

## CASE REPORT

## A Case of Endometrial Carcinoma and Pregnancy in a Cat

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**Abstract:** This case report describes a rare condition of a pregnant cat that has endometrial carcinoma. A 5-year-old cat was presented because of vaginal discharge on the 40th day after the mating. USG examination revealed small embryonic structures, and thickened endometrium. It was decided to perform an ovariohysterectomy operation. The ovaries and uterus were sent to the laboratory for histopathological examination. The uterine mucosa showed papillary growth and atypical cells with mild to moderate anisokaryosis and occasional mitotic figures. The estrogen beta receptor was mildly positive in some neoplastic epithelium and stromal cells. The progesterone receptor was significantly positive in the lamellar layers of the placenta and myometrium but only slight positivity was observed in neoplastic cells. In summary, the gestational sacs were still at the implantation stage on the 40th day after mating may have been due to the carcinoma in the uterine endometrium and implantation could not occur for this reason. Our case might suggest that estrogen-dependent uterine tissue negatively affects embryonal development in cats and thus pregnancy couldn't be completed properly.

**Keywords:** Endometrial carcinoma, Neoplasm, Queen, Pregnancy

## Bir Kedide Endometriyal Karsinoma ve Gebelik Olgusu

**Öz:** Bu olgu raporu, nadir görülen endometriyal karsinomlu gebe bir kedinin durumunu anlatmaktadır. Beş yaşında bir kedi çiftleşme sonrası 40. günde vajinal akıntı nedeniyle getirildi. USG incelemesinde küçük embriyonik yapılar ve kalınlaşmış endometriyum belirlendi. Ovariohistektomi operasyonu yapılmasına karar verildi. Ovaryumlar ve uterus histopatolojik inceleme için laboratuvara gönderildi. Uterus mukozasında papiller büyüme ve hafif ila orta derecede anizokaryoz, bazı bölgelerde de mitotik yapılar içeren atipik hücreler görüldü. Östrojen beta reseptörü, bazı neoplastik epitel ve stromal hücrelerde hafif pozitifliği. Progesteron reseptörü, plasenta ve miyometriyumun lameller tabakalarında önemli ölçüde pozitifliği, ancak neoplastik hücrelerde sadece hafif pozitiflik gözlemlendi. Özetle, gebelik keselerinin çiftleşmeden sonraki 40. günde hala implantasyon aşamasında olması uterus endometriyumdaki karsinomdan kaynaklanmış olabilir ve bu nedenle implantasyon gerçekleşmemiştir. Olgumuz östrojene bağımlı uterusun kedilerde embriyonal gelişimi olumsuz etkilediğini ve bu nedenle gebeliğin tam olarak tamamlanamadığını düşündürebilir.

**Anahtar sözcükler:** Dişi kedi, Endometriyal karsinoma, Gebelik, Neoplazma

## INTRODUCTION

Endometrial carcinoma is a tumor formed by the irregular division and proliferation of cells in the endometrium of the uterus. One of the most important factors in the

formation of this disease is that the level of estrogen in the circulation is higher than normal<sup>[1]</sup>. Although cases of endometrial carcinoma are commonly observed in humans, rabbits, and cows, they are rarely observed in cats<sup>[2,3]</sup>.

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Table 1. Vital parameters, complete blood count, and biochemical findings

Parameter	Value	Reference Value	Parameter	Value	Reference Value
WBC (x10 <sup>9</sup> /L)	16.35	5.5-19.5	GGT (U/L)	2	0-5
RBC (x10 <sup>12</sup> /L)	7.32	5-10	Glucose (mg/dL)	94.48	56-153
HGB (g/dL)	9	8-15	Total Bilirubin (mg/dL)	0.30	56-13
HCT	50.1	24-45	ALT (U/L)	64.3	26-128
MCV (fL)	41	39-55	AST (U/L)	46.1	14-54
PLT (x10 <sup>9</sup> /L)	430	300-800	Albumin (g/dL)	2.57	2.3-3.9
Oestradiol (pg/mL)	5.2	<20	BUN (mg/dL)	35.51	18-36
Progesterone (ng/mL)	28.3	>2	Body temp (°C)	38.5	37.5-39
Creatine (mg/dL)	0.64	0.6-2	Heart rate (bpm)	124	120-140
Urea (mg/dL)	76		Respiratory rate (rpm)	18	15-30
Total Protein (g/dL)	6.32	5.9-8.4			

According to the data of one study, endometrial carcinomas accounted for 0.29% of carcinoma cases in cats [4]. The most common symptoms observed in endometrial carcinoma cats include abdominal mass, weight loss, loss of appetite, pain, and vaginal bleeding [3,4].

