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Case Report

Ovarian Fibrothecoma in a Mare-Case Report

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Simple Summary: The 6-year-old KWPN mare was present to Lithuanian University of Health Sciences, Large Animal Clinic with colic signs. During diagnostic laparotomy an altered right ovary was found and removed. Macroscopically, one part of the ovary was hard and gray. The other parts were smaller, soft, yellowish, with abundant hemorrhages. Ovarian neoplasia was suspected. During microscopical examination tumor showed a mixed histological appearance. The predominant population of cells showed ovoid to round nuclei and pale gray abundant oval, round cytoplasm, indistinct cell membranes impart a syncytial appearance. A diffuse growth pattern was observed. Cell's nucleus showed minimal atypia – large distinct nucleoli, moderate mitotic index (10 mitosis). Mentioned features were consistent with fibrothecoma. The tumor was mixed part of thecoma in the region of their borders or showed a sharp border in places. The fibroma showed very fine storiform pattern which was composed of uniform spindle shaped cells with oval nucleus and minimal atypia. The normal histological structure of ovary was fully destroyed –any primordial, primary, secondary, or tertiary follicles were not found. Usual ovarian stroma also was not detected. Based on histological findings, tumor was consistent with ovarian fibrothecoma.

Abstract: Ovarian tumors in mares are not common in comparison to other neoplasms and are divided into three categories: gonadal stromal tumors, coelomic epithelium surface tumors, and germinative cell tumors [17]. Some ovarian neoplasms histologically show a mixture of multiple cell types in the same tumor, such as fibrothecoma, therefore the differentiation between fibroma and thecoma is often difficult [1]. According to World Health Organization, fibrothecoma is classified as sex cords stromal tumor (pure stromal tumor) [18]. Neoplasms, such as fibrothecoma have a very scarce morphology, clinical signs, ultrasonographic view and endocrine profile. To diagnose this type of tumor, a broad clinical examination is needed, but histopathology remains the most accurate. Herein, we report a case of incidentally found ovarian fibrothecoma during diagnostic laparotomy in 6-year-old KWPN mare which was presented to the clinic with colic symptoms. After unilateral ovariectomy, the altered right ovary, based on histopathological features was diagnosed as fibrothecoma.

Keywords: thecoma; ovarian tumor; neoplasia; histopathology

1. Introduction

Fibrothecoma is the rarest ovarian tumor type for equids which is seldomly reported in mares. There is scarce information about equine fibrothecoma in veterinary literature. In human medicine, fibrothecomas represent only 1%-4.7% of ovarian tumors [18]. Clinical signs of ovarian neoplasms can be nonspecific [29]. In human medicine these tumors are asymptomatic, usually detected during routine gynecologic examination [4]. Fibrothecoma is a benign neoplasm that can be hormonally active and can secrete estrogen and androgens. Estrogen production can cause infertility by inducing defects in ovulation or implantation [18]. However, hormone assays can show a normal concentration of testosterone and progesterone [27]. According to the literature apart from behavior and estrous changes, fibrothecoma may occur as infertility, weight loss, or colic. There is no information about its

malignancy in the veterinary literature [3]. This study aims to report a case of ovarian fibrothecoma in a mare.

2. Case History

In December 2023, a 6-year-old KWPN mare was presented with colic symptoms (apathy, depression, refusing to eat and drink, no passing of manure) to the Lithuanian University of Health Sciences Large Animal Clinic. According to anamnesis, mare had colic a month ago, which was solved only conservatively. Mare presented a low body score (2 out of 5). On physical examination, all parameters were within normal ranges, except weakened peristalsis in small colon. No significant changes were observed during abdominal ultrasound. Hematological examination revealed lymphopenia ($1.48 \cdot 10^9 /l$), leukopenia ($4.45 \cdot 10^9 /l$), hypochromia (MCHC 296 g/l), thrombocytopenia ($99 \cdot 10^9 /l$). Serum biochemistry was within the physiological limits. Blood lactates were 1.8 mmol/l (LACTATE PRO 2, Arkray Inc, Japan), glucose 4.9 mmol/l (eBGK-VET, VISGENEER INC., Taiwan), PCV 37%. Per-rectal palpation revealed formed, very hard and dry feces in ampulla and small colon, also edge of the spleen was slightly displaced medially from abdominal wall. The rectal palpation of the uterus and ovaries did not find any significant changes also mare did not show any discomfort during rectal palpation of reproductive system. Five liters of water and electrolytes were applied through a nasogastric tube to the stomach. Intravenous fluid therapy [Ringer lactate, B.Braun, Germany] and metamizole natrium salt [Biowet Drwalew, Poland 30 mg/kg bw i.v.] were applied.

