



## Diagnosis and surgical removal of a granulosa-theca cell tumor in a mare

Kathy T. Maurice

**Abstract** — An 8-year-old mare showed stallion-like behavior and aggressiveness. A granulosa-theca cell tumor was tentatively diagnosed based on history, transrectal palpation, and ultrasonography, and surgically removed. Serological levels of testosterone and inhibin were elevated. Histopathological examination confirmed the diagnosis. The mare recovered and by day 45 could be turned out with other horses.

**Résumé** — Diagnostic et ablation d'un folliculothécome chez une jument. Une jument de 8 ans a manifesté un comportement et de l'agressivité semblables à ceux d'un étalon. Une tumeur de cellule de la granulosa-theca a été provisoirement diagnostiquée, en se fondant sur les antécédents, une palpation transrectale et une échographie. On a ensuite procédé à l'ablation chirurgicale de la tumeur. Les taux sérologiques de testostérone et d'inhibine étaient élevés. Un examen histologique a confirmé le diagnostic. La jument s'est rétablie et a pu être mise à l'herbe avec d'autres chevaux 45 jours après l'intervention.

(Traduit par Docteur André Blouin)

*Can Vet J 2005;46:644-646*

**A**n 8-year-old quarter horse mare was presented with a 1-month history of gradual changes in behavior, characterized as stallion-like, including aggressiveness towards people and other horses.

No abnormalities were noted on physical examination. However, on palpation per rectum, the right ovary was identified as a smooth, slightly lobulated mass, > 15 cm in diameter, located ventrally to the right of the midline. The left ovary was small and inactive. Transrectal ultrasonographic examination revealed a mass composed of multiple, irregularly shaped cystic areas with a honeycomb appearance. The left ovary was confirmed to be small and inactive. Possible differential diagnoses considered at this time were a granulosa-theca cell tumor (GTCT), ovarian teratoma, dysgerminoma, and serous cystadenoma (1). Based on the history of aggressive, male-like behavior, the findings made by transrectal palpation and ultrasonography, a tentative diagnosis of GTCT was made. Surgical removal of the affected ovary was chosen as the treatment of choice.

Blood was collected for an in-clinic complete blood (cell) count (CBC) (IDEXX QBC VetAutoread

Hematology System; CDMV, St-Hyacinthe, Quebec). The results revealed a severe thrombocytopenia ( $6 \times 10^9/L$ ; reference range,  $90$  to  $350 \times 10^9/L$ ). Because there were no clinical signs, such as petechiation of the mucous membranes to support this abnormality, it was disregarded. Serum was sent to the Animal Health Laboratory (University of Guelph, Guelph, Ontario) for a biochemical profile. The results showed a mild hypercalcemia ( $3.29$  mmol/L; reference range,  $2.75$  to  $3.25$  mmol/L), a severe hyperkalemia ( $7.3$  mmol/L; reference range,  $3.1$  to  $4.3$  mmol/L), mildly decreased total carbon dioxide ( $23$  mmol/L; reference range,  $25$  to  $36$  mmol/L) and urea ( $3.7$  mmol/L; reference range,  $4.2$  to  $8.9$  mmol/L), a mild hypoglycemia ( $3.6$  mmol/L; reference range,  $3.7$  to  $6.7$  mmol/L), moderately decreased total bilirubin ( $10$   $\mu$ mol/L; reference range,  $21$  to  $57$   $\mu$ mol/L) and free bilirubin ( $7$   $\mu$ mol/L; reference range,  $18$  to  $55$   $\mu$ mol/L), and a moderate increase in haptoglobin ( $3.76$  g/L; reference range,  $0.1$  to  $1.7$  g/L). The sodium and potassium ratio was also moderately decreased ( $19$ , reference range,  $31$  to  $44$ ). These biochemical changes are not specific for GTCTs in horses; therefore, they were not investigated further.

The mare was prepared for surgery by placement of an 18-gauge IV catheter in the right jugular vein. Lactated Ringer's solution was administered at a rate of  $2$  mL/kg bodyweight (BW)/h to a total of  $3$  L by the end of the surgery. Procaine penicillin G (Prodain Penicillin G; Dominion, Winnipeg, Manitoba),  $20$  000 IU/kg BW, IM, and flunixin meglumine (Banamine; Schering-Plough, Pointe-Claire, Quebec),  $1.1$  mg/kg BW, IV, were administered. Neuroleptanalgesia was induced by administering detomidine (Dormosedan; Pfizer, Kirkland,

Ontario Veterinary College, University of Guelph, Guelph, Ontario N1G 2W1.

Address all correspondence and reprint requests to Dr. Maurice.

Dr. Maurice's current address is Perth Veterinary Clinic, 118 Sunset Boulevard, RR #4, P.O. Box 631, Perth, Ontario K7H 3K4.

Dr. Maurice will receive 50 free reprints of her article, courtesy of *The Canadian Veterinary Journal*.

**Table 1. Blood hormone levels in an 8-year-old mare pre- and postsurgical removal of a granulosa-theca cell tumor**

Analyte	Result		Reference range for mares and geldings
	Presurgery	Postsurgery	
Testosterone mmol/L	< 1.73	< 1.73	< 0.69
Inhibin ng/ml	3.6	0.22	0.1 to 0.7

Quebec), 0.02 mg/kg BW, and butorphanol (Torbugesic; Wyeth, Guelph, Ontario) at 0.01 mg/kg BW, IV. The area of the right paralumbar fossa was anesthetized with a line block, using 60 mL 2% lidocaine hydrochloride (Lidocaine HCL 2%; Wyeth) with the horse standing.

