Hypoglycemia and ketosis in a pregnant bitch

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Summary

A four-year-old female Afghan hound in near-term gestation presented for dystocia. On presentation the patient had dull mentation, a low body condition score (2.5/9) and was unable to ambulate. The patient had delivered two pups before presentation and on physical examination a palpable pup in the vagina. Fetal heart rates were measured with transabdominal ultrasound and fetal bradycardia was observed (measured between 155-190 beats per minute). A cesarean section was indicated. Clinical pathology showed a marked hypoglycemia (2.1mmol/L), ketonemia and lymphopenia. Urinalysis showed hypersthenuria, ketonuria, mild proteinuria and bilirubinuria. Dextrose 50% was administered parenterally at 1g/kg and isotonic fluid therapy was commenced. The patient was anaesthetized and a routine cesarean was performed. Prior to discharge the patient had normal mentation, was eating, ambulatory and blood glucose was 8.8mmol/L. A catabolic energy state for a bitch in late gestation may result in hypoglycemia, ketonemia and ketonuria. Inappropriate energy balance throughout the periparturient period may be detrimental to both the bitch and her pups.

Keywords: Hypoglycemia, ketonemia, ketonuria, pregnancy, cesarean section

Background

Hypoglycemia with ketonemia and ketonuria in the preparturient bitch has been poorly described in the literature, hence the pathophysiology and definition of the disorder in the bitch has been difficult to demonstrate.[1] Pregnancy toxemia, as defined in other domestic species, is a metabolic disorder, commonly occurring in the final third of gestation. It is associated with an inability to maintain glucose homeostasis and a negative energy balance. Undernourishment in late gestation and exposure to stressors (environmental and physiological) that can promote glucose consumption has been associated with the disease.[2] Clinicopathological findings of pregnancy toxemia in species where it is well defined, namely sheep and other small ruminants, include severe hypoglycemia, cortisol-induced hematology changes (neutrophillia, lymphopenia, eosinopenia) and evidence of dehydration.[3] Ketonemia and ketonuria are also common findings in pregnancy toxemia of small ruminants and occur as a result of the altered metabolism of carbohydrates and fats,[4] allowing for the production and accumulation of ketone bodies. Hypoglycemia is generally considered an unlikely cause of dystocia in the bitch.[5] To the authors' knowledge, there have been five reported cases of suspected pregnancy toxemia in dogs. Irvine[6] briefly reported a case series of three patients with hypoglycemia in 1964, and Jackson[7] reported a case of hypoglycemia-ketonemia in a bitch in 1980, with minimal database and information. Another more recent brief communication was published in 2009 detailing preparturient hypoglycemia in a Great Dane bitch,[8] which was the first report in a large breed dog. The aim of the present case report is to contribute to the limited database of cases pertaining to the rare occurrence of severe hypoglycemia and ketosis in the pregnant bitch.

Case presentation

History

A four-year-old female Afghan hound presented to the theriogenology services at a private specialist hospital for dystocia. She had commenced stage II labor five hours prior to presentation, and the caregiver had found a deceased pup. A second pup was delivered two hours after the first, which was a male and clinically normal at birth. No further pups were delivered, and the owner had observed no abdominal straining prior to presentation. History at presentation indicated that the patient had been particular about eating; she had initially been fed a dry dog food following insemination, however in the later stage of gestation she had been fed chicken frames and necks. Recently her appetite had been reduced and she had subsequently become inappetent.

The patient had been inseminated surgically 56 days prior to presentation. Clinical examination at time of insemination, including reproductive examination and vaginal cytology, was normal and in accordance with the stage of estrous. Three progesterone profiles were obtained prior to surgical insemination. A body condition score (BCS) of five out of nine was given at time of

insemination and was determined as normal. The bitch was inseminated with 140 million frozen-thawed sperm. Pregnancy examination occurred four weeks after insemination and the bitch was found to be healthy and normal. Transabdominal ultrasound identified a minimum of eight conceptuses with heartbeats, which were all of appropriate size for the stage of gestation. Uterine and placental anatomy was normal.

Clinical findings

On presentation to the clinic, the patient was unable to right, rise or ambulate on her own and had dull mentation. The patient had a body weight (BW) of 23-kg (50.7lb) and BCS of 2.5/9. Cardinal signs were as follows: temperature 37.5°C (99.5°F), heart rate 90 beats per minute (bpm), respiratory rate 16 breaths per miute with appropriate effort, mucous membranes were pink and dry with capillary refill time of two seconds. On reproductive examination the patient had a swollen vulva consistent with parturition, and a soft and dilated vagina. A pup in caudal presentation with normal posture was palpated in the cranial vagina. No Ferguson reflex was detected. Transabdominal ultrasound revealed a normal uterus and abdomen; multiple pups were visible and fetal heart rates were measured on M-mode. Fetal heart rates were measured between 155-190 bpm.