In the literature review, it was determined that cases of endometrial carcinoma during pregnancy have been reported in humans before, and it was evaluated that it would be significant to prepare a case report of endometrial carcinoma observed during pregnancy in a female cat. [5-8]. In this case, clinical, laboratory, ultrasonographic and histopathological findings of a pregnant cat with endometrial carcinoma and recovery status after an ovariectomy operation are presented.

### CASE HISTORY

Before the patient was examined, the owner approved the informed consent form that she accepted all the

procedures to be performed.

The material of this case was a 5-year-old cat brought to Burdur Mehmet Akif Ersoy University Veterinary Faculty Obstetrics and Gynecology clinics on 7 September 2023 with the complaint of vaginal discharge on the 40th day after the mating. It was learned that 40 days ago, the cat stayed with a male cat in another house for three days and left that house after mating, did not run away from the owner's house, and did not mate with another male cat for 40 days. In the physical examination, it was seen that the patient's pulse, respiratory rate, and rectal body temperature were within the reference ranges. It was determined that the cat felt pain on abdominal palpation, the general appearance of the cat was normal, there was a transparent discharge from the vagina, and it was learned that her appetite was good. Complete blood count (H60 Vet, Edan, China) and serum biochemical (Respon's910, DiaSys, Germany) examination were performed by taking blood samples from the cephalic vena. Serum E2 and

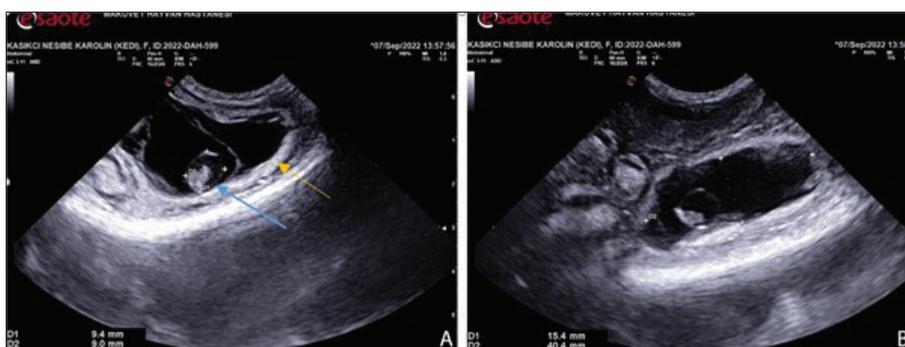


Fig 1. A- Image of uterine endometrium (yellow arrow) and embryonic sac (blue arrow), B- Size of the uterus

P4 concentrations were measured (Cobas E800, Roche, Switzerland) in accordance with the relevant instructions using electrochemiluminescence immunoassay kits (Elecsys Estradiol III and Elecsys Progesterone III, Roche, USA). All values were determined to be within the reference range (*Table 1*).

It was decided to perform a B-mode ultrasonography (7.5-MHz micro-convex; MyLab™X8 Platform, Esaote, Italy) examination for pregnancy examination. During the examination, the uterus and gestational sacs were detected. The embryonic structures that could be identified were quite small compared to the 40th day and there was no sign of life [9], the lumen in cervix uteri, corpus uteri and cornu uteri was thicker than those of normal (*Fig. 1-A*), and the dimensions of the uterus were determined in the area where pregnancy occurred (*Fig. 1-B*).

Since the patient's general condition was good and the owner did not want his cat to have kittens in the future, it was decided to perform an ovariohysterectomy operation. Chemotherapy could not be performed because the patient owner did not accept chemotherapy treatment.

