

Adenomyosis in a domestic feline: a case report

Adenomióse em felina doméstica: relato de caso

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ABSTRACT: Adenomyosis is a non-neoplastic condition which affects the female reproductive system. This condition is rare in domestic animals, and is characterized by the invasion and abnormal growth of the endometrium into the uterine muscle region. Herein, we describe the histopathological findings of uterine adenomyosis with delayed diagnosis in a three-year-old domestic female cat, of undefined breed, with a history of periodic administration of exogenous progestagens. The cat underwent ovariohysterectomy, during which macroscopic incidental changes of increased volume in the left uterine horn were observed. Microscopic analysis further revealed marked glandular epithelial hyperplasia in the endometrium, along with multiple cystic areas composed of well-differentiated columnar epithelial cells, mild multifocal hemorrhage, and deposition of amphophilic amorphous material. Some glandular structures and cystic dilations were noted in the myometrium. Based on histopathological findings, a diagnosis of cystic endometrial hyperplasia with endometritis and adenomyosis was made. Despite the delayed diagnosis, surgical treatment proved effective in this case.

KEYWORDS: Surgery; diagnosis; feline; progestagens.

RESUMO: A adenomióse é uma afecção não neoplásica que acomete o sistema reprodutor das fêmeas. Considerada rara nos animais domésticos e caracterizada pela invasão e crescimento anormal do endométrio na região de musculatura uterina. O presente relato descreve o achado histopatológico de adenomióse uterina com diagnóstico tardio em uma felina doméstica, de três anos de idade, sem raça definida, com histórico de administração periódica de progestágenos exógenos. Esta foi submetida ao procedimento de ovariossalpingohisterectomia, onde foram observadas as alterações incidentais macroscópicas de aumento de volume em corno uterino esquerdo. Na análise microscópica observou-se, no endométrio acentuada hiperplasia epitelial glandular, além de múltiplas áreas císticas, compostas por células epiteliais colunares e bem diferenciadas, discreta hemorragia multifocal e deposição de material amorfo anfófilico. Algumas glândulas e dilatações císticas foram observadas no miométrio. Baseado nos achados histopatológicos, o diagnóstico foi de hiperplasia endometrial cística com endometrite e adenomióse. Conclui-se que apesar do diagnóstico tardio, o tratamento cirúrgico foi efetivo para o caso.

PALAVRAS-CHAVE: Cirurgia; diagnóstico; felino; progestágenos.

INTRODUCTION

In mammals, the uterus features glands in the endometrium responsible for synthesizing, transporting, and secreting substances within its lumen (Spencer, 2014; Spencer, Kelleher, Bartol, 2019). Incidentally, these glands may proliferate abnormally and penetrate the layers of the myometrium, typically occurring in a diffuse manner. This phenomenon is due to the distribution pattern of these glands in the endometrium, while the resulting condition is referred to as adenomyosis and is of a benign nature (Bulman-Fleming, 2008; Stöckun-Gautschi *et al.*, 2001).

Adenomyosis is typically found as an incidental lesion, with diagnosis commonly occurring late, postoperatively, following elective procedures. Throughout the majority of its development, this disease often lacks clinical signs and tends to be investigated only as an incidental finding, following discovery of pathological alterations of the uterus requiring surgical intervention, such as in cases of endometritis, pyometra, and cystic glandular hyperplasia (Perez-Marin *et al.*, 2008; Stöckun-Gautschi *et al.*, 2001).

Due to the absence of clinical signs and the low frequency of abdominal imaging requests in the preoperative

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phase of elective procedures, such as castration, diagnosis of adenomyosis is rare. Additionally, the practice of submitting postoperative collected tissue for analysis and recommending histopathological examination is not considered routine, leading to the neglect of adenomyosis diagnosis and subsequent underreporting in the majority of cases (Perez-Marin *et al.*, 2008; Stöckun-Gautschi *et al.*, 2001).

