

Hematometra associated with fetal death in a fennec fox (*Vulpes zerda*)

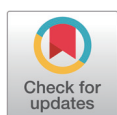
Hyo-Min Kang¹, Hye-Jin Jang², Jeong-Ho Kim³, Dong-Woo Chang⁴,
Hyun-Gu Kang⁴, Ki-Jeong Na^{4*}

¹Animal Medical Center, Bucheon 14427, Korea

²Department of Biomedical Laboratory Science, Dong-Eui Institute of Technology, Busan 47230, Korea

³Cheongju Zoo, Cheongju 28311, Korea

⁴College of Veterinary Medicine, Chungbuk National University, Cheongju 28644, Korea



Received: Dec 20, 2021

Revised: Dec 23, 2021

Accepted: Dec 23, 2021

*Corresponding author

Ki-Jeong Na

College of Veterinary Medicine,
Chungbuk National University,
Cheongju 28644, Korea

Tel: +82-43-261-3151

E-mail: sigol@cbnu.ac.kr

Copyright © 2021 Research Institute of Veterinary Medicine, Chungbuk National University. This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID

Hyo-Min Kang

<https://orcid.org/0000-0002-4003-5828>

Hye-Jin Jang

<https://orcid.org/0000-0003-4884-3675>

Jeong-Ho Kim

<https://orcid.org/0000-0002-8562-6306>

Dong-Woo Chang

<https://orcid.org/0000-0002-7721-773X>

Hyun-Gu Kang

<https://orcid.org/0000-0002-3827-6112>

Ki-Jeong Na

<https://orcid.org/0000-0001-6076-3147>

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Acknowledgements

The authors would like to thank Dr. Yunkeyong Song. This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (NRF-2016R1D1A1B03932312).

Abstract

A 5-year-old female fennec fox weighing 1 kg presented to the Veterinary Medical Center, Chungbuk National University with swelling of the mammary glands and hematuria. There were no significant complete blood count (CBC) or serum chemistry findings. The uterus obtained by ovariohysterectomy was filled with blood-clot-like material. The uterine fluid contained erythrocytes, a few leukocytes, and bilirubin crystals without bacteria. The progesterone concentration in the blood serum the day before ovariohysterectomy was 7.3 ng/mL, which is higher than anestrus and lower than a true pregnant condition in a fennec fox. Despite the low blood progesterone concentration and absence of a fetus in the uterus, the histopathological zonary placental findings indicated that the fennec fox had been pregnant. This is the first case report of hematometra associated with fetal death in a captive fennec fox.

Keywords: fennec fox; hematometra; fetal death; ovariohysterectomy; progesterone

INTRODUCTION

The fennec fox (*Vulpes zerda*) is the smallest canid and inhabits the deserts of North Africa and the Arabian region. The IUCN Red List has classified them in the “least concern” category. Fennec foxes have been imported for exhibition in zoos or sale as pets in Korea. All canid species studied to date are reported to be monestrous, and most have only one seasonal cycle per year in the wild [1]. The ovulation cycles of fennec foxes are monestrous, but a second litter was reported in a captive individual a year after the first litter was lost. However, the fennec fox is reported to breed seasonally in the wild, and the pups are seen out of dens in March and April [1]. Cystic endometrial hyperplasia (CEH) in the canid can result in pyometra, hematometra, or hydrometra, and many features of these uterine diseases can make them difficult to differentiate. Hematometra is an accumulation of sterile and bloody fluid. It is normal for the canine to develop a small degree of hemorrhage from the endometrium during estrus [2]. With subinvolution of placental sites, there is prolonged bloody vaginal discharge after birth, and it is also excluded, as is open pyometra [3]. Abnormal bleeding not associated with estrus or the postpartum period is called metror-

Ethics Approval
Not applicable.

rhagia [4]. Uterine hemorrhage is very rare; there are only a few reports in dogs, and it has not been reported in fennec foxes.

CASE REPORT

A 5-year-old female fennec fox weighing 1 kg was referred to the Veterinary Teaching Hospital, Chungbuk National University from Cheongju Zoo with swelling of the mammary gland, hematuria, and anorexia. On physical examination, all mammary glands, especially the fifth and sixth, were slightly distended (Fig. 1). A complete blood count (CBC), serum clinical biochemistry, hormone analysis, and abdominal ultrasonography were performed.

