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Case report

Managing retained placenta in first-parity doe and administering vitamin A, D, and E as supportive treatment

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ABSTRACT

This study aims to report the treatment of retained placenta in a doe by administration of intrauterine antibiotics, accompanied by intramuscular injection of antibiotics, anti-inflammatory, and injection of vitamins A, D, and E as supportive treatment. The Saanen doe was brown, approximately two years old with a BCS of 3/5 and kidding for the first time on January 11, 2023. The following day, it was reported that the doe's placenta had not been expelled until 24 hours after kidding. Physically the doe was weak, unable to stand, and reddish-brown discharge was seen came out of the vulva. Based on these conditions the doe was diagnosed as having retained placenta with a fausta prognosis. The doe was treated with a bolus of antibiotics contained 250 mg sulphadiazine and 50 mg trimethoprim which was diluted with 5 mL of 0.9% NaCl for uterine lavage. Systemic treatment consisted of intramuscular injection of ceftiofur at 1.1 mg/kg bw, flunixin meglumine at 1.1 mg/kg bw, as well as a combination of 300,000 IU of vitamin A palmitate, 100,000 IU of vitamin D3, and 50 mg of vitamin E acetate as supportive treatment. The treatment was successful, the doe was able to stand and eat when examined the next day after treatment. The doe returned to estrus 42 days after treatment. It could be concluded that treatment of retained placenta in a doe with intrauterine broad-spectrum antibiotics, beta-lactamase antibiotics and intramuscular anti-inflammatory, with vitamins A, D and E as supportive therapy was effective and the doe returned to estrus 42 days after treatment.

Keywords: ceftiofur, flunixin meglumine, Saanen doe, sulphadiazine, trimethoprim

INTRODUCTION

Retained placenta was a failure to release the cotyledon villi of the fetal placenta from the caruncle crypts of the maternal placenta more than 8-12 hours after parturition (Majeed *et al*., 2003). The process of placental separation began before parturition. After the fetus was expelled and the umbilical cord was severed, no blood flowed to the fetal villi, and the villi contracted and loosened. The uterus continued to contract and the large amount of blood that previously flowed to the uterus was greatly reduced. The maternal caruncle became smaller because the blood supply was reduced and the crypts in the caruncle widened. In a detached placenta, the detachment process is caused by chronic villous autolysis (Li *et al*., 2022). In retained placenta, the separation and detachment of the fetal placental villi (cotyledons) from the maternal placental crypts (caruncles) was disrupted and fusion occured, causing the placenta to not be

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expelled. After a few days, there were leukocytes in the placentome, so that inflammation of the placenta easily occured (Inaba *et al*., 2022).

Several factors identified as causes of placental retention were diet (selenium, calcium, vitamins A, and vitamin E deficiencies), infections (toxoplasmosis, chlamydiosis, and listeriosis), predisposing factors (obesity and dystocia) (Pugh *et al*., 2021), immature placenta (for example due to abortion or induction), edema or necrosis of the villi, placentitis or metritis (Leonardo *et al*., 2018), physical factors (uterine atony due to old age or lack of movement of the doe, torsion of the uterus, fluid-filled uterus), and excitation during parturition (Pugh *et al*., 2021). Retained placenta was characterized by the placenta hanging from the vulva more than six hours after parturition. There was foul-smelling bloody discharge in the vulva area. The vulva lips were swollen, and reddened (Harwood and Mueller, 2018). It was also possible that the cotyledons of the fetal placenta were still firmly attached to the maternal caruncle, and there were no detached parts hanging out of the vulva (Dervishi *et al*., 2016). In new cases of retained placenta, does were still able to stand and their general condition were still good. However, if the case had been going on for a long time, bacteria had developed, then the general condition became worse and a specific foul smell, brownish fluid came out accompanied by shreds of placenta.

