

Short Communication

Fetal demise and delayed parturition following post-mating administration of depot progesterone for contraception in three hunting dogs

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ABSTRACT

Depot medroxyprogesterone acetate (MPA) is used in dogs to suppress estrus or prevent pregnancy. This report describes three cases in which post-mating administration of MPA resulted in failure of parturition and fetal death in hunting dogs. In all cases, MPA was administered within 1–7 days post-mating at a fixed dose of 150 mg. The dogs presented with signs of prolonged pregnancy and absence of labor. Ultrasonographic examinations confirmed the presence of non-viable fetuses, and ovariohysterectomy was performed in each case. In these dogs, serum progesterone concentrations ranged between 2.20 and 9.03 ng/mL at the time of parturition and remained within this range for up to two weeks postpartum. These hormonal alterations were likely due to exogenous MPA, which interfered with luteolysis, delaying the onset of labor. These findings underscore the importance of restricting depot progesterone use to appropriate reproductive stages to prevent iatrogenic reproductive failure and to ensure animal welfare.

Introduction

Contraceptive methods are frequently utilized to prevent unwanted pregnancies in hunting dogs, ensuring optimal performance during the hunting season and avoiding interruptions associated with pregnancy and parturition. Synthetic progestins, particularly megestrol acetate, medroxyprogesterone acetate (MPA), and proligestone, have been used for decades as contraceptives in dogs. Progestin-based contraceptives are marketed in various forms, including pills, slow-release depot injections, and implants.¹ Progestins exert a negative feedback effect on the hypothalamus and pituitary gland, suppressing the production of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) at consistently high concentrations. This suppression prevents follicular growth and ovulation.^{1,2}

Under appropriate clinical conditions, MPA can be administered to healthy, adult, non-pregnant, postpubertal female dogs in anestrus to temporarily postpone the onset of estrus or for estrus suppression when surgical sterilization is not an option. However, the treatment must be limited in duration and applied only after confirming that the dog is not pregnant, not mating or in diestrus.^{1,3} Additionally, although naturally occurring primary hypoluteoidism has not been clearly documented in

dogs, exogenous progestins have been used in selected clinical situations to support pregnancy when luteal insufficiency is suspected⁴. Their misuse can lead to adverse effects, including dystocia, pyometra, insulin resistance, and behavioral changes fetal abnormalities, masculinization of female fetuses or fetal death.^{1,5-8}

The present case series describes three hunting dogs whose owners administered depot MPA after mating for contraceptive purposes without veterinary guidance, resulting in fetal death and delayed parturition. The objective of this report is to highlight the clinical consequences of such inappropriate treatment and to raise awareness among practitioners regarding the life-threatening reproductive complications that may result from the use of depot progestogens in mated female dogs without appropriate veterinary oversight and a valid veterinarian-owner-patient relationship.

Case history

Case 1 was a 6-year-old intact female Zagar dog presented to the clinic approximately 90 days after mating. The dog exhibited clinical signs including lethargy, anorexia, and abdominal distension. No vaginal discharge was noted on clinical examination. According to the

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owner, a single 150 mg dose of depot medroxyprogesterone acetate (MPA; Depo-Provera, Pfizer) had been administered two days after mating to prevent pregnancy. The product was obtained directly from a human pharmacy without a veterinary prescription or clinical consultation. Transabdominal ultrasonography revealed anechoic fluid accumulations with multiple hyperechoic foci, suggestive of mineralized fetal tissue, within the uterine region of the abdominal cavity. Radiographic evaluation further confirmed the presence of multiple radiopaque fetal skeletal structures within the uterus, consistent with prolonged pregnancy and fetal maceration (Fig. 1). The dog underwent en bloc ovariectomy under general anesthesia (medetomidine 40 µg/kg, midazolam 0.25 mg/kg, butorphanol 0.3 mg/kg IM; induction with ketamine 7 mg/kg IM). Surgical exploration revealed a markedly enlarged uterus with severe vascular congestion and discoloration ranging from dark red to brownish-black. The uterine wall was thinned and friable, and the lumen was filled with malodorous and reddish-brown fluid. The endometrium appeared necrotic, with multifocal areas of hemorrhage and mural thinning, consistent with advanced autolysis and ischemic necrosis due to retention of macerated fetuses. During surgery, decomposed fetal remains lacking recognizable anatomy were recovered from the uterus, consistent with advanced intrauterine maceration (Fig. 2).

