# Cabergoline Administration after Ovariohysterectomy in a Queen with Fibroepithelial Hyperplasia

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## Abstract
In this case report, the diagnosis and treatment process of fibroepithelial hyperplasia developing in the mammary glands of an 11-month-old Tabby queen is presented. Anamnesis that the queen had been in estrus once before, it mammaries were gradually swollen in the last 15 days, her appetite and general condition were normal, and there was no previous progesterone administration. On physical examination, all mammary lobes were excessively tight bilaterally, swollen mammaries were gel-like and painless on palpation, hyperemia and milk secretion around the nipples were noted. Laboratory tests showed that serum progesterone level was 3.02 ng/mL and estrogen level was 5.2 pg/mL. Fibroepithelial hyperplasia was diagnosed based on anamnesis, clinical examination, and laboratory analysis. Ovariohysterectomy operation was performed as the treatment. One day after the operation, cabergoline was administered orally at a dose of 5 µg/kg/day for 5 days. At the two weeks-follow-up examination, a significant regression in the mammary glands size and a end of milk production were observed. In conclusion, fibroepithelial hyperplasia in the mammary glands of a young queen that was brought to our clinic were successfully cured endogenously by surgical method and exogenously by medical drug administration.
**Keywords:** Cabergoline, fibroepithelial hyperplasia, ovariohysterectomy, queen.

# Fibroepitelyal Hiperplazili Bir Kedide Ovaryohisterektomi Sonrası Kabergolin Uygulaması

## Öz
Bu olgu sunumunda 11 aylık dişi tekir kedinin meme bezlerinde gelişen fibroepitelyal hiperplazinin tanı ve tedavi süreci sunulmaktadır. Anamnezde kedinin daha önce bir kez kızgınlık geçirdiği, son 15 gündür memelerinin giderek şiştiği, iştahının ve genel durumunun normal olduğu, daha önce progesteron uygulaması olmadığı öğrenildi. Fiziksel muayenede tüm meme loblarının iki taraflı aşırı gergin olduğu, memelerinin şişmiş, jel kıvamında ve palpasyonda ağrısız olduğu, meme başı çevresinde hiperemi ve süt salgısının olduğu görüldü. Laboratuvar testlerinde serum progesteron düzeyi 3,02 ng/mL, östrojen düzeyi ise 5,2 pg/mL olarak belirlendi. Fibroepitelyal hiperplazi tanısı anamnez, klinik muayene ve laboratuvar analizine dayanarak konuldu. Tedavi olarak ovaryohisterektomi operasyonu uygulandı. Operasyondan bir gün sonra kabergolin 5 gün süreyle 5 µg/kg/gün dozunda oral olarak uygulandı. İki haftalık kontrolde meme bezlerinin boyutunda belirgin bir gerileme ve süt üretiminin sona erdiği görüldü. Sonuç olarak kliniğimize getirilen genç bir dişi kedinin meme bezlerinde oluşan fibroepitelyal hiperplazi oluşumunun endojen olarak cerrahi yöntemle, eksojen olarak ise medikal ilaç uygulamasıyla başarılı bir şekilde iyileştirildiği görüldü.
**Anahtar kelimeler:** Kabergolin, fibroepitelyal hiperplazi, ovaryohisterektomi, dişi kedi.

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## Introduction

Feline mammary fibroepithelial hyperplasia (MFH) is a condition marked by the rapid, non-cancerous growth of both the ductal epithelium and stroma within the mammary glands, leading to the enlargement of one, multiple, or all of the glands (Allen, 1973). This condition usually occurs during first estrus (5-12 months), pregnancy or pseudopregnancy. It is often seen in young queens (13 weeks to 2 years old). Cases of MFH can also be seen in male and queens of all ages that receive exogen progesterone compounds such as megestrol acetate (MA) and medroxyprogesterone acetate (MPA) to suppress estrus (Görlinger et al., 2002).