The etiology of this condition is still unknown. However, many authors believe that hormonal disturbances play a significant role in the development of uterine adenomyosis, supporting the idea that the use of exogenous progestagens (contraceptives) may contribute to an increased disease frequency (Bezerra *et al.*, 2016; Maclean; Hayashi, 2022; Perez-Marin *et al.*, 2008).

Data on the incidence of adenomyosis are inconsistent due to variability in criteria. Reports in animals are rare, and publications indicate a wide prevalence range across all species. Values ranging between 5-8% and 40-70% have been reported (Graziano, Lo Monte, Piva, 2015; Kitawaki, 2006; Levgur, Abadi, Tucker, 2000). Current studies demonstrate that approximately 4 out of every 5 cases of adenomyosis coexist with uterine fibroids and endometriosis (Aleksandrovych, Basta, Gil., 2019).

In this context, the present report describes the accidental occurrence of adenomyosis in a feline patient undergoing ovariectomy.

CASE REPORT

A 3-year-old female feline, weighing 3.8 kg, of undefined breed, and with no previous history of illnesses, was admitted for pre-surgical assessment of elective ovariectomy. During the anamnesis, the caretaker reported the periodic use of exogenous progestagens as a contraceptive measure. The animal showed no noteworthy alterations on general preoperative physical examination. Subsequently, preoperative tests, including complete blood count, total plasma protein, platelets, alanine aminotransferase, and creatinine were performed, with all results within normal limits for the species.

Following a preoperative fasting period, pre-anesthetic medication was administered, including methadone1 [Mytedom®] (0.3 mg/kg), midazolam2 [Dormonid®] (0.3 mg/kg), and ketamine3 [Cetamin®] (4 mg/kg), all administered intramuscularly. Subsequently, anesthesia induction was performed using propofol4 [Propovan®] (4 mg/kg, intravenously). The animal was then intubated and maintained under spontaneous breathing with inhaled isoflurane5 [Isoforine®] coupled with 100% oxygen in an open system (double T-bar circuit).

In the surgical anesthetic plane, with a wide abdominal region trichotomy, the animal was positioned in dorsal recumbency for surgical antisepsis with 70% alcohol6 [Rialcool®] and 2% compounded chlorhexidine. After placing the surgical drape, a midline retro-umbilical incision was made.

Following celiotomy, the left uterine horn and uterine body were identified, revealing a significant increase in volume (Figure 1), with a floating appearance and multiple areas of thickening, firm to the touch. Subsequently, excisional tissue biopsy was performed via ovariectomy. For the procedure, the ovaries and proper ovarian ligament region were located, and the modified three-clamp technique was employed for mass ligation of the ovarian pedicle (arteriovenous plexus), with non-absorbable synthetic suture7 [mononylon® 3-0].

After both pedicles were ligated to isolate the uterus and vessels, the broad ligament of the uterus and the round ligament were severed. Following the three-clamp technique positioned on the uterine body anterior to the cervix, block excision of the tissues was performed, and thereafter, transfixing ligature on the remaining uterine body near the cervix was accomplished using non-absorbable synthetic suture7 [mononylon® 3-0]. After inspecting the cavity for the absence of bleeding, omentalization in the uterine stump region and celiorrhaphy were performed. Further, myorrhaphy was carried out using Sultan stitches with mononylon 3-0. Subcutaneous reduction was achieved with continuous simple sutures using synthetic absorbable thread7 [polygalactin 910® 3-0], while dermorhaphy was conducted with non-absorbable synthetic suture7 [mononylon® 2-0] in an interrupted simple pattern. No anesthetic or surgical complications were observed during the intraoperative period.

As postoperative medication, the patient received tramadol hydrochloride1 [Tramadol®, 2 mg/kg, subcutaneously, every 8 hours for 3 days], dipyrone10 [Novalgina®, 25 mg/kg, orally, every 8 hours for 5 days], and meloxicam9 [Maxicam®,



Source: Axys Análises

Figure 1. Uterine Horn and Uterine Body Showing a Significant Volume Increase.

