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EXPLORING THE ROLE OF FETAL PITUITARY IN PROLONGED GESTATION: A CASE STUDY OF A JERSEY CROSSBRED COW

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Abstract

Prolonged gestation in cattle can have various causes, including pituitary abnormality which can disrupt the physiological mechanism of parturition. In this case study, a 3-year-old Jersey crossbred cow with suspected pituitary hypoplasia was treated with dexamethasone and cloprostenol sodium to terminate her pregnancy after 15 months. A dead male calf was vaginally delivered within 48 hours, and histopathological analysis revealed an underdeveloped pituitary. The cow was then treated with oxytocin and successfully inseminated twice after showing estrus signs. The role of the fetal pituitary gland in parturition and the difficulty in reversing this process once it has started are also discussed. Diagnosis of prolonged gestation may involve rectal examination, ultrasonographic scans, and fetal fluid analysis. Treatment for inducing parturition in cows typically involves administering cloprostenol and dexamethasone. This case highlights the importance of considering pituitary abnormality as a possible cause of prolonged gestation in cattle and the need to manage such cases with minimal harm to the cow.

Introduction

Prolonged gestation due to adenohypophyseal hypoplasia is a well-known disorder in many cattle breeds (Jackson. 2005). The fetal pituitary gland plays an important role in the initiation of parturition at the end of gestation. In the final stage of gestation, the maturing fetal hypothalamic-pituitary-adrenal axis is able to respond to chronic stimuli and acute stressors such as hypoxia and hypercapnea with the production of Corticotropin-Releasing Hormone (CRH) (Nathanielsz 1993, Jackson, 2005, Wood, 2005). CRH causes the release of high levels of ACTH from the adenohypophysis into the blood stream. Fetal cortisol is essential in the conversion of placental progesterone and pregnenolone to oestrogens and stimulating the initial sequence of the birth process (Wood, 2005). The lack of any crucial element in parturition sequence, such as the adenohypophysis in the present case, disables the entire chain of events and parturition fails to occur. The present case reports a case of prolonged gestations of 15 months due to pituitary abnormality.

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Case history and Observation

A 3 year old Jersey cross bred cow was presented to the Teaching veterinary clinical complex, Orthanadu for pregnancy diagnosis and pregnancy was confirmed on November 2018 with signs of 7 months pregnancy. Again the animal was brought for pregnancy due and confirmed on January 2019 with same signs of 7 months pregnancy and reviewed on March 2019 with no signs of approaching parturition. On clinical observation, rectal examination revealed cervix on the pelvic brim and uterus in the abdominal cavity. The uterus was filled with fluid and fetal mass was palpable but not able to differentiate the fetal parts. Vaginal examination showed pink and moist mucous membrane, vaginal passage was severely constricted and there was a mucoid discharge. The external os the cervix has 1 finger dilatation. Ultrasonographic examination revealed hyper-echoic reflections and greyish particles in the uterus fluid which seems to be quite abnormal. Since it was an overdue fetus based on the clear breeding history, the pregnancy has been terminated with the help of dexamethasone @ 32 mg and cloprostenol sodium @ 0.5 mg intramuscularly. After 48 hours of termination rectal examination revealed fetal mass and fremitus. On vaginal examination the fetal limb was palpable and cervix has 3 finger dilatation. Since the cervical dilatation is not sufficient for the fetus to come out, to enhance the cervical dilatation fanning and feathering of the cervix with luke warm water was done. During this process the chorioallontoic sac was ruptured and greenish mucoid discharge of about 30 litre was flushed out (normal volume is around 4-8 litres). Since there is no presentation, position and posture abnormality, by slight pull a dead male fetus was delivered per vaginally. On examining the removed fetus it possess several abnormalities such as first degree hydrocephalus, absence of hair on both the thighs and the teeth was covered by the pink spongy cartilage. As per the reference since most of the case of prolonged gestation has occurred because of pituitary abnormality we collected the pituitary from the dead calf and subjected to histo-pathological examination. The histo-pathological result revealed exposed more of vacoules in the pars distalis region suggestive of under developed pituitary. The animal was treated with oxytocin @ 40 IU on first day along with ceftriaxone @ 4.5 g I/V, meloxicam @ o.5 mg I/V, chlorphenaramine maleate @ 0.5 g I/M, involon 150 ml P/O and supportive fluid therapy for the following 5 days. After 28 days the animal showed estrus signs such as bellowing. On clinical examination all the vital parameters were normal. Rectal examination revealed proper uterine involution. Ultrasonographic examination revealed cystic corpora lutea (15.7x19.1mm) on left ovary and dominant follicle (8.8x10mm) on right ovary. It clearly indicates that the animal has been already ovulated results in the formation of cystic corpora lutea and now the animal is in the stage of mid cycle estrum. In order to lyse the cystic corpora lutea injection cloprostenol sodium @ 0.5 mg has been injected intramuscularly. After 60 days the animal again showed estrus signs such as bellowing, mounting and vaginal discharge. External examination of the genitalia revealed edematous vulva and pink & moist vaginal mucous membrane. Rectal examination revealed relaxed cervix and turgid uterus. Ultrasonographic examination revealed dominant follicle (15.7x13mm) on the right ovary and multiple small follicles on the left ovary. The animal was inseminated followed by GnRH @ 10 mg injection to ensure the ovulation. On next day of GnRH injection ultrasonographic examination showed ovulatory site on the right ovary and the animal has been inseminated successfully second time to improve the chance of fertilisation. Hence a successful case of prolonged gestation and its therapeutic management was reported.

