

## Scientific Report

# A case of spontaneous abortion related to ovarian endometriosis in a Golden Retriever dog

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## Summary

This report describes a case of spontaneous abortion in a 4-year-old Golden Retriever dog with ovarian endometriosis. Clinical findings indicated that there was not any sensitivity in the abdomen and the viability parameters were within the reference values. On vaginal examination, serosanguineous discharge was determined. Ultrasonographic examination revealed that no fetus was observed in cornu uteri and an hypoechoic cystic structure, measuring  $3.2 \times 3.4$  cm was found behind the left kidney. Ovarian cyst was suspected, and then ovariohysterectomy was performed. On laparotomy, the presence of a cystic structure was confirmed in the left ovary similar to ultrasonographic findings. Cyst was smooth, flat, hemorrhagic and thick-walled structure. Histopathologic examination of the ovarian stroma revealed covered luteinizing cells and midline hemorrhagic cyst. However, the internal surface of the cyst wall was covered by an endometrial lining. Interestingly, the endometriotic tissue had a maximal penetration into the cyst wall. It was thought that the ovarian endometriosis caused a failure in the luteinizing hormone action which is responsible for luteal function and spontaneous abortion was observed in this case. Although ovarian endometriosis is quite usual in human, this case could be the first report to describe ovarian endometriosis in a dog, and thus it has been reported to cause spontaneous abortion.

**Key words:** Abortion, Dog, Endometriosis, Ovarian

## Introduction

Spontaneous abortion is the death and resorption or expulsion of a fetus before the pregnancy has come to term. The causes of spontaneous abortion can be divided into maternal and fetal causes. Maternal causes include severe illness from preexisting disease, bacterial (Shambulingappa, 2010) or viral agents, uterine diseases, ovarian disorder leading to low progesterone levels. Fetal causes are primarily related to abnormal development and early fetal death (Romagnoli, 2002; Fontbonne, 2011).

Endometriosis is a gynecologic disease, characterized by the growth of endometrial-like tissue outside the uterine cavity (Kim *et al.*, 2013; Taylor and Lebovic, 2014). Uterine endometriosis (adenomyosis) is the presence of endometrial tissue within the myometrium. Adenomyosis is a rare and sporadic disorder in dogs. It results in no symptoms during much of its development, and it is incidentally diagnosed in adult dogs (Stocklin-Gautschi *et al.*, 2001; Tamada *et al.*, 2005; Perez-Marin *et al.*, 2008; Kim *et al.*, 2010; Karagiannis *et al.*, 2011). Furthermore, ovarian endometriosis is a non-neoplastic hyperplastic lesion, estrogen dependent, characterized by endometriotic deposition within the ovary. Regarding ovarian endometriosis, there is no scientific data in dogs. However, in woman, precise incidence of the disease commonly associated with infertility is unknown, while

it is found in approximately 15-20% of women in pelvic laparotomy for other indications (Alborzi *et al.*, 2006; Mukherjee and Rekhi, 2012; Carnahan *et al.*, 2013). Ovarian endometriosis has been associated with inadequacy of corpus luteum and progesterone secretion (Ayers *et al.*, 1987; Pluchino *et al.*, 2014). This could be the first report to describe a case of spontaneous abortion related to ovarian endometrioma in a 4-year-old Golden Retriever dog.

## Case history

A 32-kg, 4-year-old, Golden Retriever dog was brought to the clinic for examination of an enlargement in the abdomen. Pregnancy was diagnosed by ultrasonography at approximately 30-35 days. However, spontaneous abortion was observed on the 2nd day after the ultrasonographic examination. According to anamnesis, the dog's general condition was good, but excessive licking of the vulva was noted. No sensitivity was detected on abdominal palpation. The viability parameters such as body temperature ( $38.1^{\circ}\text{C}$ ), heart rate (98 bpm), and respiratory rate (20 breaths/min) were within the reference ranges. On vaginal examination, serosanguineous discharge was determined by speculum. While no fetus was observed in uterine horns, a hypoechoic structure, measuring  $3.2 \times 3.4$  cm was determined behind the left kidney on the abdominal

