



## Diagnostic and Surgical Treatment of a Mare with Granulosa Theca Cell Tumor

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**How to cite this article:** Ayad et al. Diagnostic and Surgical Treatment of a Mare with Granulosa Theca Cell Tumor. *Veterinary Medicine and Public Health Journal* 1(2); 2020:30-33.

**DOI:** <https://doi.org/10.31559/vmph2020.1.2.1>

**Received Date:** 12/2/2020

**Accepted Date:** 2/4/2020

### Abstract

Granulosa theca cell tumors (GTCTs) are the most common neoplasia of the equine ovary, comprising about 2.5% of all equine neoplasms. Historical facts include reports of failure to cycle, unusual sexual behavior (nymphomania or stallion like), or a change in sexual behavior. The present study reports a case of a 10-year-old crossbreed mare with GTCT presenting nymphomania behavior (continuous estrus) and no pregnancy. This tumor was diagnosed by clinical history, rectal palpation and ultrasonography before surgical removal. Histopathological examination confirmed the diagnosis by showing irregular aggregates of neoplastic granulosa resembling cells. Serological levels of testosterone and inhibin were not evaluated. The mare recovered and by one month and 15 days was evacuated out with other horses. To our knowledge, this is the first report of Granulosa theca cell tumors in a mare in Algeria. The only form of treatment is surgical removal of the affected ovary that will eliminate the behavioral changes and allow recrudescence of cyclicity of the remaining ovary.

**Keywords:** *Granulosa theca cell tumor; Histopathology; Ultrasonography; Ovary.*



### 1. Introduction

Granulosa theca cell tumors (GTCTs) are the most frequent ovarian neoplasia of the mare, comprising about 2.5% of all equine neoplasms. They arise from the sex cord-stromal elements of the ovary. The tumors vary in composition and may be primarily composed of granulosa cells, while others may contain substantial amounts of theca cells (Almeida *et al.*, 2011; Sharkey and Wellman, 2011; Sivakumar *et al.*, 2005). It has been reported that most GTCT have both neoplastic elements, which is why they are termed granulosa theca cell tumors; other authors refer to the same class of tumor as a granulosa cell tumor (GCT) (Sellon *et al.*, 2014; Sharkey and Wellman, 2011). The tumors are usually slow growing and the mean age of detection is around 10 years. Maiden, open and pregnant mares may be affected and rarely newborn and young fillies have been reported to have GTCT tumors (Manning and Sleeman, 2012; Masters and Flach, 2015).

Typically one ovary is affected; however, bilateral GTCTs have been reported (Hines *et al.*, 2007; Kennedy and Miller, 1993). The GTCT is the only ovarian tumor associated with a small inactive contralateral ovary. Regular and irregular follicular activity has been reported prior to the detection of a GTCT (Delano *et al.*, 2002; Dungworth, 1985).

Historical facts include reports of failure to cycle, unusual sexual behavior (nymphomania or stallion like), or a change in sexual behavior. Commonly the GTCT results in unilateral ovarian enlargement. Occasionally mares with GTCT are found to have estrous cycles or are pregnant (Sharkey and Wellman, 2011). Excessively large tumors may result in colic or other problems in the mare, and tumors in excess of 50 kg have been reported. Some mares with GTCT tumors that grow slowly or do not progress may have estrous cycles and become pregnant. Mares with tumors have been reported to carry to term (Almeida *et al.*, 2011).

The hormone secretory profile of the tumor dictates the behavior expressed, with mares having elevated plasma testosterone concentrations (>100 pg/ml) exhibiting stallion-like behavior. The ultrasonic appearance of the affected ovary ranges from a homogenous echogenic mass to a multicystic or 'honeycomb' pattern. The contralateral ovary is behavior, presence of a unilaterally enlarged ovary with an inactive contralateral ovary, transrectal palpation, ultrasonography and in some cases, elevated plasma testosterone, and inhibin (McCue *et al.*, 1991).