Laboratory medical analysis

The results are shown in Tables 1 and 2. CBC, white blood count (WBC) differential count, and serum clinical biochemistry were done with ProCyte Dx (IDEXX, Westbrook, ME, USA), a manual method, HITACHI 7020 (Hitachi, Tokyo, Japan), and IMMULITE 1000 (Siemens, Germany), respectively. International Species Information System (ISIS, March 2002) reference intervals were used. WBC was increased with normocytic normochromic slight anemia (Table 1). Despite the increased amylase and lipase serum concentrations (Table 2), there was no evidence of pancreatitis.

The serum progesterone concentration was 7.3 ng/mL, indicating mating during ovulation or just before parturition [1]. Cytology of the fluid from the uterus by fine needle aspiration showed many red blood cells (RBCs) and bilirubin crystals (Fig. 5). Bacterial culture of the uterine fluid was negative in both aerobic and anaerobic conditions of MacConkey broth culture. Urine analysis results were pH 7, protein 500 mg/dL, and WBC 500 /hpf. For the cytology, a uterine fluid sample that was collected after ovariohysterectomy was used. The fluid-smear slide glass was stained with Wright-Giemsa. Cytologic examination showed low and high numbers of RBC and WBC, respectively. Many bilirubin crystals were observed upon microscopic examination, which implied a hemorrhagic condition in the uterus.



Fig. 1. Physical examination. Fennec fox (A) and swelling of mammary glands (B).

Table 1. CBC of fennec fox

Item	Patient	Reference [*]	Unit
WBC	9.82	5.96±2.33	× 10 ³ /μL
Differential count			
Monocyte	0.26	0.26±0.18	× 10 ³ /μL
Lymphocyte	3.06	2.40±1.43	× 10 ³ /μL
Segmented neutrophil	6.32	2.86±1.57	× 10 ³ /μL
Eosinophil	0.17	0.38±0.25	× 10 ³ /μL
Basophil	0.01	0.05±0.02	× 10 ³ /μL
RBC	5.69	8.72±1.27	× 10 ⁶ /μL
PCV	32.7	48.6±0.07	%
Hemoglobin	10.6	16.2±2.4	g/dL
MCV	57.5	56.0±7.7	fL
MCHC	32.4	33.2±3.7	g/dL
Platelet	677	471±222	× 10 ³ /μL

^{*} Reference value of fennec fox from ISIS (March 2002).

CBC, complete blood count; WBC, white blood count; RBC, red blood cell.

Table 2. Serum clinical biochemistry and hormone analysis of fennec fox

Item	Patient	Reference [*]	Unit
Total protein	5.6	5.6±6	g/dL
Albumin	2.9	3.0±0.5	g/dL
Globulin	2.7	2.5±0.6	g/dL
A/G ratio	1.07		
Glucose	153	66.6±19.98	mg/dL
ALT	86	88±63	IU/L
GGT	<0	4±5	mg/dL
ALP	41	54±55	IU/L
Amylase	268	54.95±21.83	IU/L
Lipase	1,310	59.21±24.46	IU/L
Total bilirubin	0.3	0.3±0.3	mg/dL
BUN	26	78.54±28.56	mg/dL
Creatinine	0.5	0.7±0.18	mg/dL
Progesterone	7.3		ng/mL

^{*} Reference value of fennec fox from ISIS (March 2002).

Diagnostic imaging

An abdominal ultrasound examination revealed that the uterus was enlarged and the mammary glands were swollen (Figs. 2 and 3). There was minimal free fluid in the abdominal cavity. The uterus was slightly distended, and both uterine horns were filled with hyperechoic floating material.

Ovariohysterectomy and histopathology

Ovariohysterectomy was performed in the fennec fox (Fig. 4) under inhalational anesthesia with isoflurane. Anesthesia was maintained using 2% isoflurane after induction using 4% isoflurane. Oxygen flow was set at 1.5 L/min. A histopathological examination was performed on

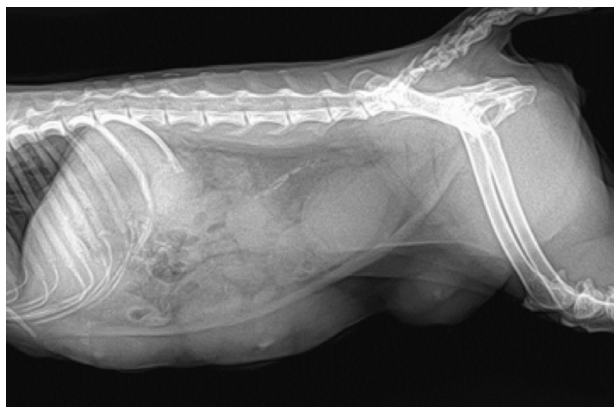


Fig. 2. X-ray image of abdomen showing enlarged uterus and swollen mammary glands.