On consecutive days intravenous fluid and pain relief therapy also fluids through the nasogastric tube were applied because mare refused to drink. Blood lactates decreased respectively 1.3 mmol/l; 1.1 mmol/l; 0.9 mmol/l, however clinical condition did not change significantly. Motility of small colon and small intestines decreased, nevertheless, the mare started to be fed a small amount of hay. After few days mare started to show acute colic symptoms (restlessness, pawing the ground, no passing of manure, apathy). Elevated heart rate (55 beats per minute) was observed. Ultrasonographically, 1cm of anechoic free fluid within the peritoneal cavity was detected; slightly dilated duodenum, decreased motility small colon loops were observed at lower flank bilaterally.

Abdominocentesis was performed. Peritoneal tap was opaque, dark yellow (Figure 1). Peritoneal tap glucose was 11.3 mmol/l (eBGK-VET, VISGENEER INC., Taiwan), lactates 1.6 mmol/l (LACTATE PRO 2, Arkray Inc, Japan), total proteins 4g/dl. Based on exacerbated clinical symptoms, appeared free fluid within peritoneal cavity and abdominocentesis results (increased glucose, lactates and total protein levels and changes in peritoneal tap color and turbidity), it was decided to perform a diagnostic laparotomy.



Figure 1. Dark yellow and opaque peritoneal tap.

The mare was premedicated with xylazine 20mg/ml [Biowet Drwalew, Poland 1.1mg/kg bw i.v.] positioned in dorsal recumbency after induction with ketamine 10% [VetViva Richter GmbH, Austria, 2.2 mg kg/bw], midazolam [Kalceks, Slovakia, 0.05mg kg/bw] and was maintained with sevoflurane [Chanelle Pharmaceuticals Manufacturing Ltd., Ireland] delivered in 100% oxygen. The surface of abdomen was prepared aseptically, and ventral midline celiotomy was made. An incision

of approximately 30 cm was performed. During routine exploratory laparotomy, no intestinal dislocation was present. Enlargement of spleen was observed. During diagnostic laparotomy an altered right ovary was found incidentally, and neoplasia was suspected. The left contralateral ovary had a normal appearance and size.

After right ovary exposure, transfixion ligations of the ovarian pedicle were made with PGA USP 3&4 [SMI, Belgium] then the ovarian pedicle was sectioned, and ovary was removed from peritoneal cavity. Finally, a routine 3-layer closure of the abdominal wall was performed.

During surgery the specimens of ovary masses were obtained. Tissue samples were fixed with 10% formalin solution and proceeded to the Pathology Center of Veterinary Academy of Lithuanian University of Health Sciences.

After surgery, the mare was treated with benzylpenicillin [Sandoz, Austria, 33,000 U.I. kg/ bw i.v BID] and gentamicin [Dopharma, Netherlands, 6.6mg kg/ bw i.v SID] for five days. Flunixin meglumine [Vet-agro, Poland 1.1 mg kg/ bw i.v] was used for postoperative pain management. Due to lack of peristalsis postoperatively neostigmine [Cenavisa S.L., Spain, 0.0044 mg kg/bw] was applied. Fluids were applied throughout nasogastric tube 3-4 times a day for the first two days, due to refusing to drink postoperatively.

Topical treatment of the incision was done daily using povidone-iodine [Valentis, Lithuania]. No complications were observed, sutures were removed within 14 days.