ultrasonographic examination (Fig. 1). For this reason, an ovarian cyst was suspected. Ovariohysterectomy was decided at the request of the owner. The right ovary and uterine horns were macroscopically normal at operation, however, a cystic structure was identified in the left ovary similar to ultrasonographic findings (Fig. 2). Surgery was performed to remove both ovaries accompanying with ovarian cyst and cornu uteris. The dog was treated with amoxicillin-clavulanic acid for 5 days after surgery. During postoperative period, the dog recovered without any complications and she is healthy on close follow-up.

The removed tissues were subjected to the histopathological examination. Macroscopically,  $5 \times 4 \times 4$  cm ovarian cyst was observed adjacent to tuba uterine,  $11 \times 3 \times 3$  cm in size. Cyst was a smooth, flat, hemorrhagic and thick-walled structure. On microscopical evaluation, ovarian stroma was revealed to be covering luteinizing cells and midline hemorrhagic cyst (Fig. 3). The internal surface of the cyst wall was covered by an endometrial lining (Fig. 4). The endometriotic tissue had a maximal penetration into the cyst wall. Histopathological analysis of the ovary revealed corpus luteum and endometriosis. There is no pathological condition in the cornu uteri.

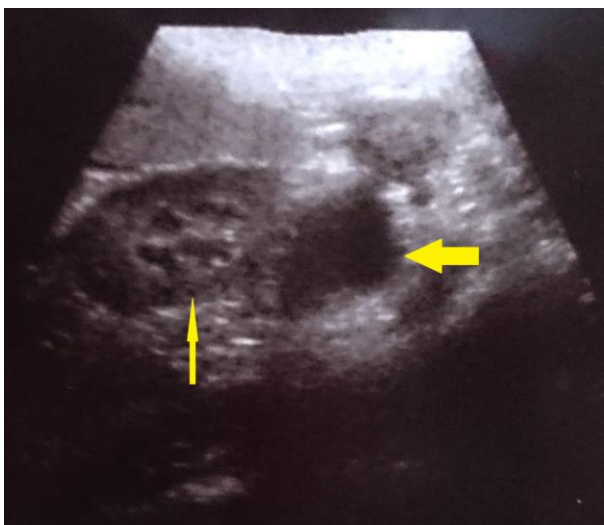
## Discussion

The progression of pregnancy is dependent on functional corpora lutea. It is known that luteal function in the dog is related to pituitary hormone such as luteinizing hormone and prolactin, rather than uterine or placental influences (Palmer and Post, 2002). Hypoluteoidism has been suggested under the causes of spontaneous (noninfectious) abortion. The maintenance of canine pregnancy is dependent on serum progesterone concentrations higher than or equal to 2 ng/ml. If the

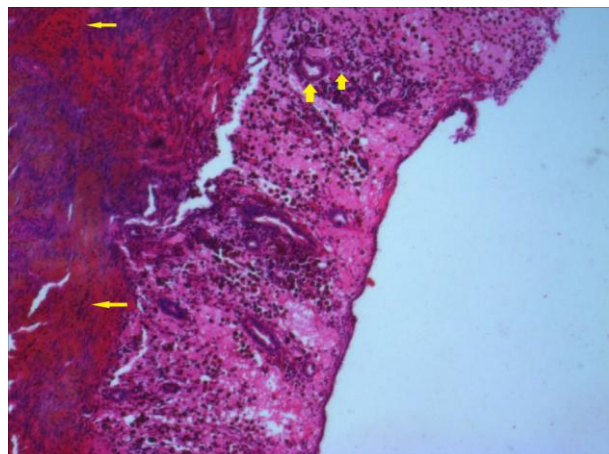
concentrations of serum progesterone drop lower than this for more than 24-48 h, spontaneous abortion becomes inevitable (Holyoak *et al.*, 2013). Ovarian endometriosis has been associated with corpus luteum inadequacy and abnormalities of luteal phase progesterone secretion. Studies in women have shown



