

Mammary Cystadenoma: Diagnosis and Treatment in a Bitch

Gabriela Corrêa de Almeida¹, Najla Ibrahim Isa Abdel Hadi², Izabelle Moutinho⁴, Vinícius Cardoso de Oliveira⁴, Victor Mendes de Oliveira⁴, Gentil Ferreira Gonçalves³, Fabiana Elias³ & Fabíola Dalmolin³

ABSTRACT

Background: Although malignant mammary alteration is highly studied in canine, data about benign lesions is sparse. A study reported 27.1% of benign alteration, being 5.9% cystadenomas. It is a unique or multiple lesion, characterized by lined and well differentiated epithelial cells. The alteration is well recognized in women, opposite to canines, which present cysts or not, and it is more frequent in ovary, kidney, salivary gland, thyroid, pancreas and mammary gland. Related to cysts, ultrasonography and cytological exams help the diagnosis and treatment. In this way, this report presents the diagnosis, the treatment and 4 years follow up canine mammary cystadenoma.

Case: A 5-year-old non-spayed Mongrel bitch, weighing 5.9 kg, presented mammary enlargement identified by the owner since 8 months before. The patient had received exogenous contraceptives 3 times, being the last one 12 months before; after detection, the enlargement increased in volume along the time. It was a 9x2x1 cm nodular and fluctuant enlargement in the left inguinal mammary gland; the ultrasound exam confirmed many fluid collection delimited by a thin echogenic capsule and anechoic content. No alterations were detected at other glands and abdomen. Fine-needle aspiration promoted the liquid drainage, which presented no cells identified by cytology for 2 times. The patient was submitted to OVH and nodulectomy and discharged after anesthetic recovery, with prescription of meloxicam, dipyrone and topic chlorhexidine digluconate 1%. After 4 days the owner verified the color change of the skin at the nodulectomy site. We identified a purplish alteration 13 days after, as well as wound healing, being sutures removed and warm compresses prescribed; normal color was verified after 8 days. Posteriorly at 1 and 4 years the patient was evaluated and no clinical, mammary and ultrasonography alterations were detected.

Discussion: The non-spayed bitches which receive exogenous contraceptive are more likely to mammary alteration development, as observed in this patient. According to the Brazilian Mammary Consensus, the malignant mammary alteration bigger than 3 cm must be treated by unilateral mastectomy and lymphadenectomy, an aggressive surgery which involves long anesthesia and hemodynamic disturbances due to the surgical stress response. Considering the absence of malignant signs, an encapsulated alteration, the absence of malignant signs and a relatively young patient, the patient was treated by nodulectomy, opposite to the recommended. The benign mammary neoplasms are more susceptible to hormonal influence compared to the malignant one after synthetic progesterone application, since the benign have more progesterone and estrogen receptors. In this way, the OVH was performed in order to reduce the hormonal influence. The OVH was performed firstly to avoid abdominal contamination by liquid or cells, according to the aseptic and atraumatic surgical principles. The histological tumor exam revealed cystadenoma with papillary formation, and mild uterine cystic endometrial hyperplasia not visible by ultrasonography image. Although it was a benign alteration, the authors considered the risk of malignant lesion after exogenous contraceptive. For this, the patient was assessed by clinical and ultrasonography exam 1 and 4 years after to verify recurrence or new lesions, which were not observed and indicated treatment effectiveness. It was recognized that surgical aggressiveness changes the immune response and it predisposes to neoplasm development. Although the authors believe in the positive effect of less aggressive surgery to patients with benign alterations, more studies are necessary to verify the benign neoplasm behavior in order to suggest the adequate treatment.

Keywords: benign neoplasm, canine contraceptive, mammary cyst, mastectomy, surgical stress, mammary nodulectomy.

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¹Private Veterinary Practitioner, Cascavel, PR, Brazil. ²Private Veterinary Practitioner, Dionísio Cerqueira, SC, Brazil. ³Veterinary Medicine & ⁴Programa de Pós-Graduação em Saúde, Bem-estar e Produção Animal Sustentável na Fronteira Sul (PPG-SBPAS), Universidade Federal da Fronteira Sul (UFFS), Campus Realeza, Realeza, PR. CORRESPONDENCE: F. Dalmolin [fabiola.dalmolin@uffs.edu.br]. Superintendência Unidade Hospitalar Veterinária Universitária. Rua Edmundo Gaievski n. 1000. Jardim Primavera. CEP 85770-000 Realeza, PR, Brazil.