After surgery mare's reproductive system was investigated ultrasonographically, slight ovarian oedema and air in the uterus was observed. Left ovary was normal in size and echogenicity, present with some 10mm to 28 mm follicles. Due to poor perineal conformation mare has pneumovagina. Caslic's vulvoplasty was performed.

3. Diagnosis

On gross examination, removed ovary was approximately $10 \times 4 \times 5 \text{ cm}^3$ in diameter. Macroscopically, right ovary was enlarged as compared to contralateral ovary. The macroscopic image of the tumor already allowed to suspect a double histological image. A major part of tumor was hard, gray (Figure 2). The other parts of tumor were smaller, soft, yellowish, with abundant hemorrhages (Figure 3).

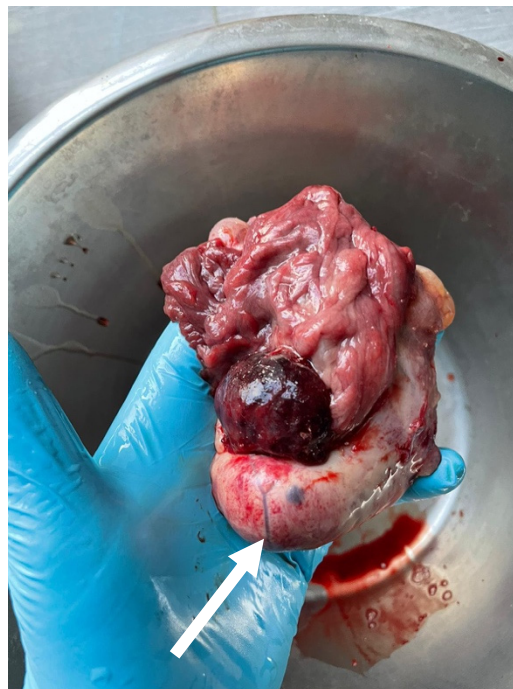


Figure 2. Macro view of mare's right ovary. Arrow shows very hard, gray ovarian edge.

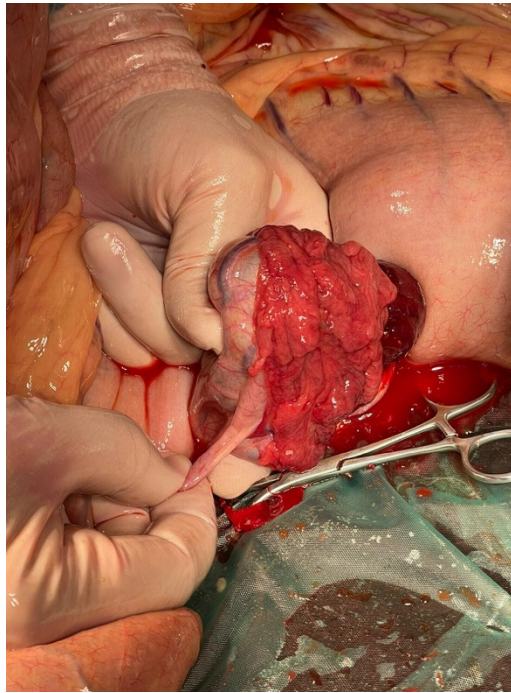


Figure 3. Macro view of mare's right ovary during diagnostic laparotomy.

Histological examination was performed. Paraffin blocks were made using „Shandon Pathcentre“ (UK) and „TES99 Medite Mediz-intechnik“ (Germany) equipment. Four micrometer sections were obtained using Shandon Pathcentre (UK) microtome. Serial 4- μ m sections were prepared with a “Sakura Accu-Cut SRM” microtome.

Sections were stained with routine hematoxylin-eosin (HE) technique using Sakura Accu-Cut SRM (Japan) equipment.

Histological slides were evaluated using the Olympus microscope supplied with a digital Olympus DP72 image camera with CellSensDimension software.