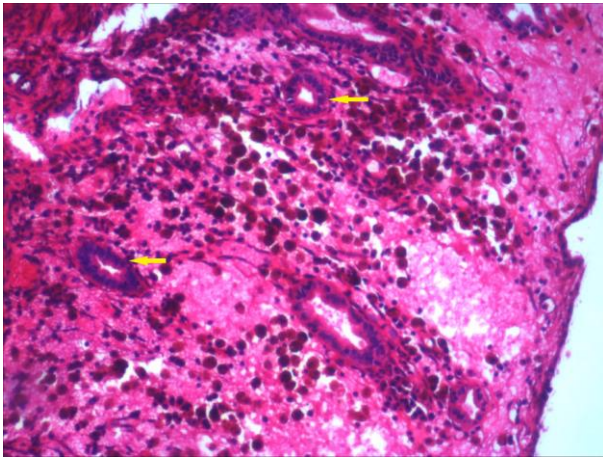
**Fig. 2:** The macroscopic appearance of the both cornu uteris (thin arrow) - ovaries and cystic structure (thick arrow)



**Fig. 1:** Transabdominal ultrasonographic appearance of cystic ovary in the left upper quadrant. Cystic hypoechoic structure (thick arrow) in behind of the left kidney (thin arrow) (5 MHz multifrequency, convex probe, B-mode real-time ultrasonography device)



**Fig. 3:** The histopathological view of thick hemorrhagic foci in ovarian stroma (thin arrow) and the presence of the endometrial glands (thick arrow), (H&E,  $\times 10$ )



**Fig. 4:** Endometrial glands (arrow) and stroma are seen at high magnification in the internal surface of the cyst

that luteinizing hormone receptor concentrations in ovarian follicles and corpora lutea in cases of ovarian endometriosis are lower than in healthy women (Kauppila *et al.*, 1982; Rönnerberg *et al.*, 1984). Therefore, it is stated that there is an association between endometriosis and spontaneous abortion (Donnez and Nisolle, 1996; Gupta, 2006; Sahu and Tempe, 2013; Perini *et al.*, 2014) since the low luteinizing hormone receptor concentration in ovarian endometriosis suggests a failure in the LH action which is responsible for luteal function and spontaneous abortion is observed (Kauppila *et al.*, 1982). Also, this can possibly be explained by alterations in humoral and cell-mediated immunity in patients with endometriosis. These immunological changes cause alterations within the follicle or oocyte, resulting in embryos with decreased ability to implant (Tomassetti *et al.*, 2006).

According to studies in human medicine, ovarian endometriosis is generally asymptomatic and found incidentally in pelvic operation or ultrasonographic examination. Ultrasound, tumor marker and determination of progesterone-estrogen levels are useful for clinical diagnosis of ovarian endometriosis. However, these methods are not useful for discriminating ovarian endometriosis from ovarian malignancy. For this purpose, histopathology is required to make a definitive diagnosis of ovarian endometriosis (Busacca *et al.*, 2006; Savelli, 2009). In this case, since ovariohysterectomy was performed in the dog that was diagnosed with spontaneous abortion by physical and ultrasonographic examination, blood hormone levels could not be evaluated. Because ovarian endometriosis was not suspected before ovariohysterectomy. However, the cystic structure, which was determined by ultrasonography, was observed to be morphologically different from previously seen cyst on operation. Therefore, removed tissues and cystic structure were sent to histopathological examination. In that, it is important to differentiate other non-neoplastic and neoplastic lesions in ovaries for determination of treatment strategies. In the present case, cyst was smooth, flat, hemorrhagic and thick-walled structure on macroscopic

evaluation. It is known that this structure is caused by endometriosis, and formed when a tiny patch of endometrial tissue bleeds, becomes transplanted, grows and enlarges inside the ovary. The blood that appears as a brown fluid grows up over months and years (Woodward *et al.*, 2001; Carnahan *et al.*, 2013). In this case report, the internal surface of the cyst wall was covered by an endometrial lining on microscopic analysis, similar to other studies (Hachisuga and Kawarabayashi, 2002; Mukherjee and Rekhi, 2012).