INTRODUCTION

The cystadenoma is a benign neoplasm characterized by a single or multiple cyst lined by well differentiated epithelial cells [5,24]. Macroscopically, the adenomas are circumscribed and solid, but sometimes it may contain disseminated cysts [7]. The alteration in animals occurs more commonly in the ovaries, kidneys, pancreas, salivary glands and thyroid [5]. A retrospective study with 35 mammary canine samples collected revealed that among the benign neoplasm, 40% were cystadenoma, 40% intraductal papilloma and 20% fibrolipoma [8].

In women, mammary cysts appear between 7-10% of the mammary alteration and it is presented as a mobile nodule with regular contour and soft consistency [18]. Considering the cystic alteration, the ultrasonography has high possibility to diagnose de affection. The exam precision varies from 95 to 100% and it identifies alterations bigger than 2 mm [1,18]. The cytological examination after fine needle aspiration allows morphological changes visualization in the puncture site cells and it helps to differentiate neoplastic, inflammatory or hyperplastic lesions [9].

In women, the mammary cystadenoma diagnosis is realized through clinical evaluation, ultrasound and cytology exams, which determine the diagnosis and guide the therapeutic approach [2,18]. To the best of the author's knowledge, no clinical reports including diagnosis, treatment and evolution of the canine cystadenoma is available. In this way, the objective of this study is to report a canine mammary cystadenoma case describing the mentioned aspects and the 4 year follow up.

CASE

A 5-year-old non-spayed Mongrel bitch, weighing 5.9 kg, presented mammary enlargement identified by the owner since 8 months before. The owner related 3 exogenous contraceptive applications, being the last one applied 12 months before; after it was observed mammary enlargement, which increased volume along the time. Clinically was verified a 9x2x1 cm tumor in the inguinal gland (Figure 1A); by palpation was nodular, with fluctuant consistency, liquid content, no ulcerated skin, no local or mammary secretion, no rise temperature or adherence. Syringe and fine needle aspiration (13x0.45 mm) promoted liquid drainage and the cytological study was performed, being inconclusive. The total blood count was realized and it identified eosinophilia.

Pulmonary alteration was detected by auscultation and radiographic demonstrated perialveolar bronchitis. It was prescribed cephalexin¹ [Rilexine® - 30 mg/kg, VO, BID, for 10 days] and pyrantel pamoate, praziquantel and febantel² [Canex plus®, VO, single dose].

The patient was reassessed after 25 days and it presented tumor recurrence; new aspiration was performed and cytology was inconclusive again. Local ultrasound exam revealed several fluid collections delimited by a thin, echogenic capsule and anechoic content; no metastasis signs or other abdominal alteration were observed, being the suggestive of benign neoplasia. In this way, the patient was referred to nodulectomy and ovariohysterectomy (OVH).

After 8 h for solid fasting and 2 h for liquid, the patient was clinically examined and it was administered acepromazine³ [Acepromazin® - 0.05 mg/kg], midazolam⁴ [Dorminum® - 0.4 mg/kg] and methadone⁵ [Mytedom® - 0.4 mg/kg] were administered IM. After 20 min, the surgical site was prepared and the Ringer's lactate therapy⁶ [Ringer com Lactato® - 3 mL/kg] was instituted by venous access. The anesthesia was induced by propofol⁷ [Propotil® - 3 mg/kg, IV], the maintenance with isoflurane⁸ [Isoflurano® - diluted in 100 % oxygen] in a calibrated device and the analgesia by meloxicam⁹ [Maxicam® - 0.2 mg/kg, SC].