Without proper treatment, retained placenta would worsen into metritis, endometritis, and pyometra, and could even caused infertility, sterility, or death. Infertility occured because retained placenta inhibited the rate of uterine involusion, late return to estrus after parturition, and a longer postpartum intervals (Faradillah and Agustina, 2023), causing economic losses for farmers (Tuscho, 2017). Treatment for retained placenta could be done by manually releasing the fetal membranes, administering broad-spectrum antibiotics such as oxytetracycline, chlortetracycline, or tetracycline, as well as hormonal therapy using oxytocin and prostaglandins (Rahim *et al*., 2023). Manual release of retained fetal membranes should be attempted by 72 hours after parturition. If the placenta could not be separated within 10 minutes, the attempt should be stopped to avoid further damage and bleeding. The doe was revisited again in 48 hours. If the second attempt failed, another attempt was made 48-72 hours later. After removal of the placenta, it was recommended to administer antibiotics in utero (Beagley *et al*., 2010). Removal of the cotyledons from the caruncula must be carried out by professionals because of the risk of bleeding and infection. Some experts believed that manual removal of the placenta was not recommended because it could cause infection. Another treatment that could also be done was to cut the hanging placenta while leaving the rest in the uterus and then inserting antibiotics into the uterus in the hope that the remaining placenta remaining in the uterus would lyse and be expelled along with the lochia (Königsson *et al*., 2001).

Only a few publications reported the treatment of cases of retained placenta in does. Therefore, this study aims to report the treatment of retained placenta on a doe which was carried out by administering intrauterine antibiotics accompanied by intramuscular injection of antibiotics, anti-inflammatory, and injection of vitamins A, D, and E as supportive treatment.

MATERIALS AND METHODS

Signalement and anamnesis

The Saanen doe, brown in color, approximateley two years old with a BCS of 3/5 was always kept in a goat pen all the time, and forage feed and drinking water was always available. The doe was kidding for the first time on January 11, 2023. The next day, it was reported that the doe's placenta had not been expelled until 24 hours after parturition.

Clinical signs

On physical examination, the doe was weak, unable to stand, and a reddish-brown discharge was seen came out from the vulva (Figure 1).

Diagnosis and prognosis

The diagnosis made based on anamnesis from the farmer and physical examination on the

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doe showing that the doe was having retained placenta with a good prognosis.

Therapy

The placenta hanging outside the vulva was gently pulled until it fell off, then the vulva and vaginal areas was cleaned of discharge. Next, an antibiotics bolus containing 250 mg sulphadiazine and 50 mg trimethoprim was diluted with 5 mL of 0.9% NaCl and used for uterine lavage. Ceftiofur at 1.1 mg/kg bw and flunixin meglumine at 1.1 mg/kg bw were both injected intramuscularly. Finally, a combination of 300,000 IU of vitamin A palmitate, 100,000 IU of vitamin D3, and 50 mg of vitamin E acetate was injected. Therapy was carried out as a single treatment (Table 1).

Table 1 Treatment of retained placenta in a doe

drugs	content	dosage	route
Sulphadiazine & Trimethoprim bolus	sulphadiazine, trimethoprim	¼ bolus + 5mL NaCl 0,9%	intrauterine
Ceftionel-50	ceftiofur	1.1-2.2 mg/kg 2 mL	im
Flunixin injection	flunixin meglumine	1.1-2.2 mg/kg 2 mL	im
Vigantol E	vitamin A, D3 dan E	2 mL	im