Laboratory findings

Biochemistry, performed in-house[a] on a plasma sample, revealed marked hypoglycemia (2.1mmol/L; reference range 4.11-7.95mmol/L), mild elevation of urea (10 mmol/L; reference range 2.5 to 9.6mmol/L), likely pre-renal (see urinalysis below), with all other values within normal range. Marked elevation of ketones in whole blood was found on in-house human Point-of-Care (POC) analyzer[b] with the value of 1.9 mmol/L. A blood sample was taken after surgery and was submitted to external pathology laboratory for measurement of B-hydroxybutyrate, which showed mild elevation (1.6mmol/L; normal reference under 0.5mmol/L). Resting cortisol level of 158 nmol/L; reference range 15 to 170 nmol/L and low insulin of 3.3 mU/L; reference range 5 to 20 mU/L. Progesterone was 3.18 nmol/L (1.0 ng/mL), appropriate with parturition.

Complete blood count, performed in-house,[c] revealed a normal hematocrit for late pregnancy (Hct, 34.5% reference range 25% to 40%), a normal WBC count (9,400 WBC/μL; reference range 5,050 to 16,760 WBC/μL), and a mild lymphopenia (760 lymphocytes/μL; reference range 1,050 to 5100 lymphocytes/μL). Urinalysis performed in-house initially on sample collected via cystocentesis, with results confirmed by an external laboratory revealed hypersthenuria (urine specific gravity of >1.060), indicating adequate urinary concentration, bilirubinuria (large), ketonuria reflecting a catabolic state (over 8 mmol/L), trace glucose (5.5mmol/L), pH of 7.0, and mild proteinuria (1g/L). Cytologic interpretation demonstrated few epithelial cells, low cellularity and low number of red blood cells on the background, likely to reflect iatrogenic contamination from cystocentesis. In-house venous blood gas analysis[d] revealed mild metabolic acidosis with compensatory alkalosis (pH 7.35; reference range 7.38 to 7.44, pCO_2 31.3mmHg; reference range 40 to 50 mmHg and HCO_3 16.8mmol/L; reference range 18 to 26 mmol/L) with a standard base excess of -7.8mmol/L, reference range -5 to 1 mmol/L. Electrolytes were within normal range (Na+ 145 mmol/L; reference range 141 to 156 mmol/L, K+ 4.42mmol/L; reference range 4.0 to 5.6 mmol/L, ionized Ca 1.13 mmol/L; reference range 0.98 to 1.45 mmol/L and Cl- 112 mmol/L; reference range 110 to 120 mmol/L).

Treatment

After the initial blood glucose test, 1g/kg (2.2g/lb) of 50% dextrose diluted 1:3 with 0.9% saline was administered slowly intravenously. Parenteral isotonic fluids (lactated Ringer's solution) were commenced at 10ml/kg/hr (4.5ml/lb/hr). General anesthesia was induced and a cesarean section was performed soon after initial examination and eleven pups (six females and five males) were delivered to neonatal intensive care for resuscitation. One pup had ruptured fetal membranes when it was isolated in the uterus and was initially resuscitated but died shortly after birth. The deceased pup delivered at home was of unknown sex and health status, with the live pup born at home male and clinically normal. The BW of all pups born alive, via cesarean or at home, ranged from 375g to 515g (0.83 to 1.14lb), with a mean of 434.6g (0.96lb). All pups were assessed and were anatomically within normal limits. Pups born via cesarean required moderate resuscitation. Single doses of

oxytocin 10 IU and meloxicam 0.2mg/kg (0.44mg/lb) were given intra-operatively subcutaneously to the bitch.

Outcome

Repeat measurements of blood glucose in the bitch with in-house human Point-Of-Care glucometer[e] 30m after dextrose administration was 7.7 mmol/L (initial 2.0 mmol/L), post-operatively 7.8mmol/L and pre-discharge levels (three and half hours after admission) was 8.8mmol/L. Blood ketone levels had dropped to 1.6mmol/L post-operatively then to 0.9mmol/L immediately prior to discharge. Venous blood gas, which was measured three hours after surgery, demonstrated pH 7.34, pCO_2 35.5mmHg, HCO_3 18.5mmol/L with a base excess -6.2 (reference ranges as above). Electrolytes were all within normal limits.