After aseptic preparation, a skin and subcutaneous incision using the scalp was performed, from the caudal umbilical scar until one third of the distance between it and the pubis. The linea alba incision was initiated by the scalp and completed with Metzenbaum scissor. The ovarian arteriovenous complex and uterine body hemostasis was performed by the modified clamp method and double circular ligature with 2-0 polyglactin 910¹⁰ [Shalon Poliglactina 910®]. The abdominal closure was done by the isolate cruciate pattern followed by subcutaneous approximation with the same thread. In a second moment, an elliptical excision around the liquid collection was performed, observing 1 cm clean surgical margins (Figure 1B). Through blunt dissection using Metzenbaum scissor, the tumor was removed, including the mammary tissue and the ligature of cranial and caudal epigastric artery and vein hemostasis was done by simple circular ligature with 3-0 polyglactin 910¹⁰ [Shalon Poliglactina 910®]. The skin edges were approximated using the walking suture pattern and the same surgical material; to the subcutaneous sutures was applied the same material in continuous pattern. Dermorrhaphy was

done by the isolated horizontal mattress pattern and 3-0 nylon¹⁰ [Shalon Nylon 910®]. The patient was discharged after anesthetic recovery and prescription of meloxicam⁹ [Maxicam® - 0.5 mg/kg, SID, for 3 days], sodium dipyrone¹¹ [Dipirona sódica EMS® - 20 mg/kg, TID, for 5 days] chlorhexidine digluconate¹² [Asseptcare Spray® - topic, TID, for 10 days] at surgical site and protective clothing. The removed ovaries, uterus, uterine tubes and tumor were immediately placed in 10% formalin solution and sent to histopathology examination.

The patient was clinically assessed 13 days after. The owner just reported skin color change (purplish) at the tumor site 4 days after, which regressed over the days (Figure 1C). No clinical alteration was detected, just mild inflammation of the surgical site skin. It was observed surgical wound healing and the stitches were removed. The prescription of warm compresses TID/8 days was done and 8 days later, by phone, the owner related physiologic skin color.

The mammary gland, uterus, uterine tube, ovary and mammary gland alteration were evaluated by H&E stain. The uterus presented endometrium cystic dilation, ectasia and vascular congestion; the ovaries presented no alteration.

The mammary gland tumor (Figure 2A) revealed a cystic formation surrounded by one squamous cellular layer (Figure 2B). A glandular proliferation and occasionally papillary formation was observed in the lining cyst epithelium, characterizing a cystadenoma with papillary formation (Figure 2C) [6]. At the periphery was identified lymphocytic infiltrate and mammary tissue with ductal ectasia (Figure 2D). A glandular proliferation and occasionally papillary formation was observed in the lining cyst epithelium, characterizing a cystadenoma with papillary formation [6].

After 1 (Figure 1D) and 4 years, the patient was clinically assessed; the surgical site and the mammary glands were evaluated by ultrasound examination. No clinical and image alteration were detected in both moments.

DISCUSSION

The mammary alterations in bitches are clinically observed as a gland tumor, which can be single when it affects 1 gland, or multiple, when more ones are involved. These alterations could be associated with a series of alterations such as hyperplasia, inflammation, cysts, benign or malignant neoplasms [10,16] with cystic neoformation, as observed in this case.

A study demonstrated that among 60 bitches with mammary neoplasia, no one has undergone OVH before the second estrous cycle; in 43.3% the surgery was realized lately and 56.7% where not spayed [15]. The patient of this case was 5-years-old and not neutered, which corroborates to this data; in the same way, other authors suggested 25% more risk to mammary neoplasia in not neutered bitches [3,14,17]. The cystadenoma is a benign mammary neoplasm and it has been already diagnosed from 5.9 to 20% of the mammary gland alteration. Due to the absence of information about the treatment and prognosis of the alteration, the authors believe in the importance of this case [19,25].

The progesterone stimulates mammary hyperplasia and the benign neoplasm development in young bitches due to the growth hormone synthesis by the gland, which causes alveolar proliferation [16,17]. The observation is reinforced by this case, since the young patient presented the alteration and had received hormonal contraceptives 3 times. A study observed that 27.77% of the bitches exposed to progesterone-based contraceptives had developed mammary neoplasia lately; in just one patient it was observed a benign neoplasm [20], as observed in this case.

In addition to the endogenous progesterone, the frequent synthetic hormone use in canine can induce mammary alteration, as well as it directly influences the cells that make up the mammary tissue [11]. The patient of this investigation received 3 exogenous progesterone applications, which probably contributed to this development change.