A 25-cm longitudinal skin incision was made in the right paralumbar fossa and carried through the muscle layers and then the peritoneum. Due to the large size of the mass (> 20 cm diameter), fluid was first aspirated from the cystic structures by using a 16-g needle attached to a 60-mL syringe. A total of 500 mL of fluid was removed, which allowed the mass enough to be exteriorized. Double transfixation sutures with No. 2 chromic catgut suture material were placed through the ovarian pedicle to facilitate hemostasis. The ovarian pedicle was transected distal to the ligatures and the ovary removed. The pedicle was carefully inspected for hemorrhage, and the abdominal wall was closed using a 4-layer closure. Two 1-cm<sup>3</sup> specimens from the affected ovary were placed in neutral buffered 10% formalin and sent to the Animal Health Laboratory, University of Guelph, for microscopic examination, which confirmed the tentative clinical diagnosis of GTCT.

Postoperatively, the mare was treated with trimethoprim/sulfadiazine (Tribrissen; Schering-Plough), 30 mg/kg BW, PO, q24h for 10 d. During this time, she was monitored closely for evidence of wound dehiscence, internal hemorrhage, or peritonitis, while being kept cross-tied in a box-stall for 21 d to restrict exercise and decrease pressure on the incision site. Following this, she was given progressively more exercise, beginning with hand-walking 5 min/d. The aggressive behavior was noted to subside gradually. By day 45, the mare could be turned out with other horses.

Testosterone levels from blood collected at the time of surgery and 3 wk postsurgery were < 1.73 mmol/L on both occasions. Serum was sent to the University of California at Davis for inhibin testing. The presurgical inhibin level was significantly elevated (3.6 ng/mL; reference range, 0.1 to 0.7 ng/mL). The postsurgical level of inhibin was within normal limited (0.22 ng/mL, reference range, 0.1 to 0.7 ng/mL) (Table 1).

Ovarian tumors have been reported to have a frequency as high as 5.6% of all neoplasms in horses. Granulosa-theca cell tumors are the most common and result in increased concentrations of plasma hormones such as testosterone, estrogen, progesterone, and inhibin. These cause a variety of reproductive and behavioral abnormalities, including anestrus, constant or erratic estrus, or stallion-like behaviors, making surgical removal of the affected ovary the treatment of choice.

Serum hormone levels are a useful adjunct for the diagnosis of a GTCT. In this case, the level of inhibin, a dimeric protein secreted by granulosa and theca cells, was significantly elevated and suggestive of a tumor of this cell type (2). Neoplastic granulosa cells express mRNA for inhibin, resulting in an increased secretion of inhibin subunits (1). However, it must be noted that extragonadal expression of these proteins may occur. For example, the adrenal glands secrete free inhibin subunits (1,3). Therefore, inhibin assays must discriminate between biologically active dimeric forms produced by GTCTs and free inhibin subunits produced by extragonadal tissues. Failure to differentiate between these 2 forms of inhibin could result in a false positive diagnosis (2).

Serum testosterone values can also be used to diagnose GTCTs, as the plasma testosterone levels are elevated in approximately 50% of mares with this type of tumor (2). Reference intervals for mares and geldings are < 0.69 nmol/L; for stallions during the nonbreeding season, < 3.5 nmol/L; and for stallions during the breeding season, 3.5 to 14.0 nmol/L. Values > 0.69 nmol/L are considered significant. In this case, both the presurgical and postsurgical blood values were < 1.73 nmol/L, but they could not be interpreted as being significant, since the test used was not sensitive enough to detect levels < 1.73 nmol/L. Serum samples could have been sent to a laboratory where a more sensitive test is used; unfortunately, this was not done. Although the testosterone test used in this case was not sensitive enough to be diagnostically useful, the mare did stop exhibiting stallion-like behavior approximately 3 wk after surgery.

History, clinical signs, findings on transrectal palpation and ultrasonography, and hormonal assays are useful in diagnosing GTCTs. However, testosterone, progesterone, and estrogen are normally produced by ovarian tissue, so the interpretation of their values can be difficult in cases of GTCTs in mares. Additionally, although unusual, mares with GTCTs may continue to have normal ovarian activity on the contralateral ovary. The final diagnosis is obtained by histopathologic examination of ovarian tissue (1).

Due to the various reproductive and behavioral abnormalities in mares with GTCTs, ovariectomy is the treatment of choice (4). Once the ovary is exteriorized, providing local anesthesia to the ovarian pedicle by applying gauze sponges soaked in 2% lidocaine prior to ligation and transection makes this less painful for the mare (5). Reducing the pain and discomfort felt by the mare makes this surgical procedure safer and decreases the chance that the mare will cast herself during the procedure. The temperament of the mare must also be considered. 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, (TA90 Premium, GIA 50 Premium; Proximate F290, Auto Suture Company, Tyco, Australia) can be used to provide hemostasis to the ovarian pedicle prior to it being incised. The use of such stapling instruments is reported to decrease surgery time compared with hand suturing techniques. In addition, the stainless steel staples create less inflammation and are easier to apply (5). However, if such a stapling instrument is not available, it is possible to achieve adequate hemostasis by careful dissection

and double ligation of the ovarian vessels, as was done in this case.

### Acknowledgment

The author thanks Dr. Steve Scott and Mary-Ellen McLellan at the Perth Veterinary Clinic, Perth, Ontario for their surgical and technical skills and advice. CVJ

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