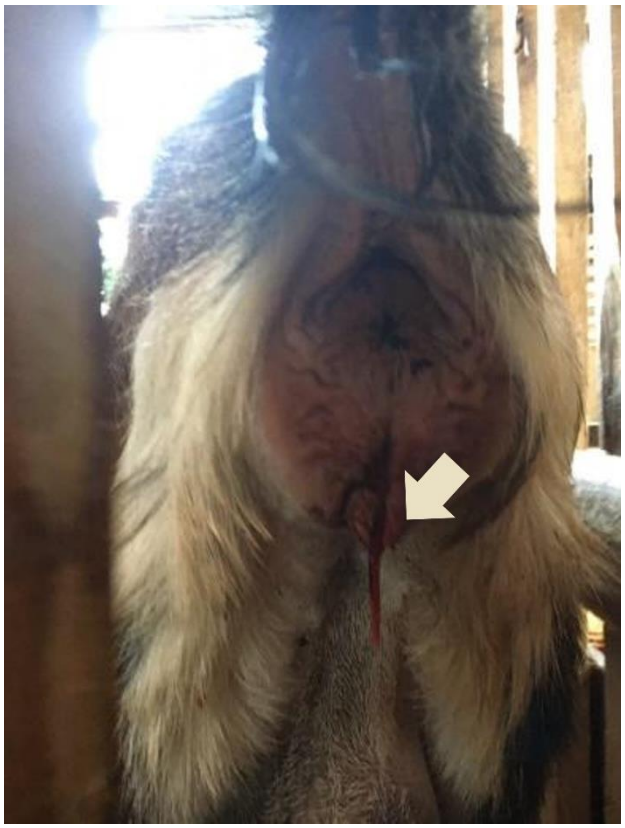

Figure 1 Saanen doe with retained placenta showing a reddish-brown discharge from the vulva (arrow).

RESULTS

The treatment was successful, the doe was able to stand and eat when examined the next day after treatment, and the doe returned to estrus 42 days after treatment.

Figure 2 Twenty-four hours after treatment, the doe that had retained placenta was able to stand and eat.

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DISCUSSION

Based on physical examination, anamnesis, and clinical signs, the doe was diagnosed as having retained placenta. Normally, the placenta came out by itself within 6 hours postpartum. The placenta was considered retained if it was not expelled within 12-18 hours after parturition. In this case, the placenta had not been expelled within 24 hours postpartum. The placenta was not expelled by itself because the fetal placenta (cotyledon villi) failed to separate from the maternal placenta (caruncle crypts) (Sheldon *et al*, 2008). The uterus usually contracted approximately 14 times during one hour after parturition and would reduce the frequency of contractions to once per hour at 42 hours after parturition (Rizzo *et al*, 2018). The parturition was accompanied by regression of the corpus luteum so that progesterone was at basal levels. Low progesterone levels reduced the threshold of myometrium response to oxytocin stimulation. Up to six hours after parturition myometrium contractions still occured due to oxytocin. Oxytocin was a neuropeptide hormone released from the neurohypophysis into the circulation. Oxytocin was an effective uterotonic drug in puerperal cows (Heppelmann *et al*., 2017).

The placenta functioned as a conduit from the doe to the fetus, such as distributing nutrients and oxygen and protecting the fetus. The surface of the placenta was widened by intimate connections between the chorionic villi and the endometrial crypts for maximum nutrient exchange, saturation, and excretion. A further expansion of the area occured due to the presence of cotyledon microvilli which branch into the caruncular crypts (Tanner *et al*., 2022). Retained placenta occured due to mechanical interference and due to the doe's lack of strength to expel the placenta and could also occur due to a deficiency of hormones that could stimulate uterine contractions during parturition such as oxytocin or estrogen. The disruption of prostaglandin formation in the doe's caruncle could cause a decrease in uterine contractions, the less prostaglandin produced, the weaker the contractions produced (Beagley *et al*., 2010).

Predisposing factors for retained placenta included dystocia, multiple births, hypocalcemia, high environmental temperature, age, premature birth, placentitis, bacterial endotoxins, and nutritional factors (Hossein-Zadeh *et al*., 2011). It was suspected that the cause of retained placenta in this case was nutritional factors, because during pregnancy the doe was only given forage. The doe was already weak when kidding and after that the doe could not stand. Lack of nutrients such as protein, selenium, iodine, vitamins A, vitamin E, and calcium were reported to be factors that could cause placental retention. Vitamin E and selenium deficiencies had been proven to damage neutrophil function and could reduce oxidative stress before parturition. Selenium was a component of the enzyme glutathione peroxidase which functioned as an antioxidant that formed enzymes that were useful for the immune system and reproduction of livestock. Deficiency of vitamin E and selenium could decrease immunity and cell defense mechanisms, thereby increasing cases of retained placenta (Xiao *et al*., 2021).

This case of retained placenta occurred in a doe at first kidding. This was in line with the finding of Majeed *et al*. (2003) that the prevalence of cases of retained placenta in the first kidding was 61.1%. However, in dairy cows retained placenta occured more often in cows aged more than seven years or parity of more than five (Rohmah *et al*., 2023). The high rate of retained placenta in dairy cows as parity increased was caused by the short gestation period, which caused retained placenta (Al-Yamani *et al*., 2021).