Fig. 3. Ultrasonographic image of uterus showing uterine cavity filled with echogenic material.



Fig. 4. Ovariohysterectomy of the fennec fox. Ovaries and uterus (A). The uterus was filled with hemorrhagic fluids and clot material (B). As the effusion was removed from the uterus, a zonary placenta was detected.

the removed uterus. Postoperative care consisted of flunixin 2 mg/kg and enrofloxacin 10 mg/kg IM BID for 7 days.

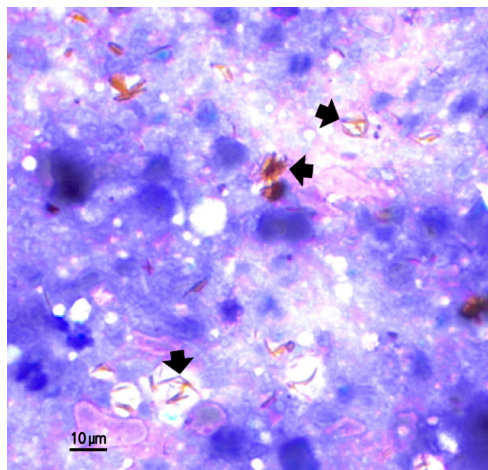


Fig. 5. Uterine fluid cytology. The arrows indicate bilirubin crystals. Wright-Giemsa stain, immersion oil (scale bar = 10 µm).

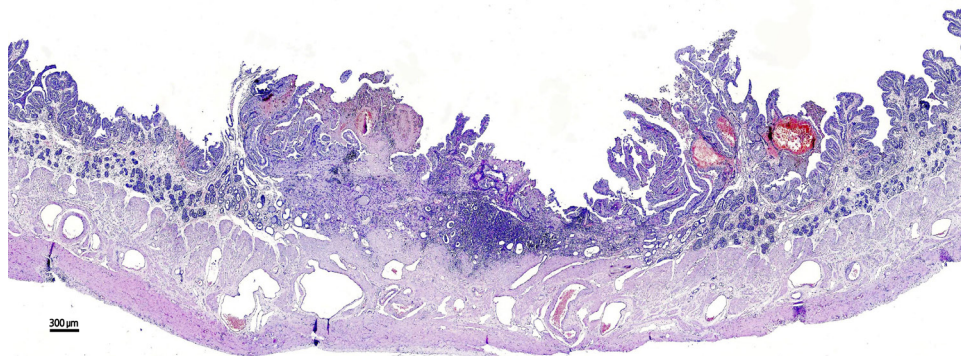


Fig. 6. Uterine cross-section. Dilated maternal blood vessels as well as papillary hyperplasia and hemorrhage were observed. Slide was scanned with virtual microscope system (BA600Mot, Motic). H&E stain (scale bar = 300 µm).

Histopathological findings

The zonary placenta papillae showed hyperplasia and enlargement change. A hyperplasia of the papillae hemorrhagic sign was observed upon histopathological examination. Moreover, mineralization was detected in the center of Fig. 6. Inflammatory cells had infiltrated the uterine tissue.

DISCUSSION

The reference interval of progesterone serum concentration for the fennec fox was limited [1]. However, the information of progesterone serum concentration change according to estrus cycle showed very similar patterns to those of the dog, wolf, and fennec fox [1, 5, 6]. The result of serum progesterone concentration in the fennec fox was 7.3 ng/mL, indicating that the fennec fox was at least in the post-ovulation phase.

Hematometra is an uncommon disease in Canidae. There are many reasons for hematometra, including uterine trauma, anticoagulant rodenticide toxicity and other acquired coagulation

deficiencies, neoplasm, placental necrosis, and postpartum endometritis. Postpartum subinvolution of placental sites is also included among these reasons [7, 8].