Discussion

Prolonged gestation due to adenohypophyseal hypoplasia is a well known disorder in many cattle breeds (Jackson, 2005). In cattle, gestation length is influenced by factors such as the breed of the cow and bull, calf gender, single vs. multiple birth, the parity of the cow, and the fetal genotype. Environmental factors, including nutrition, ambient temperature, and the season of the year, have a smaller influence. The breed of cattle has the greatest influence on gestation length. In European cattle of the *Bos taurus* species, considerable breed variation is recognized (eg, 279 days mean gestation in Holstein-Friesian to 287 days in Charolais). In breeds of the *Bos indicus* species, a slightly longer gestation length is often seen (eg, Zebu cattle have a mean gestation

length of 296 days). Within breeds, individual bulls may sire calves with longer gestation length than normal, leading to a higher incidence of dystocia. The fetal pituitary gland plays an important role in the induction of parturition at the end of gestation, and its importance in the physiological mechanism of parturition has been extensively studied in the sheep (Liggins and others 1967, Nathanielsz 1993, Wood 2005). In the final stage of gestation, the maturing fetal hypothalamic-pituitary-adrenal axis is able to respond to chronic stimuli and acute stressors such as hypoxia and hypercapnea with the production of corticotropin-releasing hormone (CRH) in the para ventricular nuclei of the hypothalamus (Nathanielsz 1993, Jackson 2005, Wood 2005). This hormone causes the release of high levels of ACTH from the adenohypophysis into the bloodstream. The fetal adrenal glands in sheep respond to this ACTH stimulus with the production of high amounts of cortisol; fetal cortisol induces the activation of cytochrome P450c17 (CYP17) in the placenta, through up regulation of prostaglandin-2 synthethase activity and production of prostaglandins. CYP17 is essential in the conversion of placental progesterone and pregnenolone to oestrogens (oestradiol). This oestradiol has a positive feedback on the production of CRH in the fetal hypothalamus; thereby further stimulating this initial sequence of the birth process (Wood 2005). In cattle, the initiation of parturition includes an additional step, which is necessary to reduce the plasma progesterone concentration in the dam. Unlike in sheep, the corpus luteum of the bovine ovary is the main source of progesterone during almost the entire pregnancy (Hoffmann and Schuler 2002). An abrupt drop in plasma progesterone levels during the two to three days before parturition is caused by luteolysis induced by prostaglandins, especially prostaglandin F2α, released from the fetal membranes, the placenta and the maternal endometrium at the end of gestation (Kindahl 2004). The increased oestrogen-to-progesterone ratio enhances the activity of the myometrium, leading to the onset of labour and delivery contractions (Wood 2005). Oxytocin is released from the neurohypophysis to further stimulate uterine contractions. In a positive feed-forward mechanism, known as the Ferguson reflex, stretching of the uterine cervix stimulates the release of more oxytocin by the maternal pituitary gland. This chain of events is impossible to reverse and very difficult to stop, making delivery inevitable (Nathanielsz 1993). The lack of any crucial element in this whole sequence, such as the adenohypophysis in the two calves, disables the entire chain of events and parturition fails to occur. Maternal ACTH is unable to cross the placental barrier and although maternal cortisol is able to diffuse through the placenta, the plasma cortisol levels in the mother never reach the required concentration of 25 to 100 ng/ml, as seen in the fetal plasma approaching delivery. (Kennedy *et al.,* 1957). In a case of suspected prolonged gestation, the dam's breeding records, if available, should be