Complications of retained placenta varied. However, in this case there were no complications, because the treatment was carried out directly by a veterinarian. Placental retention could develop into a uterine infection due to the opening of the vulva because there was a hanging membrane, so that bacteria could enter the vulva and reached the uterus. Retained placenta could inhibit uterine involution, and cause infertility in cows related to uterine infections. The incidence of retained placenta accompanied by metritis had been reported to

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reduce fertility (Sheldon *et al*., 2008). Currently there are no publications regarding the management and treatment of retained placenta in does. A study compared the treatment of retained placenta in local does in Iraq by manual removal, oxytocin (20 IU/im), and prostaglandin F2 (7.5 mg im) with effectiveness of 55.6, 66.6, and 88.8% respectively (Majeed *et al*. al., 2003). Retained placenta in beef cattle was successfully treated with a bolus of broad-spectrum antibiotics and oxytocin. In cases of retained placenta in beef cows that were treated immediately, reproductive performance was not affected. Delayed treatment could cause toxemia and ultimately infertility or death of the animal (Brahmanand *et al*., 2022). Dairy cows with retained placenta could recover and return to estrus after 14 days if treated appropriately. The retained placenta was carefully removed manually, followed by uterine lavage using 0.2% povidone-iodine solution in warm water, intrauterine antibiotics, and intramuscular injection of penicillin-streptomycin. Intramuscular injections of vitamin E and selenium were given as supportive treatment (Rahim *et al*., 2023).

In this case of retained placenta, treatment was by intrauterine administration of broad-spectrum antibiotics (250 mg Sulphadiazine and 50 mg Trimethoprim) diluted with 5 mL of 0.9% NaCl. Systemic treatment given was intramuscular injection of ceftiofur, and flunixin meglumine. Ceftiofur was a beta-lactam antibiotic which could inhibit bacterial cell wall synthesis and cause cell death. The dose given to goats was 1.1 mg/kg bw intramuscularly or subcutaneously. Flunixin meglumine was a non-steroidal anti-inflammatory that could work as an analgesic, anti-inflammatory, and antipyretic. The dose of flunixin meglumine given to goats was 1.1 mg/kg bw intramuscularly or intravenously (Papich, 2021).

There were still few publications regarding the use of vitamins A, D and E as supportive therapy in cases of retained placenta. Vitamin A deficiency was reported to result in a high incidence of retained placenta due to the role of vitamin A in maintaining the lining of the reproductive tract (Akar and Gazioglu, 2006). In dairy cows, vitamin D supplementation reduced the incidence of retained placenta (Poindexter *et al*., 2022). Less exposure to sunlight which was beneficial for vitamin D synthesis was correlated with a high incidence of placental retention (Rohmah *et al*., 2023). Meanwhile, vitamin E functioned as an antioxidant which helped the healing process of retained placenta in dairy cows (Xiao *et al*., 2021; Rahim *et al*., 2023).

In this case, supportive treatment was carried out with a combination injection of 300,000 IU vitamin A Palmitate, 100,000 IU vitamin D3, and 50 mg vitamin E acetate. Vitamin A (beta carotene) was a natural antioxidant that prevented the negative effects of free radicals. Vitamin A contributed to the cellular activation of the immune system, helped the cell healing process, increased hydration and elasticity, increased cell regeneration, increased collagen, and restored damaged tissue (Bozhkov *et al*., 2023). Vitamin A deficiency could result in a high incidence of retained placenta because of vitamin A's role in maintaining the lining of the reproductive tract, accelerating wound healing, and helping tissue repair after parturition. Vitamin D in serum correlated with antioxidant capacity in post-calving cows and was associated with reduced cases of retained placenta. Vitamin D also played an important role in calcium absorption (Eder and Grundmann, 2022). Calcium ion played a role in myometrial contractions in the third phase of labor (Strickland *et al*., 2021). Sunlight was useful for vitamin D synthesis in cow skin (Weir *et al*., 2017). Dairy cows that were given regular exposure to sunlight tended to reduce cases of retained placenta (Rohmah *et al*., 2023). Vitamin E was a lipophilic molecule that could neutralize lipid peroxyl radicals so that it could inhibit lipid peroxidation in cell membranes (Niki, 2014). Administration of vitamin E caused an increase in tocopherol concentrations in tissues, including leukocytes, which was thought to increase the function polymorphonuclear leucocyte (Pontes *et al*., 2015). Lack of vitamin E intake several weeks before parturition followed by low serum of α-tocopherol levels, raised the risk of retained placenta (Haga *et al*., 2021). Vitamin E injections once a week for three weeks before