During microscopical examination, the predominant population of cells showing ovoid to round nuclei and pale gray abundant oval, round cytoplasm, was found (Figure 4). Indistinct cell membranes impart a syncytial appearance. Diffuse growth pattern was observed. Cells nucleus shows minimal atypia – large distinct nucleoli, moderate mitotic index (10 mitosis HPFX400) at thecoma part. The fibroma part was mixed part of thecoma in region of their borders or showed a sharp border in places. The fibroma shows very fine storiform pattern. The fibroma tissues were composed from uniform spindle shaped cells with oval nucleus with minimal atypia. The normal histological structure of ovary was fully destroyed – the any primordial, primary, secondary, or tertiary follicles were not found. Ovary usual stroma also was not detected.

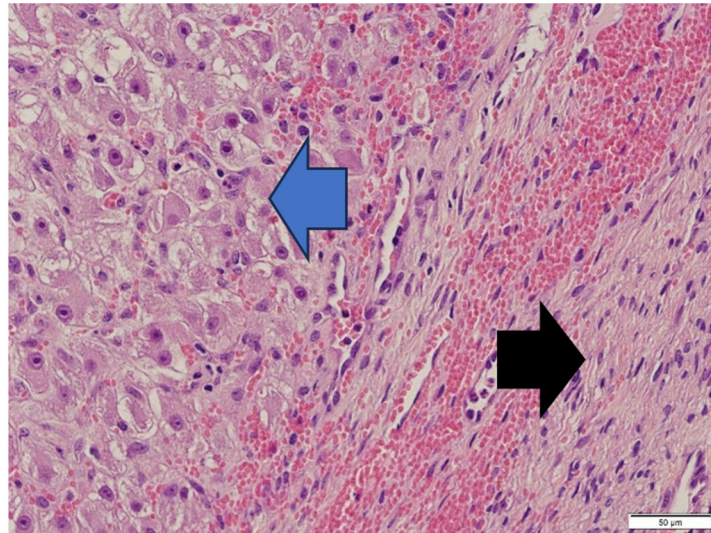


Figure 4. The part of thecoma: population of cells showing ovoid to round nuclei and pale gray abundant oval, round cytoplasm. The distinct large nucleolus inside nucleus is present (blue arrow). HE, medium magnification. Black arrow – part of fibroma.

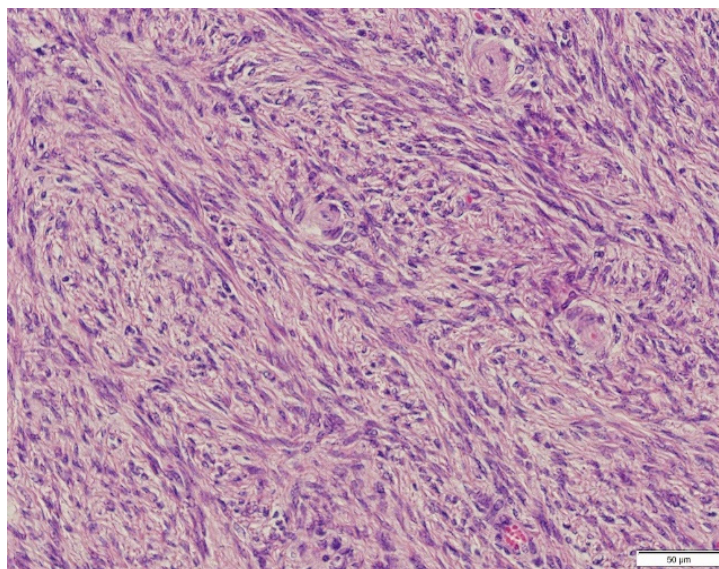


Figure 5. The part of fibroma. Uniform spindle shaped cells with oval nucleus with minimal atypia, storiform histological pattern. HE, medium magnification.

4. Discussion

Macroscopically fibrothecoma is variably sized, thick, solid and firm consistency, often whitish or yellowish [16]. Surface varies from regular [9] to irregular [1]. Areas of hemorrhage and necrosis also evident [27]. Cysts filled brownish [9] or green gelatinous secretions [2] also observed. Hemorrhagic areas were observed both inside [27] and outside of neoplasia.