In summary, the case of spontaneous abortion related to ovarian endometriosis in a Golden Retriever dog was reported for the first time in the present study. It was concluded that ovarian endometriosis could be one of the possible causes of abortion in dogs. Therefore, it can be suggested that in the case of the spontaneous abortion in a dog, the ultrasonographic examination of ovaries and the measurement of progesterone concentrations are important diagnostic parameters. Moreover, histopathological evaluation should be carried out to detect the differentiation of neoplastic ovarian lesions which should be analyzed for a definitive diagnosis in order to determine appropriate treatment strategies.

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## References

- Alborzi, S; Zarei, A; Alborzi, S and Alborzi, M (2006). Management of ovarian endometrioma. *Clin. Obstet. Gynecol.*, 49: 480-491.
- Ayers, JW; Birenbaum, DL and Menon, KM (1987). Luteal phase dysfunction in endometriosis: elevated progesterone levels in peripheral and ovarian veins during the follicular phase. *Fertil. Steril.*, 47: 925-929.
- Busacca, M; Riparini, J; Somigliana, E; Oggioni, G; Izzo, S; Vignali, M and Candiani, M (2006). Postsurgical ovarian failure after laparoscopic excision of bilateral endometriomas. *Am. J. Obstet. Gynecol.*, 195: 421-425.
- Carnahan, M; Fedor, J; Agarwal, A and Gupta, S (2013). Ovarian endometrioma: guidelines for selection of cases for surgical treatment or expectant management. *Expert Rev. Obstet. Gynecol.*, 8: 29-55.
- Donnez, J and Nisolle, M (1996). *Definition and history of endometriosis: peritoneal, ovarian and recto-vaginal endometriosis: the identification of three separate diseases*. 1st Edn., USA, CRC Press. PP: 15-30.
- Fontbonne, A (2011). Infertility in bitches and queens: recent advances. *Rev. Bras. Reprod. Anim.*, Belo Horizonte. 35: 202-209.
- Gupta, S (2006). Impact of ovarian endometrioma on assisted reproduction outcomes. *Reprod. BioMed. Online*. 13: 349-360.
- Hachisuga, T and Kawarabayashi, T (2002). Histopathological analysis of laparoscopically treated ovarian endometriotic cysts with special reference to loss of follicles. *Hum. Reprod.*, 17: 432-435.
- Holyoak, GR; Makloski, C and Morgan, GL (2013). Abortion, abnormal estrous cycle, and infertility. In:

- Lorenz, MD; Neer, TM and DeMars, P (Eds.), *Small animal medical diagnosis*. (3rd Edn.), Iowa, USA, Wiley & Sons. PP: 337-357.
- Karagiannis, GS; Pelekanis, M; Loukopoulos, P; Ververidis, HN and Kaldrymidou, E** (2011). Canine uterine leiomyoma with epithelial tissue foci, adenomyosis, and cystic endometrial hyperplasia. *Case Rep. Vet. Med.*, 2011: Article ID 901874.
- Kauppila, A; Rajaniemi, H and Rönberg, L** (1982). Low LH (hCG) receptor concentration in ovarian follicles in endometriosis. *Acta Obstet. Gynecol. Scand.*, 61: 81-83.
- Kim, JH; Jung, SH; Yang, YI; Ahn, JH; Cho, JG; Lee, KT; Baek, NI and Choi, JH** (2013). Artemisia leaf extract induces apoptosis in human endometriotic cells through regulation of the p38 and NFκB pathways. *J. Ethnopharmacol.*, 145: 767-775.
- Kim, HS; Kang, SC; Zhang, HS; Kang, JS; Kim, JH; Kim, KH; Kang, BH and Yoon, BI** (2010). Uterine adenomyosis in beagle dogs. *Lab. Anim. Res.*, 26: 211-213.
- Mukherjee, T and Rekhi, B** (2012). Ovarian endometriosis with co-existing granulomatous inflammation-a rare association. *Med. J. Armed Forces India*. 68: 182-184.
- Palmer, CW and Post, K** (2002). Prevention of pregnancy in the dog with a combination of prostaglandin F<sub>2α</sub> and bromocriptine. *Can. Vet. J.*, 43: 460-462.
- Perez-Marin, CC; Molina, L; Dominguez, JM; Millan, Y and Martin de las Mulas, J** (2008). Incidental finding of uterine adenomyosis in a bitch with reproductive disorders: a case report. *Vet. Med-Czech*. 53: 636-640.
- Perini, JA; Cardoso, JV; Berardo, PT; Vianna-Jorge, R; Nasciutti, LE; Bellodi-Privato, M; Machado, DE and Abrão, MS** (2014). Role of vascular endothelial growth factor polymorphisms (-2578C>A, -460T>C, -1154G>A, +405G>C and +936C>T) in endometriosis: a case-control study with Brazilians. *BMC Women's Health*. 14: 117.
- Pluchino, N; Drakopoulos, P; Wenger, JM; Luisi, S; Russo, M and Genazzani, AR** (2014). Endocrinology of pregnancy loss. In: Carp, HJA (Ed.), *Recurrent pregnancy loss: causes, controversies, and treatment*. (2nd Edn.), New York, CRC Press. PP: 111-123.
- Romagnoli, S** (2002). Complications in canine pregnancy and their clinical approach. *Congresso de Ciências Veterinárias [Proceedings of the Veterinary Sciences Congress]*, SPCV, Oeiras, 10-12 Out., PP: 159-162.
- Rönberg, L; Kauppila, A and Rajaniemi, H** (1984). Luteinizing hormone receptor disorder in endometriosis. *Fertil. Steril.*, 42: 64-68.
- Sahu, L and Tempe, A** (2013). Laparoscopic management of endometriosis in infertile women and outcome. *Int. J. Reprod. Contracept. Obstet. Gynecol.*, 2: 177-181.
- Savelli, L** (2009). Transvaginal sonography for the assessment of ovarian and pelvic endometriosis: how deep is our understanding? *Ultrasound. Obstet. Gynecol.*, 33: 497-501.
- Shambulingappa, BE; Manegar, GA and Ananda, KJ** (2010). Study on aerobic bacterial flora in canine abortions. *Vet. World*. 3: 111-112.
- Stocklin-Gautschi, NM; Guscetti, F; Reichler, IM; Geissbühler, U; Braun, SA and Arnold, S** (2001). Identification of focal adenomyosis as a uterine lesion in two dogs. *J. Small Anim. Pract.*, 42: 413-416.
- Tamada, H; Kawate, N; Inaba, T; Kuwamura, M; Maeda, M; Kajikawa, T and Sawada, T** (2005). Adenomyosis with severe inflammation in the uterine cervix in a dog. *Can. Vet. J.*, 46: 333-334.
- Taylor, R and Lebovic, DI** (2014). Endometriosis. In: Strauss, JF and Barbieri, RL (Eds.), *Yen & Jaffe's reproductive endocrinology*. (7th Edn.), Philadelphia, Elsevier Saunders. PP: 565-585.
- Tomassetti, C; Meuleman, C; Pexsters, A; Mihalyi, A; Kyama, C; Simsa, P and D'Hooghe, TM** (2006). Endometriosis, recurrent miscarriage and implantation failure: is there an immunological link? *Reprod. BioMed. Online*. 13: 58-64.
- Woodward, PJ; Sohaey, R and Mezzetti, TPJr** (2001). Endometriosis: radiologic-pathologic correlation. *Radiographics*. 21: 193-216.