Case 2 was a 5-year-old intact female Zagar dog that was evaluated 74 days after reported mating. The owner stated that a depot MPA injection had been administered one day after mating. In the following weeks, the dog developed mammary gland enlargement and progressive abdominal distension, raising the owner's suspicion that pregnancy had occurred despite hormonal intervention. However, the owner stated that no pregnancy check or veterinary consultation had been sought during the presumed pregnancy. When parturition did not occur as expected, the dog was brought in for assessment. On clinical examination, the dog appeared bright, alert, and in good general condition, with no vaginal discharge. Transabdominal ultrasonography revealed multiple hyperechoic fetal skeletons and markedly reduced intrauterine fluid. No fetal cardiac activity, movement, or positional changes were detected during the examination, findings consistent with intrauterine fetal death and

resorption of fetal fluids. Radiographic evaluation corroborated these findings, confirming the presence of eight well-developed fetuses with overlapping skeletal structures. The dog underwent en bloc ovariectomy under general anesthesia (medetomidine 40 µg/kg, midazolam 0.25 mg/kg, butorphanol 0.3 mg/kg IM; induction with ketamine 7 mg/kg IM). During surgery, the uterus was markedly enlarged, hyperemic, and thin-walled. The uterine lumen contained a small volume of thick dark green-to-black fluid, and eight autolyzed fetuses were recovered, none showing gross congenital abnormalities (Fig. 3). The endometrium was friable and edematous but without cystic hyperplasia or neoplastic changes, and the ovaries appeared normal, bearing corpora lutea on their surface.

Case 3 concerned a 3-year-old intact female Zagar dog that was presented 73 days after mating. The owner reported that MPA had been administered one week after mating. Similar to Case 2, mammary development and abdominal distension were observed in the weeks following the injection, leading the owner to assume that the contraceptive had failed. However, the owner stated that no pregnancy check or veterinary consultation had been sought during the presumed pregnancy. When parturition did not occur as expected, the dog was brought in for assessment. On admission, the dog was bright, alert, and clinically healthy, with no vaginal discharge. Transabdominal ultrasonography revealed several hyperechoic fetal skeletons surrounded by echogenic material and markedly reduced intrauterine fluid, findings consistent with resorption of amniotic fluid. No fetal movement or cardiac activity was detected. Radiographic imaging confirmed the presence of five fully developed fetuses with overlapping skeletal structures and complete ossification, indicating intrauterine fetal death and prolonged retention. The dog underwent en bloc ovariectomy under general anesthesia (medetomidine 40 µg/kg, midazolam 0.25 mg/kg, butorphanol 0.3 mg/kg IM; induction with ketamine 7 mg/kg IM). During surgery, the uterus was markedly enlarged, congested, and thin-walled. On incision, a small quantity of thick dark green-to-black fluid was released, and five autolyzed fetuses were removed, each exhibiting variable degrees of soft-tissue disintegration (Fig. 4). The endometrium appeared friable, necrotic, and diffusely hemorrhagic on macroscopic

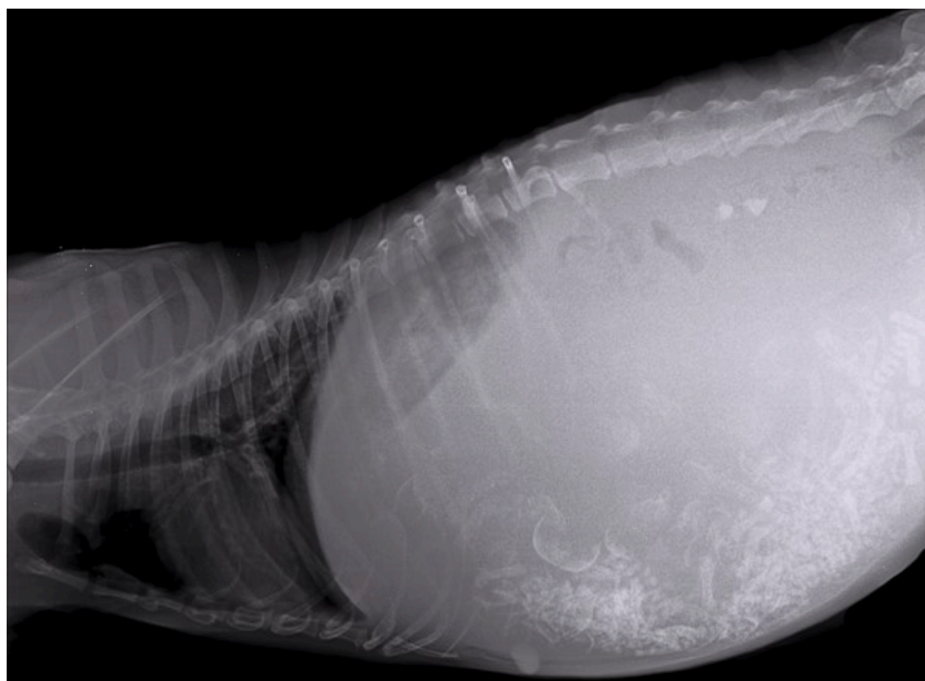


Fig. 1. Lateral abdominal radiograph of Case 1 demonstrating intrauterine fetal retention.