The affected mammary glands of the queen with fibroepithelial mammary hyperplasia is soft, sharply limited, fluctuant, and jelly-like. Furthermore, it has been reported that some patients have erythematous, dark, and necrotic areas on the their skin of the relevant mammary gland (Bonatto et al., 2021; Voorwald et al., 2021). Fever, tachycardia, lethargy, anemia, and anorexia can be seen as systemic effects of the disease (Loretti et al., 2004). Although fibroepithelial hyperplasia can be diagnosed commonly by clinical findings (inflammation of the mammary gland, etc.), the homogeneous and granular structure of the parenchyma of the affected mammary glands can be seen characteristically during ultrasonographic examination. In addition, histopathological examination of fine needle aspiration biopsy or excision biopsy specimens is also recommended as an additional diagnostic technique (Vitasek & Dendisova, 2006). Treatment can be done by using drugs with luteolytic effect and/or ovariectomy, ovariohysterectomy (OHE), and other methods to prevent endogenous progesterone effect (Johnston et al., 2001; Keskin et al., 2008). Treatment options include surgical methods such as total and partial mastectomy, however, it can be successfully treated with the application of progesterone receptor blockers as medical treatment (Görlinger et al., 2002).

In this case report, the diagnosis of fibroepithelial hyperplasia in the queen and the rapid and nonrecurrent treatment process are presented.

## Case Description

The study material consisted of an 11-month-old tabby queen, weighing 4 kg, which was brought to the Animal Hospital of the Faculty of Veterinary Medicine of Harran University. Anamnesis taken from the patient's owner revealed that the queen had been in heat once before, her mammaries had been gradually swollen in the last 15 days, and her appetite and general condition were normal. The queen was fed a commercially available dry diet, vaccinated regularly, and no medication use (steroid, antifungal or progestin) was reported in her anamnesis.

Physical examination revealed that the queen's body temperature (38.7 $^{o}$C), pulse (114/min), and respiration (14/min), were within normal limits. It was observed that the mammary lobes were extremely tight, the swollen mammaries were gel-like and painless on palpation, and there was also milk secretion (Figure). Furthermore, it was noted that the swellings did not have a connection with the abdominal wall. In the complete blood count analysis (pocH-100 IV Diff, Sysmex, Norderstedt, Germany), all parameters (WBC: 6.2 x $10^3$/µL, RBC: 9.7 x $10^6$/µL, HGB: 13.0 g/dL, HCT: 41.4 %, MCV: 40.6 fL, MCH: 14.7 pg, MCHC: 30.1 g/dL, PLT: 206 x $10^3$/µL) were found to be within normal limits. Serum progesterone level was 3.02 ng/mL and estrogen level was 5.2 pg/mL. Based on the medical history, clinical examination, and serum progesterone level, the diagnosis of MFH was made.

**Figure.** Appearance of the mammary glands before treatment.

In the treatment, an ovariohysterectomy operation was performed through a median line incision. During the operation, corpus luteums that had become cystic on the ovary were observed. Antibiotic (containing 140 mg amoxicillin trihydrate and 35 mg clavulanic acid per ml, Synulox®, Zoetis New York, USA) and vitamin (Nervit® composition/Vetaş, Türkiye) support was given for 5 days after the operation. One day after the operation, cabergoline (Dostinex®, Pfizer, New York, USA) was administered orally at a dose of 5 µg/kg/day once a day for 5 days. In the follow-up examination two weeks later, a significant regression of the mammary glands and a end of milk production were observed. Follow-up examination performed one month later revealed that the mammary glands were completely recovered and the serum progesterone value was 0.217 ng/mL and the estrogen value was less than 5 pg/mL. No complications were encountered during and after the treatment.

## Discussion

Fibroepithelial hyperplasia is formed due to the hypersensitivity of mammary gland tissues to progesterone during the estrus period of the reproductive cycle. This problem spontaneously disappears in a long period of 40-45 days following the natural regression of the corpus luteum (Loretti et al., 2004). However, as waiting for this process can result in several adversities in the mammary glands, this process should be accelerated by early intervention (Allen, 1973; Görlinger et al., 2002). Although fibroepithelial hyperplasia is generally seen in young queens (Baştan et al., 2004; Uçmak et al., 2011), cases can also be observed in male and female cats of all ages who are administered exogenous synthetic progestins for a short or long time (Görlinger et al., 2002; Nak et al., 2004; Bonatto et al., 2021). Similar to the report of Görlinger et al., (2002), a case of MFH was encountered in a queen at a very early age without any treatment, therefore, estrogen and progesterone hormones of individual mammary glands were encountered, suggesting that MFH may have occurred as a result of increased susceptibility due to factors such as genetics and age.