Surgical removal of the affected ovary is recommended. The tumor may continue to increase slowly in size and may eventually cause colic (Barker and Van Dreumel, 1985; Barker *et al.*, 1993), weight

## 2. Case report

A 10-year-old crossbreed horse mare was presented at the clinic of equine reproduction in the Veterinary Institute of Tiaret-Algeria with a 2-year history of infertility and estrus persistence behavior, characterized as nymphomania.

Physical examination showed no abnormalities, however, transrectal palpation of the left ovary revealed a smooth, slightly lobulated mass of about 10 cm in diameter, located ventrally to the left of the midline while the right ovary was very small and inactive. Transrectal ultrasonography showed a mass composed of multiple, cystic irregularly shaped structures with a honeycomb-like appearance (Fig 1).



**Fig (1):** Ultrasound image of the left ovary showing a GTCT; note the anechoic areas separated by echogenic trabeculae in the form of a honeycomb

At this time, possible differential diagnoses considered were an ovarian teratoma, a granulosa-theca cell tumor (GTCT), dysgerminoma and serous cystadenoma. A tentative diagnosis of GTCT was made based on the history of nymphomania behavior, the findings made by ultrasonography and transrectal palpation. Accordingly, removal of affected ovary by surgery was the treatment of choice.

usually small and inactive, although one mare with a functional contralateral ovary was recently described (Gee *et al.*, 2012). Mares with an inactive contralateral ovary resume normal cyclic ovarian activity 2-16 months after removal of the affected ovary. Clinical diagnosis of a GTCT is based on history,

loss (Maxie, 2007), gastrointestinal obstruction, or other problems. Ovarian tumors can be surgically removed by a colpotomy approach (Maxie, 2007) or through a flank, ventral midline, paramedian, or diagonal paramedian laparotomy approach (Maxie, 2007). In addition, standing flank and ventral abdominal laparoscopic techniques for removal of GTCTs have been described (Edwards and Pojeto, 1997).

## Surgical procedure

Preparation of the mare for surgery was initiated by placement of an 18-gauge intravenous catheter in the right jugular vein. A total of 2 L NaCl 0.9 % solution was administered at a rate of 1 mL/kg of body weight (bw)/h by the end of the surgery. Benzylpenicilline and dihydrostreptomycine (peni&strep; Norbrook, Northern Ireland), 20,000 IU/kg bw, IM, and flunixin meglumine (Lhiflunex; Livisto, zaragoza, la libertad, el Savador, Centromerica), were administered intravenously at 1.1 mg/kg bw. Neuroleptanalgesia was induced by administering acepromazine 0.025-0.05 mg/kg bw, and butorphanol (Torbugesic® vet; Zoetis, USA) at 0.02 mg/kg bw, and IV. Xylazine at 0.5 mg/kg bw. A line block anaesthesia of the left paralumbar fossa was induced with 80 mL 2% lidocaine hydrochloride (Xylocaine 2%) with the horse standing.

Longitudinal skin incision of 20-cm was then made in the left paralumbar fossa and carried through the muscle layers and then the peritoneum, the pedicle of the ovary was supplied by lidocaine 2% then the mass was exteriorized.

In order to facilitate hemostasis, a double transfixation sutures with chromic catgut No. 2 were placed through the ovarian pedicle which was then cut distal to the ligatures and the ovary removed. The pedicle was carefully inspected for hemorrhage, and a 4-layer abdominal wall closure was performed (Fig 2).



**Fig (2):** Section of ovarian tumor mass showing irregular multicystic structures separated by a few areas of solid tissue

Postoperative treatment of the mare was started with trimethoprim/sulfadiazine (Tribrissen; Schering-Plough), 30 mg/kg bw, IM, every 24h for 5 days. Meantime, the mare was closely observed through clinical exam and transrectal ultrasound for evidence of wound dehiscence, internal hemorrhage, or peritonitis for 21 days. The mare was cross-tied in a box-stall to limit exercise and decrease pressure on the incision. Mare has developed a local peritonitis and treated with gentamycin at 6 mg/kg bw, IM, for 5 days. Next, the mare was given gradually more exercise, starting with hand-walking 5 min/d. The aggressive behavior decreased gradually and the mare joined other horses by day 45.