The surgical excision of the mammary neoplasm in bitches is the recommended treatment to the most part of the cases. Techniques such as nodulectomy, simple mastectomy, regional mastectomy, unilateral or bilateral mastectomy, with or without the removal of lymph nodes are the indicated procedures [6]. According to the "Brazilian Consensus regarding the diagnosis, prognosis and treatment of canine and feline mammary tumors" [6], the patients presenting inguinal mammary neoplasms larger than 3 cm should be referred to unilateral mastectomy. In this case, due to the patient and tumor characteristics, the authors opted for neoplasm excision and OVH at the same surgical time. In this case it was considered an option due to the patient age (relatively young), the absence of malignancy characteristics, and the presence of an encapsulated and localized tumor.

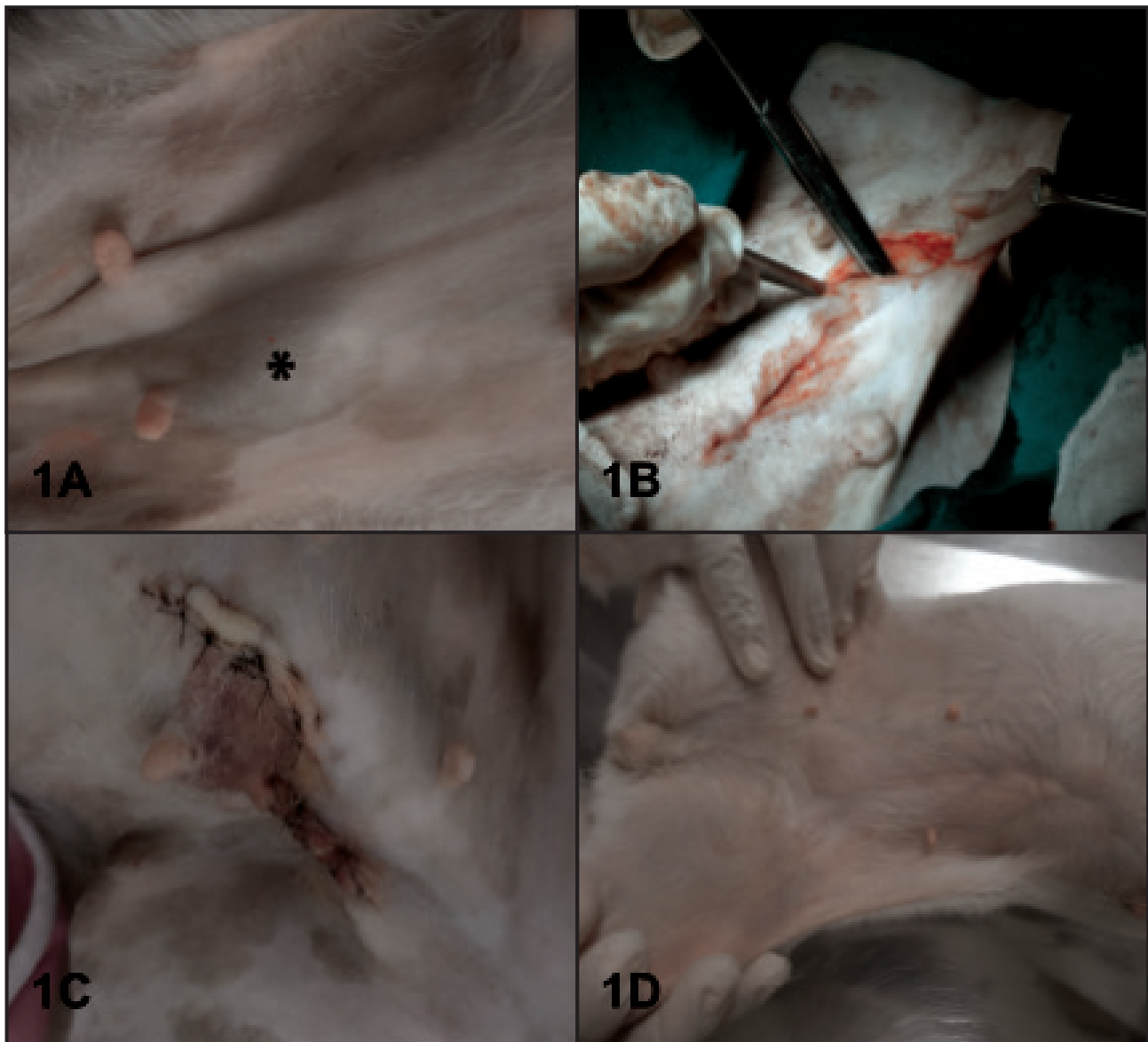


Figure 1. A 5-year-old non-spayed Mongrel bitch. A- A 9x2x1 cm increasing volume in the left inguinal mammary gland with fluctuant consistency, liquid content, no ulcerated skin, no local or mammary secretion, no rise temperature or adherence (*). B- Transoperative image of the ovariohysterectomy and nodulectomy. C- Thirteen days after surgery, when the skin suffusion was registered and the suture removed. D- No clinical signals of recurrence or new alteration at mammary glands 12 months after surgery.

The benign neoplasms are subjected to a greater hormonal influence, due to the bigger number of estrogen and progesterone receptors compared to the malignant ones [6,12]. It is believed that OVH and no subsequent exogenous hormone application had a positive effect in this patient case. In this sense, despite the unilateral or bilateral mastectomy being curative in the most part of the mammary neoplasm cases, these procedures are more aggressive and provoke surgical stress, which can culminate in metabolic alteration, cell damage and changes in the genetic material, which predispose to the mutagenesis and carcinogenesis [22,23]. In the same way, the mastectomy is associated with increased

surgical complications, which may not improve the survival time of the affected bitches [6,22,24], and it should be pondered, as realized in this case.

The histopathology examination revealed cystadenoma papillary formation in the mammary gland and mild multifocal cystic endometrial hyperplasia in the uterus. The administration of exogenous progesterone in bitches causes endometrial estrogen and progesterone receptors increasing. Consequently, the endometrium suffers thickening due to the cystic dilatation, secretion of the endometrial glands and proliferation of the epithelial cell surface [4]. A study promoted the application of exogenous progesterone in