In queens with fibroepithelial mammary hyperplasia, increases in tissue volume lead to perfusion problems, erythema, pain, ulceration, dark and necrotic areas on the mammary gland skin (Bonatto et al., 2021; Voorwald et al., 2021), as well as systemic effects such as high fever, tachycardia, anorexia, and sepsis are also observed (Loretti et al., 2004; Voorwald et al., 2021). In this case, growth was observed to cover all mammary lobes, similar to other researchers (Baştan et al., 2004; Vitasek & Dendisova, 2006; Küçükbekir et al., 2020), and there were no local and general symptoms except hyperemia in some mammary lobes. It was assumed that this might be since the queen was not exogenously exposed

to progestins, and therapeutic intervention was commenced in the clinic in a short time.

In a study where aglepristone (15 mg/kg/ 2-3 weeks) and cabergoline (5 µg/kg/oral/ 7 days) were administered together, it was found that the size of the mammary glands was reduced significantly and milk secretion was ceased at the 3rd week, and the mammary glands were completely regressed after 6 weeks (Uçmak et al., 2011). In another study, it was reported that the treatment with aglepristone and cabergoline (5µg/kg/14 days) in combination was effective in stopping milk production and ensure regression in the mammary glands in a pregnant queen with mammary gland hyperplasia (Keskin et al., 2008). When the hyperplastic change in the mammary gland is due to an endogenous source of progesterone, ovariohysterectomy is one of the most effective treatment methods, as suggested by other researchers (Baştan et al., 2004; Kutzler & Wood, 2006; Silva & Silva, 2012). When making this decision, it should also be taken into consideration that this is an operation that will prevent it from being possible to have offspring in the future (Melo et al., 2021). Baştan et al. (2004) reported that in a case of mammary hypertrophy observed in a 5-month-old queen, all mammary glands, except the mammary gland where hypertrophy started, returned to normal after the follow-up performed only on the 7th day after the OHE operation, and clinical improvement was observed in all mammary glands on the 14th day. However, in a study in which the effect of OHE was seen on MFH, it was reported that persistent swelling of the mammary gland was encountered more frequently after the operation, and treatment with antiprogestogen would provide a better success in these complicated cases (Melo et al., 2021). In our study, the combination of OHE and cabergoline was administered to the mammary glands in two different ways (Nak et al., 2004; Uçmak et al., 2011; Küçükbekir et al., 2020). A significant regression was noted within a week and no complication related to both the operation and the regression process in the mammary gland was observed. It was thought that the success in this rapid regression period in the mammary glands might be related to the combination of treatment and the fact that medications such as MPA were not used in the anamnesis. Furthermore, it is stated that OHE performed through the median incision before the complete involution of the mammary glands is impossible, and it should be performed after the complete involution of the hyperplasia (Munson, 2006), and no operative complication was encountered in this presented case. The dose of cabergoline administered in this case, especially in which there was milk secretion, was consistent with other study data (Keskin et al., 2008; Uçmak et al., 2011), and it was seen that cabergoline administration at the specified dose did not cause any adverse events. Contrary to some studies (Keskin et al., 2008; Uçmak et al., 2011), the administration time was kept short, limited to 5 days in terms of supporting OHE operation and not for therapeutic purpose. It was proved to be successful. It has been stated that the regression process of the mammary gland is rather long, especially in cases where short or long-term progestagen was used in the past and in those receiving only medical treatment. The mammary lobes become ulcerated and relapses occur shortly after the application in those cases (Keskin et al., 2008; Uçmak et al., 2011). Therefore, it has been observed that combined treatment, including surgery, is an effective treatment method in MFH cases that do not respond to treatment.

## Conclusion

As a result, fibroepithelial hyperplasia was successfully treated and possible recurrences were avoided through OHE operation, suppressing milk secretion with cabergoline and accelerating mammary glands regression,

especially in queens that are not planning to become pregnant.

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**Ethical Statement**

This study does not present any ethical concerns.

**Author Contributions**

Investigation: T.A. and Ö.Y.; Material and Methodology: T.A. and Ö.Y.; Supervision: T.A. and Ö.Y.; Visualization: Ö.Y.; Writing-Original Draft: T.A. and Ö.Y.; Writing- review & Editing: T.A.

**Conflict of Interest**

The authors declared that there is no conflict of interest.

**Data Availabilty Statement**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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