Despite the fact that the clinical signs and physical examination results implied a pregnancy, a fetus was not discovered from the ultrasonography. A presumptive diagnosis of pyometra or uterine hyperplasia was made based on the physical examination and diagnostic findings. Ultimately, an ovariohysterectomy was performed. Canine pyometra may present clinically with inappetence, depression, polydipsia, lethargy, and abdominal distension, with or without vaginal discharge. Typically, the bitch is feverless and often has an elevated WBC. Prerenal azotemia commonly accompanies dehydration present with hyperproteinemia and hyperglobulinemia. The histopathological examination revealed endometrium hyperplasia from pyometra, hypertrophy, and small endometrial cysts scattered throughout the endometrium.

In this case, histopathological examination of the uterus indicated that the fennec fox had neither pyometra nor endometrium hyperplasia. Considering the results of several examinations, hematometra occurred from fetal death in the uterine cavity or pseudo-placental hyperplasia.

The canid has a zonary placenta, completely surrounding the fetus, and complex lamellar organization of the maternal and fetal tissues. It consists of the chorioallantoic membrane, the placental labyrinth, the necrosis zone, the maternal glandular chambers, the supraglandular layer, and the deep endometrial glands [9]. The amnion is avascular in the early stages but becomes vascularized by blood vessels of the internal allantoic membrane in the later stages of pregnancy [10].

In dogs, coagulation necrosis has been observed in two of the placentation sites early after fetal death. Edematous swelling of the maternal endothelium of blood vessels might contribute to hypoxia [9]. Hematometra is a very uncommon disease in pet animals like dogs and cats. Pyometra, endometrial hyperplasia, or fetal death in the uterus can possibly cause hematometra. However, in most cases of pets, the owners notice the clinical signs of pyometra and fetal death in the early stage and take appropriate action.

On the contrary, in wild animals, detecting clinical signs is very difficult because they tend to hide them. Thus, in this case, hematometra occurred because of fetal death. Hematometra from fetal death in canids and fennec foxes has not yet been studied. Thus, further investigations are needed for a more detailed understanding of the morphological processes occurring in hematometra after fetal death. In conclusion, we can assume that the fetus had died in the uterine cavity in the early stage and had been lysed by the uterus but that the hemorrhage had continued because the placenta remained after fetal absorption and that these events were the cause of the hematometra.

REFERENCES

1. Valdespino C, Asa CS, Bauman JE. Estrous cycles, copulation, and pregnancy in the fennec fox (*Vulpes zerda*). J Mammal 2002;83:99-109.
2. Asa CS, Bauman KL, Devery S, Zordan M, Camilo GR, Boutelle S, Moresco A. Factors as-

- sociated with uterine endometrial hyperplasia and pyometra in wild canids: implications for fertility. *Zoo Biol* 2014;33:8-19.
3. Schlafer DH, Gifford AT. Cystic endometrial hyperplasia, pseudo-placentational endometrial hyperplasia, and other cystic conditions of the canine and feline uterus. *Theriogenology* 2008;70:349-358.
 4. Voorhorst MJ, Brederode JC, Albers-Wolthers CHJ, de Gier J, Schaefers-Okkens AC. Successful treatment for subinvolution of placental sites in the bitch with low oral doses of progestagen. *Reprod Domest Anim* 2013;48:840-843.
 5. Gräf KJ. Serum oestrogen, progesterone and prolactin concentrations in cyclic, pregnant and lactating beagle dogs. *J Reprod Fertil* 1978;52:9-14.
 6. Seal US, Plotka ED, Packard JM, Mech LD. Endocrine correlates of reproduction in the wolf. I. Serum progesterone, estradiol and LH during the estrous cycle. *Biol Reprod* 1979;21:1057-1066.
 7. Troxel MT, Cornetta AM, Pastor KF, Hartzband LE, Besancon MF. Severe hematometra in a dog with cystic endometrial hyperplasia/pyometra complex. *J Am Anim Hosp Assoc* 2002;38:85-89.
 8. Gumber S, Springer N, Wakamatsu N. Uterine endometrial polyp with severe hemorrhage and cystic endometrial hyperplasia—pyometra complex in a dog. *J Vet Diagn Invest* 2010;22:455-458.
 9. Steiger K, Politt E, Hoeffmann T, Meyer-Lindenberg A, Schoon HA, Günzel-Apel AR. Morphology of canine placental sites after induced embryonic or fetal death. *Theriogenology* 2006;66:1709-1714.
 10. Miglino MA, Ambrósio CE, Martins DS, Wenceslau CV, Pfarrer C, Leiser R. The carnivore pregnancy: The development of the embryo and fetal membranes. *Theriogenology* 2006;66:1699-1702.