Histologically, fibrothecoma consists of oval or spindle shaped cells and intersecting fascicles [10]. Lipid vacuoles, presence of hemosiderin can also occur [2]. Vesicular nuclei vary from ovoid to fusiform in shape, slightly eosinophilic and foamy, vacuolated cytoplasm [4], with poorly defined borders. Mitotic figures were not evident [29], in other case- mitotic amount was less than 2 cells per 10 HPF [16]. Well-circumscribed and variably sized vascular spaces filled with erythrocytes are also characteristic [10].

However, both macroscopic and microscopic view of fibrothecoma is very variable. Some ovarian neoplasms histopathologically show a mixture of multiple cell types in the same tumor [2].

Sometimes impossible to differentiate between thecoma and fibroma so term “fibrothecoma” can be used to describe neoplasms with altered theca cells and fibroma characteristics. Both macroscopic and microscopic view corroborates with this case report.

To diagnose fibrothecoma more specific tests are required: tomography, histopathology, immunohistochemistry and hormonal level testing [29]. Due to relatively nonspecific features, definitive diagnosis is mostly based on histological findings. At present case due to incidental finding during exploratory laparoscopy also convenience and financial limitations, it was decided to perform only histopathological examination.

Sonographic characteristics can also provide useful information in diagnosing ovarian neoplasms. In Raoofi A. et al. 2006 report, fibrothecoma ultrasonographically has a thick 2 to 4 cm wall; the inner surface had a villous-like appearance. Stroma of the mass was mottled, with an accumulation of speckled and hypoechoic to slightly hyperechoic fluid. Fibrothecoma is sonographically characterized as an echogenic mass without posterior acoustic shadowing but a homogenous echogenic pattern with marked posterior acoustic absorption [5]. Fibrothecoma is also described as smooth and thick ovarian stroma which interior is filled with anechoic fluid. In this case, ultrasonographic examination of reproductive system before laparotomy was not performed. Mare did not have history of estrous disorders and did not show discomfort during rectal palpation, so ultrasonographic examination was not indicated at this case.

The clinical signs of ovarian tumors are relatively nonspecific. In humans fibrothecoma causes pelvic pain and metrorrhagia [2]. In horses, apart from reproductive behavior changes, masculinization, persistent anestrus [22], anovulatory follicle persistence during breeding season, [18] clinically fibrothecoma often appeared asymptomatic. It can also occur as progressive weight loss [20], anorexia and pyrexia [29]. It is reported cases, that ovarian neoplasms in mare may cause colic [26,33]. In this present case, we hypothesized, that ovarian neoplasm fibrothecoma in the right ovary may be one of the reasons for low body score and possibly cause colic symptoms for this mare.

Fibrothecomas may or may not interfere with steroid production and levels [20]. It might be endocrinologically functional and produce testosterone and inhibins. Fibrothecoma might produce estrogen and can cause infertility by inducing defects in ovulation or implantation [23,32]. Serum progesterone, estradiol, testosterone, Anti-Müllerian hormone assays can be a useful adjunct for detecting hormone producing ovarian neoplasms, however, some authors have reported hormone levels within physiological limits [27]. Fibrothecoma was an incidental finding also mare did not show any obvious changes in behaviour such as masculinization or changes in estrous cycle, so no hormonal assays were performed in this case.

Hormone producing neoplasms in mares can influence reproductive behavior that may range from estrogenic activity to masculinization [10]. The most common signs of hormonally productive sex-cord tumors are stallion-like behavior and infertility [7]. In this case, owners observed only excessive vocalization to other horses. Also, mare showed no masculine physical changes such as large clitoris or a heavily crested neck [21]. Otherwise, no other stallion-like behavior was observed, as owners did not use mare for reproductive purposes.

In animals, ovarian neoplasms are more prominent in elderly than in young horses [2,20]. However, there are reported cases, when thecoma and fibrothecoma occurred for young, 4-5 years-old mares [4,29]. In this clinical case, fibrothecoma was diagnosed for young, 6 years-old mare.

