 - 695.0
pH	7.37	
pCO_2 (mmHG)	42.9	
pO_2 (mmHG)	354	
Be (mmol/L)	-1	
HCO_3^- (mEq/L)	24.4	
TCO_2 (mEq/L)	26	
$SatO_2$ (%)	100	
Sodium (mEq/L)	154.0	144.0 - 155.0
Potassium (mEq/L)	4.1	4.0 - 5.7

to the cria at 45 mL/kg/h speed. An ultrasound examination of the cria abdomen revealed a C1 fluid accumulation, thus a gastric tubing was performed, C1 was emptied and an IV supportive fluid therapy associated to sodium bicarbonate was carried. Glycaemia was monitored every 2 hours through stick glucometer and corrected when necessary by infusion of bolus of 33% glucose diluted in a saline solution. Due to the non-responsiveness to therapy, the cria was euthanized at 36 hours of life.

Dam's condition improved in terms of appetite and rumination and fecal output rapidly reached normality. After assessing complete expulsion of fetal membranes, the female alpaca was dismissed, at day 7 after admission.

DISCUSSION

Pregnancy toxemia arises in ruminants from negative energy balance, thus causing lipid mobilization, liver lipidosis and ketosis[7]. However, camelids are slightly different by the digestive and metabolic point of view: glycaemia is higher and ketones are lower compared to true ruminants. Finally, it is not completely clear how much camelids rely on ketogenesis to support energy metabolism[8]. In addition to simple starvation or competition for food, various stressors may promote lipolysis. These include transport, extreme temperatures, hypoproteinemia, and systemic diseases. Concerning hypoproteinemia, a possible explanation is that gluconeogenesis also relies on amino acids as substrates, especially during periods of anorexia[9].

The two patients herein reported belonged to two different farms, so it was difficult to relate the onset of pregnancy toxemia to a herd-related condition. However, it is possible that competition could lead to lesser feed intake in less dominant animals.

Some Authors report that abnormal lipid metabolism is associated to pregnancy toxemia due to fat mobilization, however other studies report that only one-third of the affected camelids show increased serum triglycerides, thus representing a low-sensitive determination[8]. However, in case of intensive lipid mobilization, blood serum could appear milky and dense, as reported in the second patient.

Induction of parturition or cesarean section are sometimes suggested for dams affected by pregnancy toxemia. In the first alpaca referred to our hospital, fetal death was identified. As no signs of abortion were noticed, induction of fetal expulsion was obtained in 24 hours after a single injection of prostaglandin agonist. Since camelids show intense enzymatic pathways for gluconeogenesis but relatively poor enzymatic pathways for ketogenesis, we hypothesized that pregnancy-associated negative energy balance induced lipid mobilization.

The second alpaca was referred to the OVUD close to the end of the pregnancy, with less severe clinical signs and with a live fetus, although fat mobilization was more intensive as demonstrated by dense and milky serum and blood biochemistry findings. Supportive medical therapy and spontaneous parturition contributed to a rapid recovery of the dam. Although the cria was born alive, it developed failure of passive transfer of immunity and the therapeutic approach herein presented failed to improve its clinical condition.

Prognosis for camelids with pregnancy toxemia depends on the timing of diagnosis and intervention. In both the cases reported, our approach showed good result in preserving the survival of the dams. The fetus from the first alpaca was diagnosed as already dead soon after admission, while the other one died within 48h from birth.

Improved feeding management for pregnant alpacas could be useful in preventing insufficient energy intake, fat mobilization and pregnancy toxemia. Ensuring animals a good quality-feed, considering hierarchy and providing easy access to feed for less dominant animals could represent an easy-to-implement strategy at the farm level, together with disease and parasite control.

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Conflict of Interest

The authors declare that there were no conflicts of interest.

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