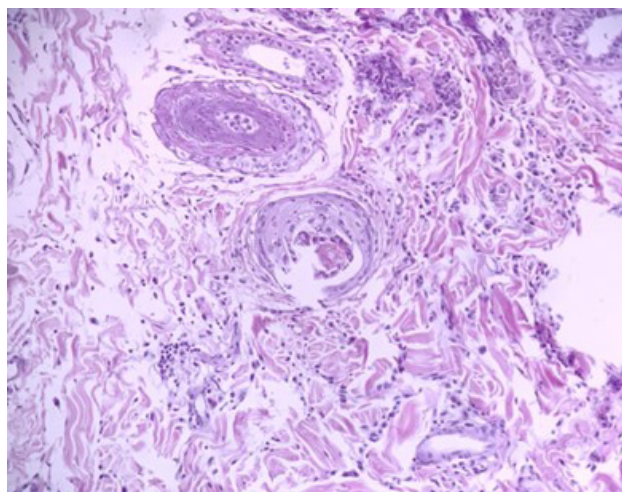
0.05 mg/kg, intramuscularly, every 24 hours for 3 days]. Homecare instructions included daily dressing changes and cleaning of the surgical wound, with a scheduled return to the hospital at the 10th postoperative day for skin stitch removal.

The excised uterus and ovaries were preserved in 10% formalin and subjected to histopathological analysis. During macroscopic histopathological examination, uterine horns were divided into A and B. In A, a 7-centimeter uterine horn with a focal thickening area of 1 centimeter, a floating appearance, and a firm uterine body were observed. Upon cutting, friable brown fluid and focal thickening were found. In the evaluation of B, a 6-centimeter uterine horn with multiple areas of discreet thickening, firm to the touch, showed a similar result to uterine horn A, with friable brown fluid and focal thickening upon cutting.

Microscopic analysis revealed marked glandular epithelial hyperplasia in the endometrium, in addition to multiple cystic areas composed of well-differentiated columnar epithelial cells. A pronounced inflammatory infiltrate comprising neutrophils, lymphocytes, plasma cells, and macrophages, as well as mild multifocal hemorrhage and deposition of amphophilic amorphous material was observed. Some glandular structures and cystic dilations were further observed in the myometrium (Figure 2). Ovarian evaluation detected the presence of follicles in all stages of development. Based on histopathological findings, a final diagnosis of cystic endometrial hyperplasia with endometritis and adenomyosis was made.

DISCUSSION

In the present case, the diagnosis was incidental, with no alterations in the preoperative exams performed. Similar occurrences have been reported by other authors, where the finding was often associated with cases of pyometritis, and there were no specific signs for adenomyosis. In the present case, the disease was diagnosed through histopathological evaluation following



Source: Axys Análises

Figure 2. Myometrium with Glands and Cystic Dilations

the performance of ovariohysterectomy (Bezerra *et al.*, 2016; Bulman-Fleming, 2008).

Adenomyosis still lacks a clear understanding among researchers, presenting various commonalities with endometriosis, despite the latter occurring outside the uterus and being exclusive to species with menstrual cycles (primates), with the exception of a single reported case in a dog (Bulman-Fleming, 2008; Paiva *et al.*, 2015). Regular use of progestagens may be related to disease onset, as progestins can promote endometrial growth through the activation of estrogen receptors, which, in turn, disrupt growth factor receptors (Munson *et al.*, 2002). A study in zoo wildcats, published in 2002, demonstrated that animals treated with melengestrol acetate were 3.6 times more likely to develop uterine hyperplasia and other reproductive diseases than those that did not receive the drug (Munson *et al.*, 2002).