Brief postmortem examination of the deceased pup delivered by cesarean section showed an externally normal female, BW 465g (1.02lb), with a small amount of serous nasal discharge bilaterally. Grossly, there was a failure in inflation of the right cranial and right caudal lung lobes. The right middle, and the left cranial and caudal lung lobes were adequately inflated. No other gross abnormalities were detected.

The patient was discharged with pups three and one-half hours after initial presentation. The bitch had normal mentation, was ambulatory and comfortable. Before discharge, all pups were assisted to nurse twice and the patient ate well. Of the 13 pups born, 11 survived and were vocal, suckling and mobile at the time of discharge. No medications were dispensed on discharge. Communication from the owner two weeks after surgery showed the patient and all pups doing well.

Discussion

During pregnancy there is a considerable change in the metabolic energy requirements of the dam, with a marked increase in glucose utilization by the fetuses and the placenta. The ability of glucagon, norepinephrine and cortisol to respond to hypoglycemia is blunted in pregnancy.[9] In pregnancy toxemia, regulatory mechanisms fail to raise blood glucose levels resulting in a catabolic state and hypoglycemia and mobilization of fat that releases fatty acids and ketones as an alternative energy source. In severe cases, as in the present report, ketones accumulate in circulation resulting in ketonemia and ketonuria alongside the hypoglycemia.

Significant hypoglycemia occurs in fasted animals (dogs, sheep, rats and guinea pigs) during late gestation and, in the ewe, the severity of hypoglycemia is directly related to the number of fetuses.[10] While a causative relationship has not been established, the bitch in the present report had a large litter size, which may have contributed to the development of hypoglycemia and ketosis. The quality and quantity of the diet may also be contributory factor for development of hypoglycemia. Starvation in pregnancy has been proven to decrease blood glucose significantly in humans and further prolonged starvation increases plasma fatty acids and β-hydroxybutyrate concentrations.[11] This was observed in the present case, where the patient had lost body condition and had been inappetent, resulting in lowered blood glucose and an increase in ketones.

There are marked species differences in the condition termed pregnancy toxemia. In the ewe there is severe metabolic disease with high mortality and poor response to treatment.[10] In ewes, pregnancy toxemia commonly occurs in the last third of the gestation, is associated with nutrition and the severity is directly proportional to the number of fetuses. In dairy cattle, it is a disease of the postpartum period and occurs at peak lactation, again associated with negative energy balance. In women it is referred to as pre-eclampsia; a multisystemic disease causing multi-organ failure, hypertension, proteinuria, abnormal placentation, premature birth and fetal death. In the canine species it appears to be prepartum disease with moderate to severe clinical signs including that of hypoglycemia; loss of appetite, restlessness, tremors, ataxia, seizures and coma. While it is likely that this patient was at or near the end of gestation at presentation (56 days following insemination), further cases would be useful to determine if hypoglycaemia and ketosis are a cause of pre-term parturition in dogs.

In all the reported canine cases, including the present case, response to treatment has been excellent, with full recovery occurring soon after the pups have been born or delivered. The present case, when considered with available literature, suggests that pregnancy toxemia in the bitch is likely associated with poor nutrition during gestation, a negative energy balance in the peripartum period,

poor body condition, litter size and environmental stressors. Bitches that have poor body condition in early gestation and in the prepartum period, as well as starvation or reduced appetite in the prepartum period are likely to have an increased risk of pregnancy toxemia. The bitch in the present report was uniparous, further studies would required to determine if this is a contributing risk factor in the development of pregnancy toxemia. In all species, treatment is aimed at rectifying the catabolic state and providing supportive care, which the present case indicates is also appropriate management in the bitch.

Learning points

- Hypoglycaemia with ketonemia and ketonuria can occur in bitchs during late gestation as a result of a catabolic energy state.
- Correction of hypoglycemia and dehydration and a cesarean section may be appropriate treatment.
- Inappropriate nutrition in the periparturient period may be a precipitating factor of the condition in the pregnant bitch.
- With early recognition and treatment, the prognosis for survival may be excellent.

a. IDEXX Catalyse in house biochemistry
b. Point Of Care analyzer for blood ketone, Optium Xceed β-Ketone
c. IDEXX Procyte in house hematology
d. Blood gas analyzer on Co-Ox ABL80 Flex
e. Point Of Care analyzer for blood glucose, Accu-Check Performa

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