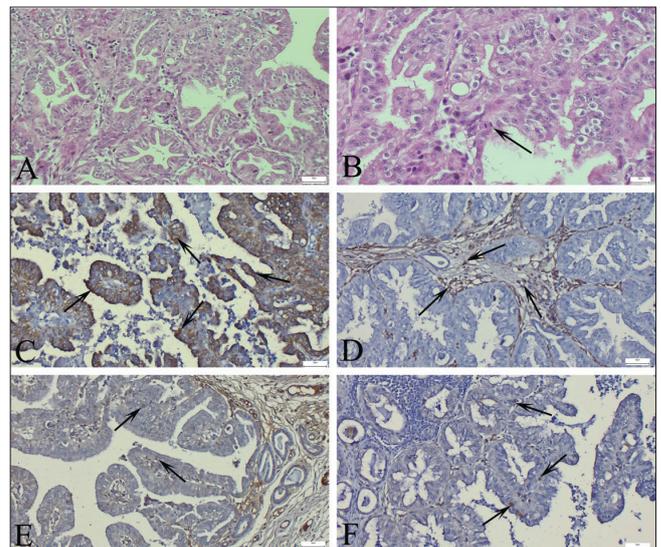
General anesthesia induction was performed with 5.5 mg/kg propofol (Propofol®, Polifarma, Türkiye). Then the patient was intubated and standard anesthesia monitoring was applied. Anesthesia was maintained with sevoflurane (Sevorane®, Abbvie, USA). The operation was performed with the routine ovariohysterectomy method. The gestational sacs were of different sizes and irregular shapes, and they were taken out. Then, the ovaries and uterus were ligated, removed, and sent to the pathology laboratory in 10% formaldehyde for histopathological examination. For prophylaxis, 10 mg/kg amoxicillin-clavulanic acid (Synulox®, Zoetis, Germany) for 5 days, and 0.2 mg/kg meloxicam (Meloxicam®, Bavet, Türkiye) for 1 day were administered s.c. after the operation. In the follow-up examination performed one week later, the patient had recovered.

### Histopathology Findings

Pregnancy was detected on the macroscopic examination of the uterine tissue. The uterus' lumen was seen to be enlarged, contain some purulent material, and occasionally have thickened mucosa (*Fig. 2*). Four kittens in the early stages of gestation were also present. Uterine samples were fixed in 10% formaldehyde and were embedded in paraffin after routine follow-up procedures. Sections of 5-micrometer thickness were taken from paraffin blocks, stained with hematoxylin-eosin, and evaluated under a light microscope. In the histopathological examinations, the uterine mucosa showed papillary growth and atypical cells with mild to moderate anisokaryosis and occasional mitotic figures. Furthermore, stromal invasion, irregular and merged cribriform pattern of glands, stromal



**Fig 2.** Macroscopical view of the gravid uterus with embryonal sacs



**Fig 3.** A- Papillary proliferation of endometrial epithelium with merged endometrial glands and stromal invasion, B- Papillary growths and occasional mitotic figures (arrow) in atypical neoplastic cells, C- Cytokeratin positivity in neoplastic cells (arrows), D- Negative vimentin reaction in neoplastic cells but a positive reaction in the stroma (arrows), E- Mild ER-beta positivity in some neoplastic epithelial cells (arrows) and prominent positivity in stromal cells, F- Mild progesterone receptor positivity in neoplastic epithelial cells (arrows)

disappearance, and surface syncytial changes were noticed (*Fig. 3-A,B*). There was no cystic formation which is characteristics of cystic endometrial hyperplasia. Immunohistochemical staining was performed with cytokeratin, vimentin, estrogen receptor alpha (ER-alpha), beta (ER-beta), and progesterone receptor. Neoplastic cells exhibited significant cytokeratin positivity (*Fig. 3-C*). Vimentin positivity was observed in stromal cells and placental cells but not in the neoplastic epithelium (*Fig. 3-D*). ER-alpha receptor was negative in all sections. ER-beta was mildly positive in some neoplastic epithelium and stromal cells (*Fig. 3-E*). The progesterone receptor was significantly positive in the lamellar layers of the placenta and myometrium but only slight positivity was observed in neoplastic cells (*Fig. 3-F*).