The image shows multiple mineralized fetal skeletons within the distended uterus, consistent with prolonged pregnancy. Absence of normal fetal positioning and overlap of skeletal structures suggest fetal death.



Fig. 2. Macerated fetal remains surgically removed from the uterus of Case 1. The image displays remnants of macerated fetuses retrieved during en bloc ovariectomy from Case 1. The absence of recognizable fetal anatomy and the presence of decomposed hair and skeletal debris are consistent with advanced intrauterine fetal maceration.



Fig. 3. Postoperative view of dead fetuses retrieved from the uterus of Case 2. The image shows eight fully developed but dead fetuses removed during en bloc ovariectomy. No macroscopic genital deformities were observed. The presence of varying degrees of autolysis is consistent with intrauterine fetal death associated with prolonged pregnancy.

examination. No macroscopic evidence of cystic endometrial hyperplasia or neoplastic lesions was observed. The ovaries were examined macroscopically, and structures consistent with corpora lutea were identified on their surface. Histopathological examination was not

performed.

No postoperative complications or abnormalities were observed during the recovery period in any of the three cases. The surgical incisions healed without complications, and no evidence of systemic



Fig. 4. Postoperative view of dead fetuses retrieved from the uterus of Case 3. The image shows four fully developed but dead fetuses surgically removed during en bloc ovariectomy. No macroscopic genital deformities were evident. The fetuses exhibited signs of intrauterine death and early autolysis, consistent with prolonged pregnancy.

illness, infection, or delayed wound healing was observed.

In addition, blood samples were collected from Cases 2 and 3 to evaluate serum progesterone concentrations using the electrochemiluminescence method (Roche, Germany). Progesterone levels measured during surgery ranged from 2.20 to 9.03 ng/mL, which are considered above the physiological threshold required to initiate parturition in dogs. One week postoperatively, serum progesterone levels were 2.51 ng/mL and 8.50 ng/mL in Cases 2 and 3, respectively. In Case 2, a follow-up measurement at two weeks postoperatively revealed a level of 2.17 ng/mL (Table 1).

Various differential diagnoses were considered to explain the prolonged gestation and intrauterine fetal death observed in our cases. Progesterone-secreting ovarian neoplasms were excluded based on the absence of such findings during surgical exploration, and an error in the estimation of gestational age was ruled out because ultrasonography revealed reduced fetal fluids and advanced fetal skeletal maturity. Considering the consistent history of MPA administration following mating and the elevated serum progesterone concentrations, the most likely diagnosis was disruption of normal parturition mechanisms due to exogenous progestin exposure.

Discussion

MPA is a long-acting synthetic progestogen that has been used for the

Table 1
Preoperative and postoperative serum progesterone levels (ng/mL) in Cases 2 and 3.

Cases	Before Surgery	One Week After Surgery	Two Week After Surgery
Case 2	2.20	2.51	2.17
Case 3	9.03	8.50	NM

NM: Not measured.

temporary suppression or delay of estrus in female dogs when surgical sterilization is not desired or possible. Its use is recommended in adult, non-pregnant, post-pubertal females during anestrus.^{1,3} When administered in depot form, a single injection effectively suppresses gonadotropin release from the hypothalamus, thereby inhibiting ovarian follicular development and ovulation while maintaining elevated circulating progestin concentrations for 6–12 months, inducing an artificial diestrus state.⁹ However, despite its theoretical benefits, MPA carries significant risk of adverse effects, including endometrial hyperplasia, pyometra, mammary hyperplasia, insulin resistance, adrenocortical suppression, and behavioral changes.^{1,7,8,10} For these reasons, its use has been largely discouraged in modern clinical practice, and no progestogen can be considered entirely safe for estrus control in dogs.¹ The cases presented in this report demonstrate the severe reproductive consequences resulting from the misuse of depot MPA in female dogs after mating. The use of long-acting progestins after mating represents a clear clinical error. In all three animals, exposure to exogenous progestogens disrupted the normal prepartum decline in progesterone concentrations required to initiate luteolysis, cervical relaxation, and uterine contractility. This hormonal disturbance consequently resulted in prolonged gestation and fetal death, representing an iatrogenic complication arising from the inappropriate use of these agents in dogs.