Considering that most cases of adenomyosis are associated with pyometritis, we can consider this condition as a predisposing factor for the occurrence of adenomyosis in intact females. Pyometritis usually arises from a previous cystic endometrial hyperplasia (CEH), which is directly related to excess basal endogenous (post-estrus) or exogenous (via progestagen administration) progesterone administration (Noakes, Parkinson, England, 2001). High concentrations of progesterone in the female's body can lead to an increase in uterine volume and excessive production of uterine secretions and fluids. This condition is termed cystic endometrial hyperplasia, and in the present case was observed in the microscopic analysis of the histopathological examination. The determining factor for the development of pyometra occurs when the uterus remains in this state for extended periods, presenting greater vulnerability and favorable conditions for the development of metritis, leading to bacterial contamination of the uterus and involvement of mucopurulent discharge (Johnston, Kustritz, Olson, 2001; Niskanen, Thrusfield, 1998; Noakes, *et al.* 2001).

Adenomyosis has rarely been reported in domestic felines in the field of veterinary medicine. In contrast, there are many scientific studies on the topic in female dogs. The authors are aware of about three reports of adenomyosis in domestic felines (Aguirra *et al.*, 2019; Bezerra *et al.*, 2016; Bulman-Fleming, 2008). In one of these reports, an association with pyometra was found, presenting alterations and clinical signs consistent with the diagnosis. In this report, adenomyosis was a late finding in the histopathological evaluation after ovariohysterectomy, similar to the present article. However, in our report, the patient had no apparent symptoms, and the procedure was considered elective, with no alterations during the physical or preoperative examination, although other studies mention associated clinical signs, such as abdominal pain, vomiting, and tachycardia. It is well known that adenomyosis is closely related to CEH, and this condition, in turn, precedes pyometritis (Niskanen, Thrusfield, 1998; Noakes *et al.*,

2001). It is generally believed that the patient in this report underwent elective ovariohysterectomy in time to avoid subsequent development of the disease, given that CEH already existed in the animal's uterus.

As reported by the caregiver of the feline in this case, continuous administration of exogenous progestagens to the patient occurred. Although the presence of pyometritis was not evident in this report, it is important to understand the pathophysiology of this disease, as it has been associated with adenomyosis findings in articles in a variety of mammalian cases. Furthermore, it is presumed that the feline did not develop a pyometra condition due to the early performance of the ovariohysterectomy procedure, considering that this condition is generally sequential to CEH (Aguirra *et al.*, 2019; Bezerra *et al.*, 2016; Bulman-Fleming, 2008; Munson *et al.*, 2002; Perez-Marin *et al.*, 2008; Tamada *et al.*, 2005).

One study published in 2019 previously reported the occurrence and histopathological aspects of adenomyosis in female cats and dogs. It concluded that, in both species, animals being administered contraceptives were significantly more affected compared to those who were not. Additionally, out of the total cases analyzed, 12% (12/100) of dogs and

3% (3/100) of cats had uterine adenomyosis, with statistically significant differences ($p < 0.05$) between the species (Aguirra *et al.*, 2019).

These studies and other reports reinforce the theory that the use of progestagens is the most influential factor in the development of uterine diseases. In women, the excess of circulating progestins (which can be of exogenous origin) can increase estrogen levels, thereby enhancing aromatase activity, estrogen receptor concentration, and epidermal growth factor (Ferenczy, 1998).

Adenomyosis is an important differential diagnosis for uterine diseases in both domestic and zoo animals, with a high risk of misdiagnosis in clinical settings. Suspected lesions warrant a detailed microscopic examination to ensure a correct and assertive morphological diagnosis. Further, the potential connection between the administration of exogenous hormones and adenomyosis deserves further investigation in veterinary medicine, considering that, despite being contraindicated, the administration of progestagens in companion animals is a common reality (Bulman-Fleming, 2008).

Overall, from the present case, we can conclude that the technique of ovariohysterectomy resulted in the resolution of asymptomatic disease in this domestic feline.

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