Metastasis in sex chord neoplasms is relatively common and is reported in bitches, queens and cattle [14,35]. Fibrothecomas with malignancy are rare [9]. Thus, metastases can occur in regional lymph nodes via bloodstream and can implant in the peritoneal cavity [14]. Even though, in extensive cases like Raoofi A. et al. 2006, no signs of metastasis were detected. At present case, no metastatic signs were detected macroscopically either.

In mares, information about reproductive life post fibrothecoma removal is lacking. The prognosis of ovariectomy is considerably successful with the mare regaining reproductive health a few months post unilateral ovariectomy [11]. Some mares may become infertile, with a small, inactive contralateral ovary [20]. Although, there are reported case that mare post unilateral ovariectomy due to fibrothecoma came to estrous cycle again and was successfully inseminated with positive embryo

transfer [18]. As far as authors are aware mare had one foal earlier. At present case, further investigation of reproductive system is needed in order to evaluate mare's fertility after unilateral ovariectomy.

Deciding surgical treatment need during colic can be more difficult in early cases with low-grade signs of colic, absence of reflux, and lack of abdominal abnormalities detected on transrectal palpation [31]. Laboratory testing is crucially important for evaluating colic severity, survival rate and prognostic information for surgery. It is reported, that mean blood lactate concentration in survivors were reported as 1.92 mmol/l and 2.0 mmol/l, compared to 4.26 mmol/l and 6.1 and 4.8 mmol/l in nonsurvivors [6,8,15,24,25]. At present case blood lactates level was within limits and decreased during conservative treatment. However, rapid blood lactates increase is more significant with small intestine lesions, especially strangulation and takes much more time to rise if there is any other pathologies within peritoneal cavity. Blood glucose is also an important prognostic indicator for horses with colics [12]. It is confirmed, that hyperglycemia is common in horses with colic and is associated with a worse surviving prognosis. For horses with acute gastrointestinal disease, hyperglycemia was a common finding with 45% of the population [12]. At present case blood glucose was within the normal range. Packed cell volume (PCV) and heart rate are correlating indicators for equine colic. The severity, site, and length of the strangulation/infarction, during colic may influence PCV elevation [19]. At present case PCV was within normal range.

Abdominocentesis are one of the most important diagnostic procedures for clinical colic assessment. Normal peritoneal fluid should be clear, transparent, light yellow and odorless. Changes in peritoneal tap color, turbidity, total proteins (TP), lactate and glucose levels can be valuable predictive measure not only for inflammation within peritoneal cavity but also characterization of pathology [28]. Significant changes in color, turbidity can signalize intraperitoneal bleeding due to organ rupture, strangulating or on strangulating obstruction, colitis and peritonitis. Additional testing of abdominal fluid may be helpful for detecting sepsis when cytology and culture are unavailable or inconclusive [13]. Normal to slight increases in total proteins (TP < 3.0 g/dL) are common with non-strangulating obstruction. However, as the duration and degree of injury increases, progressive elevations in TP are noted. At present case changes in peritoneal tap signaled inflammation within peritoneal cavity.

At present case, slight lymphopenia and leukopenia was detected. Usually, lymphopenia and leukopenia is caused by corticosteroid use, viral infections, neoplasia [34]. Article authors hypothesize, that slight lymphopenia and leukopenia can be caused by chronic inflammation at this case. Thrombocytopenia usually occur secondary to severe trauma or hemorrhage, neoplasia, viral or bacterial infection, endotoxemia. It is important to note, that pseudothrombocytopenia can be caused by poor venipuncture technique and delays in processing, so thrombocytopenia as single indicator should be evaluated with caution [30]. Hypochromia for horses is usually associated with iron deficiency and anemia [34]. We hypothesize, that slight hypochromia is not significant at this case, because no changes in red blood cells, iron, PCV, hemoglobine values were observed.

5. Conclusion

In this study diagnosis of fibrothecoma was based on histopathologic observations. Sex cord-stromal tumors such as fibrothecomas have seldom been reported in mares [2], so further investigations are needed in order to expand knowledge in recognition, diagnosing and prognosing reproductive potential post unilateral ovariectomy.

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authorized the use of their data and the excess specimens for research purposes, formal approval from the University's Ethical Committee was not required.

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