In the cases reported here, depot MPA was administered between 1 and 7 days post-mating, which falls well within the window during which fertilization and early embryonic development are likely to occur. It is well established that behavioral estrus period in dogs can last up to 21 days, and viable sperm can persist within the reproductive tract for up to six days.¹⁰ Thus, conception may have already taken place by the time of MPA administration, rendering its contraceptive purpose ineffective. The macroscopic identification of structures consistent with corpora lutea at the time of ovariectomy is compatible with MPA administration occurring after ovulation and fertilization. Moreover, because the drug artificially maintains high progesterone levels, it

inhibits luteolysis and the physiological decline in serum progesterone that triggers cervical softening and uterine contractions.^{11,12}

Serum progesterone concentrations observed in the present cases further support this pathophysiological mechanism. In two dogs, serum progesterone levels at the time of surgical intervention were between 2.20 and 9.03 ng/mL values higher than those typically observed in the immediate prepartum period. Previous studies have reported that serum progesterone concentrations decrease to below 2 ng/mL within 12–24 hours before parturition and further decline to below 1 ng/mL at parturition, enabling cervical dilation and fetal expulsion.^{13,14} The sustained elevation of progesterone, likely due to exogenous MPA, may have inhibited this critical hormonal transition, ultimately preventing the onset of parturition. Furthermore, previous reports indicate that following ovariectomy, serum progesterone concentrations rapidly decline, reaching approximately 0.33 ± 0.2 ng/mL by day 7 post-operatively.¹⁵ In contrast, the persistently elevated progesterone levels observed in our cases (measuring 2.51 ng/mL and 8.50 ng/mL one week post-surgery) highlight the prolonged systemic activity of exogenous MPA and its potential to delay hormonal clearance despite ovariectomy.

The doses administered in these cases also warrant attention. While the recommended dose of depot MPA for contraception in dogs is approximately 2 mg/kg every five months,³ each dog in this report received a fixed 150 mg dose, irrespective of body weight. Considering their weights ranged from 17 to 21 kg, this corresponds to a dose of approximately 7–8.8 mg/kg more than three times the advised amount. Such suprathreshold exposure may have intensified the suppression of hypothalamic-pituitary-gonadal axis activity and contributed to the pathological delay in parturition.

Although congenital anomalies were not macroscopically observed in Cases 2 and 3, and could not be assessed in Case 1 due to fetal maceration, earlier studies have reported teratogenic effects and fetal malformations following early pregnancy exposure to exogenous progestins.^{6,16} In addition to their effects on pregnancy maintenance and parturition, exogenous progestins may also interfere with normal lactation by suppressing mammary gland development and disrupting the endocrine cascade required for milk production and let-down. Persistently elevated progesterone concentrations prevent the physiological withdrawal of progesterone necessary to release progesterone-mediated inhibition of lactogenesis and initiate milk secretion.^{17,18}

Our findings highlight that the administration of depot MPA after mating is contraindicated and represents a medical error, emphasizing the need for strict veterinary supervision when using hormonal contraceptives in clinical practice

Conclusion

The findings of this case series demonstrate that administration of depot MPA after mating in female dogs resulted in fetal death and prolonged gestation. The persistently elevated serum progesterone concentrations observed in these dogs indicate that exogenous progestins interfere with the natural hormonal decline required to initiate parturition, leading to fetal retention. Depot MPA should never be administered when mating may have occurred, as it do not terminate existing pregnancies and may instead cause life-threatening reproductive complications. In cases of mismating, safer and evidence-based alternatives such as aglepristone or cabergoline should be considered under appropriate veterinary supervision. The present report highlights the importance of owner education and veterinary oversight in the use of hormonal contraceptives. Unsupervised administration of depot progestins represents a serious threat to animal welfare. Raising awareness of these risks is essential to prevent the recurrence of similar cases in clinical practice.

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Ethical approval

This study involved clinical case management of owned animals. Informed consent was obtained from all owners prior to diagnostic and surgical procedures. As the cases were part of routine veterinary care and did not involve experimental interventions, formal ethical approval was not required under national or institutional guidelines.