## DISCUSSION

It is known that the sudden increase in the level of estrogen in the circulation stimulates the formation of endometrial carcinoma in female mammals and accelerates its development<sup>[8]</sup>.

While progesterone suppresses estrogen-induced endometrial growth during the luteal phase, it also prepares the endometrium for blastocyst implantation. In this balance between growth-stimulating estrogen and growth-suppressing progesterone, the hormone that triggers cancer formation is usually estrogen. In domestic animals, estrogen levels that are not suppressed by progesterone can lead to endometrial hyperplasia or cancer<sup>[10]</sup>. In this case, the fact that the progesterone level was high and the estrogen level was relatively low during pregnancy suggests that the carcinoma may have formed in the first days of pregnancy or before pregnancy.

Histological differentiation of well-differentiated endometrial carcinoma with atypical hyperplasia is challenging. According to Kurman and Norris<sup>[11]</sup>, stromal invasion, irregular infiltration of glands, desmoplastic response, confluent glandular pattern, and extensive papillary pattern are indicators of malignancy. Yet, Silverberg<sup>[12]</sup> suggested that papillary growth is not a reliable criterion but stromal invasion with stromal disappearance, desmoplasia and necrosis or combination of them are the best criteria of low-grade carcinoma. In our case, mild to moderate nuclear atypia, extensive papillary growth with surface syncytial changes, irregular and merged cribriform pattern of glands, stromal invasion, and stromal disappearance were encountered. Thus, well-differentiated carcinoma was diagnosed based on histopathological findings.

The expression of estrogen and progesterone receptors in tumor masses in humans has been linked to the prognosis of endometrial carcinomas<sup>[13,14]</sup>. In feline endometrial carcinomas, ERs- $\alpha$  are positive in 50-83.3% of cases, whereas progesterone receptors are generally positive<sup>[3,15]</sup>. In another study, loss of ER- $\alpha$  expression was detected in the endometrium and myometrium, while progesterone receptor expression was observed in the stroma and myometrium<sup>[16]</sup>, and suggested that alternative pathways involving local growth factors can influence epithelial proliferation. Similarly, in the presented case, the lack of the progesterone receptor in the tumoral tissue and its presence in the myometrium were observed. ER- $\alpha$  was also found to be negative throughout the section, however, the ER- $\beta$  was revealed to be positive in some tumoral epithelial and many stromal cells. Negative ER- $\alpha$  expression has been linked to the loss and methylation of transcriptional activators in tumor tissue, as well as the trans domination of ER- $\beta$ <sup>[16,17]</sup>. It has also been

observed that ER- $\alpha$  deficiency is associated with a poor tumor prognosis in feline endometrial carcinomas<sup>[16]</sup>. Furthermore, the ER- $\beta$  receptor has been discovered as a uterine proliferation controller<sup>[19]</sup>. In our case, the negativity of ER- $\alpha$  and the very low positivity of ER- $\beta$  might be interpreted as a negative prognostic factor.

In this case, it was observed that the embryonic sacs were approximately 9 mm in diameter on the 40th day after the mating. In cats, implantation occurs between 12-14 days of pregnancy. It has been determined in previous studies that the outer embryonic sac diameter is approximately 8 mm in diameter at this stage<sup>[9,20]</sup>. In the early stages of pregnancy, endometrial carcinoma adversely affects embryo development and implantation<sup>[6]</sup>. In summary, we think that the reason why the gestational sacs were still at the implantation stage on the 40th day after mating may have been due to the carcinoma in the uterine endometrium and implantation could not occur for this reason. Our case and clinical review of the literature might suggest that estrogen-dependent uterine tissue negatively affects embryonal development in cats and thus embryos may not have developed properly.

### Availability of Data and Materials

The datasets analyzed during the study available from the corresponding author (A. Çortu) on request.

### Competing Interests

The authors declared that there is no conflict of interest.

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### Author Contributions

Ultrasonographic examination was done by AA and AC, histopathological examination was done by VI and LEOA, and the article was written by AC, AA, VI and LEOA.

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