#### Gross pathology and histopathology

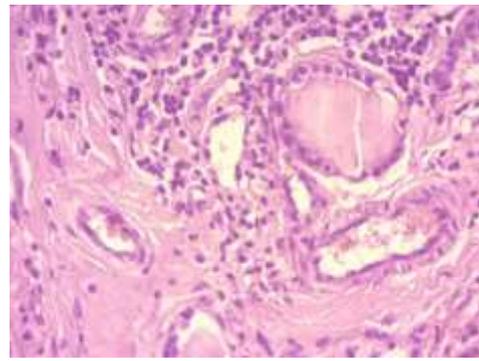
The tumor presented as an irregularly lobulated mass of approximately 12 x 6 cm with a smooth shining surface. Cut surface showed multiple cavities of up to 3 cm in diameter, most filled with clear serous liquid and others with blood. Cavities were separated by pale to yellow, moderately solid tissue (Fig 3).



**Fig (3):** Post-operative appearance. This mare was subjected to surgical removal of the granulosa theca cell tumor (GTCT) affected ovary

The ovarian mass was trimmed and small sections were placed in neutral buffered 10% formalin and sent to Veterinary Pathology Laboratory of Veterinary Institute at the University of Tiaret. Paraffin embedded sections were cut on rotary microtome, mounted on slides, deparaffinized with xylene before being stained with hematoxylin and eosin (H&E) stain according to (Suvarna *et al.*, 2018).

Microscopic examination of tissue sections revealed the presence of highly cellular, multicystic neoplastic proliferations deforming the architecture of the ovary. Irregular aggregates of neoplastic granulosa resembling cells were observed, sometimes organized in multiple layers and forming follicle-like cystic structures separated by thick bundles of fibrous stroma containing numerous blood vessels (Fig 4).



**Fig (4):** Irregular aggregates of neoplastic granulosa resembling cells organized in multiple layers and forming follicle-like cystic structures separated by thick bundles of fibrous stroma containing numerous blood vessels

Neoplastic cells presented a central round nucleus and they show low degree of anisocytosis and anisokaryosis.

### 3. Discussion

Confirmation of the diagnosis prior to ovariectomy can be achieved or at least suggested by hormonal analysis. The two most common hormones analyzed are testosterone and inhibin, although comparisons between the 2 have suggested that inhibin is more accurate. A definitive diagnosis relies on histological examination from either a biopsy specimen or tissues from surgical removal of the affected ovary (Muskens *et al.*, 2001).

Differential diagnoses of GTCTs are associated with either an enlarged ovary or behavioral changes. Behavioral changes are noted in mares on occasion with increased androgens during pregnancy and during the vernal transition into the breeding season, whereby mares are often in estrous for extended periods of time. There are not many conditions that cause true male-like behavior in female horses apart from iatrogenic anabolic steroid administration and intersex conditions such as male pseudohermaphrodites (Muskens *et al.*, 2001).

Although uncommon, mares with GTCTs may continue to have normal activity of the contralateral ovary. The final diagnosis is obtained by histopathologic examination of ovarian tissue (McKinnon *et al.*, 2011)

Ovariectomy is the only form of treatment that will eliminate the various reproductive and behavioral abnormalities in mares with GTCTs, and permit recrudescence of cyclic activity of the contralateral ovary (Muskens *et al.*, 2001; Patrick *et al.*, 2003). The ovarian pedicle can be ligated by a variety of techniques, but it must be done because of the increased blood supply to the ovary. Different stapling instruments have been used to facilitate hemostasis of the ovarian pedicle prior to transection. The use of stapling instruments is reported to decrease surgery time compared with hand suturing techniques (Maurice, 2005).

**Acknowledgments:** The authors would like to thank the surgical clinic staff and pathology laboratory technician for their assistance.

**Conflict of interest:** The authors declare that there is no conflict of interest.

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