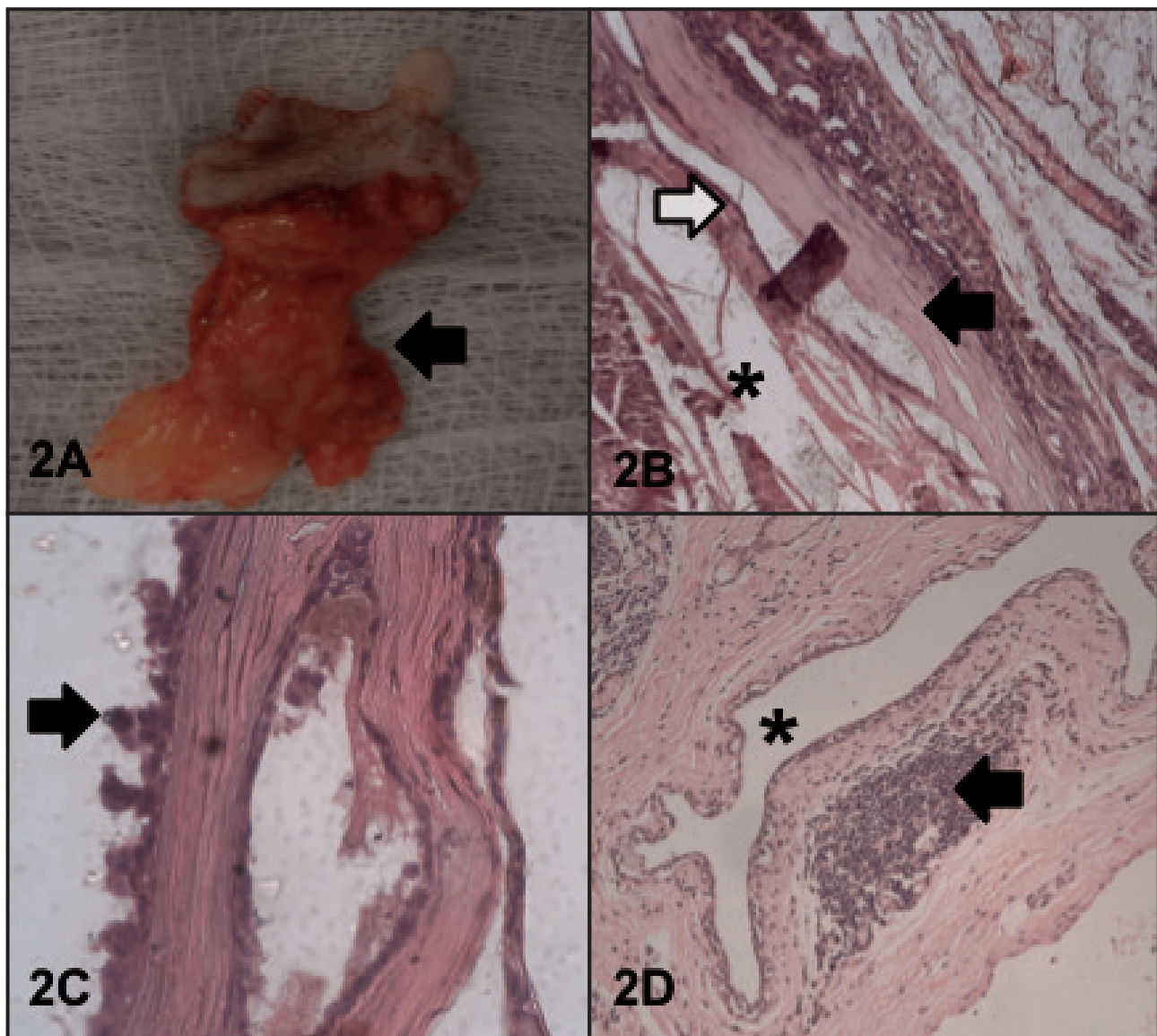


Figure 2. Inguinal mammary increasing volume of a 5-year-old non-spayed Mongrel bitch. A- Macroscopic lesion removed by nodulectomy sent to histological evaluation; macroscopic aspect of the left inguinal mammary gland and the cyst, which lost the liquid during manipulation after surgery (arrow). B- Cystic formation with a single layer of squamous cells (white arrow), covered by fibrous tissue (black arrow); in the lumen there is amorphous eosinophilic content (*) [HE 10x]. C- Presence of papillary cell proliferation in the cyst wall (arrow) [HE; 40x]. D - Breast tissue with ductal ectasia (*) and inflammatory infiltrate (arrows) [HE; 10x].

20 healthy bitches followed by OVH after 90 days. At the uterine histopathology examination, 18 of the patients presented cystic endometrial hyperplasia ranging from mild to severe [21], as observed in this patient. When the cystic endometrial hyperplasia is associated with pus presence, it characterizes pyometra, a uterine infection recognized as surgical urgency [13], which was prevented by OVH in this patient.