checked to ensure that parturition truly is overdue. Treatment of a case in which gestation is not genuinely prolonged may result in the delivery of a premature fetus that is unlikely to survive. Once the true length of gestation is established, a full clinical examination of the dam should be conducted. In cattle; rectal examination of the uterus and its contents is an important diagnostic aid. Fetal parts may be palpable, and in some cases it is possible to detect an abnormal cranium. An ultrasonographic scan may confirm the presence of fetal abnormalities, including a thin-walled, fluid-filled cranium. The weight of an overdue fetus may cause it to pass under the rumen while still within the uterus, so that it cannot be palpated per rectum. In some animals, prolonged gestation is accompanied by development of excessive amounts of fetal fluid. The origin of excessive fetal fluid can be assessed by analysis of sodium and chloride levels in an aspirated sample. Amniotic fluid contains sodium at ~120 mmol/L and chloride at ~90 mmol/L. Allantoic fluid contains sodium at 50 mmol/L and chloride at 20 mmol/L. The correlation between hydrops amnion and hydrops allantois and prolonged gestation is tenuous, however. Most fetal giants suffer from oligoamnios. In true prolonged gestation; the fetus is unlikely to be of any economic value. Treatment should be aimed at fetal delivery with minimal damage to the dam. Birth in both cows and sheep can be successfully induced by administering both prostaglandin $F_2\alpha$ (and its synthetic analogue cloprostenol) and the corticosteroid dexamethasone by IM injection. Luteolysis is induced by the prostaglandin, and the maternal hormone cascade that precedes parturition is initiated by the corticosteroid. In cows, 500 mcg cloprostenol and 20 mg dexamethasone are

given; in sheep 125 mcg cloprostenol and 16 mg dexamethasone are recommended. A single dose of these two drugs is normally effective. Parturition should begin in 24–72 hr. Induced parturition should be monitored carefully. Assistance may be required if there is evidence of uterine inertia or damage to the abdominal wall, either of which might make expulsive efforts ineffective. Fetal malposition requiring obstetric assistance may occur once birth begins. If the fetus is very large, dystocia due to fetal-pelvic disproportion may occur, and assisted delivery by careful traction may be attempted. If this is not possible, cesarean section may be required. If the dam is seriously ill but considered well enough to withstand surgery, an elective cesarean without an attempt at vaginal delivery may be considered. Fetal dysmaturity can be a problem, especially in very valuable cloned offspring, and intensive care facilities may be needed. After fetal delivery, uterine involution may be encouraged by administration of oxytocin. Fluid therapy, antibiotics, and treatment with NSAIDs such as flunixin meglumine may aid recovery and provide analgesia.

Bovine viral diarrhoea, Akabane or bluetongue virus infections can cause severe brain damage in the fetus, including anencephaly, hydrocephaly or porencephaly, resulting in rupture of the hypothalamus and/or hypophysis (Hanzen 2005, Jackson 2005). Ingestion of Veratrum californicum or Veratrum album has also been associated with prolonged gestation due to severe cranial deformities and brain defects in the bovine fetus (Jackson, 2005). Ingestion of insecticide during early pregnancy in the agriculture fields also would have caused the impairment in brain development. Even though the pars tuberalis region was having normal follicles the pars distalis region was predominantly occupied by vacuolar region which is also a source for release for hormones. However analysis of gene expression and toxicology studies will throw better light in understanding the micro impairment of fetal development

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