CRediT authorship contribution statement

Buse Öztürk: Writing – original draft, Investigation, Data curation, Conceptualization. **Aslıhan Ayalp-Erkan:** Investigation, Data curation, Conceptualization. **Yusuf Bilal Çetinkaya:** Visualization, Investigation. **Tunahan Öztürk:** Investigation, Data curation. **Nevzat Saat:** Supervision, Investigation. **Barış Güner:** Writing – review & editing, Visualization, Investigation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- Asa CS. Contraception in dogs and cats. *Vet Clin N Am: Small Anim Pract.* 2018;48:733–742. <https://doi.org/10.1016/j.vcsm.2018.02.014>.
- Beijerinck NJ, Bhatti SFM, Okkens AC, Dieleman SJ, Mol JA, Duchateau L, et al. Adenohypophyseal function in bitches treated with medroxyprogesterone acetate. *Domest Anim Endocrinol.* 2007;32:63–78. <https://doi.org/10.1016/J.DOMANIEND.2005.12.008>.
- Romagnoli S, Concannon PW. Clinical use of progestins in bitches and queens: a review. *Recent Adv Small Anim Reprod Int Vet Inf Serv.* 2003;1206:0903 (Www Ivis Org), Ithaca, New York, USA A.
- Günzel-Apel A, Urhausen C, Wolf K, Einspanier A, Oei C, Piechotta M. Serum Progesterone in pregnant bitches supplemented with progestin because of expected or suspected luteal insufficiency. *Reprod Domest Anim.* 2012;47:55–60. <https://doi.org/10.1111/RDA.12029>.
- Eilts BE, Paccamonti DL, Hosgood G, Causey RC, Milliken JL. The use of allyltrenbolone as a progestational agent to maintain pregnancy in ovariectomized bitches. *Theriogenology.* 1994;42:1237–1245. [https://doi.org/10.1016/0093-691X\(94\)90872-9](https://doi.org/10.1016/0093-691X(94)90872-9).
- Görlinger S, Galac S, Kooistra HS, Okkens AC. Hypoluteoidism in a bitch. *Theriogenology.* 2005;64:213–219. <https://doi.org/10.1016/J.THERIOGENOLOGY.2004.12.011>.
- Von Berky AG, Townsend WL. The relationship between the prevalence of uterine lesions and the use of medroxyprogesterone acetate for canine population control. *Aust Vet J.* 1993;70:249–250. <https://doi.org/10.1111/J.1751-0813.1993.TB08041.X>.
- Rutteman GR. Contraceptive steroids and the mammary gland: Is there a hazard? - Insights from animal studies. *Breast Cancer Res Treat.* 1992;23:29–41. <https://doi.org/10.1007/BF01831473/METRICS>.
- Concannon PW, Meyers-Wallen VN. Current and proposed methods for contraception and termination of pregnancy in dogs and cats. *J Am Vet Med Assoc.* 1991;198:1214–1225. <https://pubmed.ncbi.nlm.nih.gov/2045343/>.
- Kutzler MA, Mohammed HO, Lamb SV, Meyers-Wallen VN. Accuracy of canine parturition date prediction from the initial rise in preovulatory progesterone concentration. *Theriogenology.* 2003;60:1187–1196. [https://doi.org/10.1016/S0093-691X\(03\)00109-2](https://doi.org/10.1016/S0093-691X(03)00109-2).
- De Cramer KGM, Nöthling JO. The precision of predicting the time of onset of parturition in the bitch using the level of progesterone in plasma during the preparturient period. *Theriogenology.* 2018;107:211–218. <https://doi.org/10.1016/J.THERIOGENOLOGY.2017.11.018>.
- Verstegen-Onclin K, Verstegen J. Endocrinology of pregnancy in the dog: A review. *Theriogenology.* 2008;70:291–299. <https://doi.org/10.1016/J.THERIOGENOLOGY.2008.04.038>.
- Kim YH, Travis AJ, Meyers-Wallen VN. Parturition prediction and timing of canine pregnancy. *Theriogenology.* 2007;68:1177–1182. <https://doi.org/10.1016/J.THERIOGENOLOGY.2007.08.018>.
- Johnson CA. Pregnancy management in the bitch. *Theriogenology.* 2008;70:1412–1417. <https://doi.org/10.1016/J.THERIOGENOLOGY.2008.09.009>.

15. Dongaonkar KR, Gulavane SU, Chariar VM, Shelar KR. Laparoscopic ovariectomy in dogs in late gestation. *BMC Vet Res.* 2019;15:1–6. <https://doi.org/10.1186/S12917-018-1770-Z>.
16. Kustritz MVR. Pregnancy diagnosis and abnormalities of pregnancy in the dog. *Theriogenology.* 2005;64:755–765. <https://doi.org/10.1016/J.THERIOGENOLOGY.2005.05.024>.
17. Wiebe VJ, Howard JP. Pharmacologic advances in canine and feline reproduction. *Top Companion Anim Med.* 2009;24:71–99.
18. Romagnoli S, Ferre-Dolcet L. Reversible control of reproduction in queens: mastering the use of reproductive drugs to manipulate cyclicity. *J Feline Med Surg.* 2022;24:853–870.