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calving had been proven to be effective in reducing the incidence of retained placenta. The strong antioxidant properties of vitamin E could increase antioxidant capacity, which was followed by increased immune competence which played a role in the release of fetal membranes immediately after parturition (Pontes *et al*., 2015).

In the case of the doe whose placenta was retained, the treatment was successful, the doe returned to estrus 42 days after treatment The postpartum period in does was very similar to the postpartum period in cows, as well as in ruminants in general. In the process of uterine involution in does, rapid uterine shrinkage and contractions occured, especially on the third to 10th day after parturition, which was determined by measuring the weight and length of the uterus, the diameter of the uterine body, and the horns that had been pregnant (Paiano *et al*., 2019). Uterine involution was complete in 20-25 days. Endometrial recovery that occurred was a major change in the structure of the caruncle with surface degeneration, necrosis, sloughing, and subsequent regeneration of the superficial layer of the endometrium (Dai *et al*., 2023). Once the placenta detached, further hyaline degeneration of the caruncular tissue occured, resulting in narrowing of the blood vessels at the base of the maternal crypt. There was necrosis in the surface layer of the caruncle so that around four days after parturition the most superficial layer was undergoing autolysis and liquefaction, causing the discharge of lochia which was reddish-brown at this time. Sixteen days after parturition, necrosis occured throughout the superficial part of the caruncle, and then brown necrotic plaque was present in the uterine lumen. The caruncle then had a clean, shiny surface, and the regeneration process was completed by re-epithelialization of the caruncle in approximately 28 days. The amount of lochia released varied. Lochia was composed of blood, fetal fluids, and placental remnants, but as the postpartum period progressed, the caruncular tissue that liquefied and sloughed off came out (Noakes *et al*., 2001).

The does usually became anestrus after kidding which occured within a few days to two weeks after parturition. Follicle growth could occur, but silent estrus or estrus was not followed by ovulation. Failure of follicular maturation and ovulation might be caused by a lack of LH release resulting from a deficiency in GnRH synthesis and secretion. As a result, basal LH levels and the pulsatile frequency of LH secretion were not sufficient to stimulate ovulation (Arrebola *et al*., 2022). The does would return to estrus 21-42 days after kidding. However, it was better not to breed them first to give enough chance for the does to nurse the kids. It was recommended to breed in the third or fourth estrus or about two months after kidding, so that a good interval between kidding was eight months (Mogiye *et al*., 2020).

Preventing retained placenta could be done by keeping the cage clean to avoid peripartum germ infections. Nutritional management could include vitamin A before the parturition period, injecting oxytocin 0-4 hours before parturition, and a ration with a balanced composition of calcium and phosphorus. Giving selenium and vitamin E before parturition could reduce the incidence of retained placenta, metritis, and ovarian cysts, even though fresh forage contained sufficient vitamin E (Harrison *et al*, 1984). Vitamin E and selenium acted as antioxidants which played a role in defense against the accumulation of hydroperoxides during cell metabolism. Selenium deficiency could result in reduced fertility, retained placenta, and the incidence of mastitis and metritis. Selenium also played a role in the formation and activity of cytotoxic T cells, helper T cells, and natural killer cells in the immune system. Providing vitamin E and selenium during the prepartum period was an important factor in preventing retained placenta (Dhara *et al*, 2022).

CONCLUSION

Immediate treatment of the retained placenta with intrauterine and intramuscular injection of antibiotics, anti-inflammatory, and supportive therapy with vitamins A, D, and E cured the case, and the doe returned to estrus 42 days after treatment.

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AUTHOR'S CONTRIBUTIONS

Dhea Salsabila: conceived the idea, record data, manuscript drafting. Viski Fitri Hendrawan: diagnosed and treated cases, revised the manuscript for intellectual content. All authors read and approved the final manuscript.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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