After 1 and 4 years after surgery, the patient was assessed and no alteration detected. In this way, it could be suggested that the neoplasm exeresis with 1-cm margin associated to OVH is effective to treat

mammary cystadenoma after exogenous hormone in unneutered canine females.

MANUFACTURERS

¹Virbac do Brasil Indústria e Comércio Ltda. Roseira, SP, Brazil.

²Ceva Saúde Animal Ltda. Paulínia, SP, Brazil.

³Syntec do Brasil Ltda. Santana do Parnaíba, SP, Brazil.

⁴União Química Farmacêutica Nacional S.A. São Paulo, SP, Brazil.

⁵Cristália Produtos Químicos e Farmacêuticos Ltda. Itapira, SP, Brazil.

⁶JP Indústria Farmacêutica S.A. Ribeirão Preto, SP, Brazil.

⁷Midfarma Produtos Farmacêuticos Ltda. Mandaguáçu, PR, Brazil.

⁸Instituto Biochimico Indústria Farmacêutica Ltda. Rio de Janeiro, RJ, Brazil.

⁹Ourofino Saúde Animal Ltda. Cravinhos, SP, Brazil.

¹⁰Shalon Fios Cirurgicos Ltda. São Luis de Montes Belos, GO, Brazil.

¹¹EMS Pharma. Hortolândia, SP, Brazil.

¹²Neoquímica. Rio de Janeiro, RJ, Brazil.

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