



An Update in Histopathology and Immunohistochemistry of Ovarian Sex Cord-Stromal Camel Tumors

IBRAHIM ELMAGHRABY*, ABDEL-BASET I. EL-MASHAD, SHAWKY A. MOUSTAFA, AZIZA A. AMIN

Department of Pathology, Faculty of Veterinary Medicine, Benha University, Toukh 13736, Egypt.

Abstract | Background: Sex cord-stromal tumors of the ovary are a rare and heterogeneous group of benign and malignant neoplasms with a wide range of histological characteristics. The current study investigated ovarian sex cord-stromal tumors in dromedary camels slaughtered at Egyptian slaughterhouses between January 2019 and February 2022. The study included 180 female single-humped camels in which all data on the animal's age, location, and gross tumor lesions were documented, and positive ovaries were collected for further histological and immunohistochemical examination. **Results:** Interestingly, our results diagnosed 15 cases of sex cord-stromal tumors (8.30 %) in the ovary of dromedary camels included; adult granulosa cell tumor (0.55 %), interstitial cell tumor (0.55 %), thecoma or fibrothecoma (1.10 %), steroid cell tumor-NOS (0.55 %), and granulosa-theca cell tumor (5.55 %). Specifically, all cases had distinctive histomorphological appearance characteristics for benign tumors, except adult granulosa cell tumor, which had sarcomatous changes and other features reliable for malignancy. Importantly, granulosa-theca cell tumor exhibited a wide spectrum of histologic patterns as micro/macrofollicular, trabecular, diffuse sheets and Call-Exner bodies; or uncommon patterns as solid follicular, luteinized, insular, tubule-like, and Sertoli-like. Immunohistochemically, the results indicated that vimentin was markedly expressed in the majority of sex cord-stromal tumors (SCSTs), and melan A was typically positive in the steroid-secreting tumors; while inhibin was less sensitive than vimentin for recognizing SCSTs. **Conclusions:** Diagnosis of sex cord-stromal tumors in camels often present a challenge familiarity with characteristics of the different histopathologic pattern where, in the current study, the granulosa-theca cell tumor was the most frequently diagnosed tumor. Additionally, the use of vimentin and melan A are reliable markers in the differential diagnosis of sex cord-stromal tumors in the ovary of dromedary camels.

Keywords | *Camelus dromedarius*, Histopathology, Immunohistochemistry, Ovarian tumor, Egypt

Received | March 28, 2023; Accepted | April 25, 2023; Published | May 25, 2023

*Correspondence | Ibrahim Elmaghraby, Department of Pathology, Faculty of Veterinary Medicine, Benha University, Toukh 13736, Egypt; Email: elmaghraby@fvvm.bu.edu.eg

Citation | Elmaghraby I, El-Mashad ABI, Moustafa SA, Amin AA (2023). An update in histopathology and immunohistochemistry of ovarian sex cord-stromal camel tumors. *Adv. Anim. Vet. Sci.* 11(7): 1097-1104.

DOI | <https://doi.org/10.17582/journal.aavs/2023/11.7.1097.1104>

ISSN (Online) | 2307-8316



Copyright: 2023 by the authors. Licensee ResearchersLinks Ltd, England, UK.

This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

INTRODUCTION

Primary ovarian neoplasms are broadly classified into epithelial tumors, germ cell tumors, and sex cord-stromal tumors. Mesenchymal Tumors derived from nongonadal supporting tissues of the ovary are uncommon in domestic animals, and not as important as the primary tumors. Specifically, sex cord-stromal tumors are diverse groups of benign and malignant neoplasms that arise from

the follicular granulosa and theca cells or their luteinized derivatives, including granulosa cell tumor, granulosa-theca cell tumor, luteoma, thecoma, Sertoli cell tumor, and interstitial gland tumor (Agnew and MacLachlan, 2017). The term sex cord-stromal refers to the looseness of the embryological and histogenetic origins of neoplastic cells in these tumors. Surprisingly, this group produces steroid hormones and exhibits a diverse range of behavioral characteristics (Schlafer and Foster, 2016). Granulosa cell tu-

mors (GCT) are tumors that develop from granulosa cells. They are the most prevalent type of tumor in this category. They account for more than 70% of sex cord-stromal tumors in humans. Adult and juvenile GCT have unique histological characteristics. Juvenile tumors are uncommon and arise at a young age, but adult granulosa cell tumors are more common, peaking in old age (Kottarathil et al., 2013). Generally, in animals, they are unilateral, usually nonmalignant tumors, and more common in the bitch, cow, and mare (Agnew and MacLachlan, 2017).

Sex cord-stromal tumors in dromedary camels are extremely rare. Only one case of granulosa cell tumor in a 14-year-old female dromedary camel has been documented (Ali et al., 2013), but not reported, in a subsequently published retrospective research on 210 adult she-camels with ovarian lesions in the Kingdom of Saudi Arabia (Al-Afalet al., 2021). However, the prevalence of ovarian tumors in dromedary camels in Egypt was revealed to be 6.8% (34/500); of the recorded cases, sex cord-stromal tumors were found in 14 camels (Elshazly et al., 2019). Whilst sex cord-stromal tumors in camels are rare, most pathologists have limited experience with their characteristic morphological appearance, as they are uncommon in the routine diagnostic setting. Additionally, some neoplasms can exhibit unusual or overlapping characteristics. Therefore, it is difficult to diagnose them by standard histological examination, especially those of similar histological origins that closely mimic each other. In these instances, the use of immunohistochemistry might be useful in confirming the diagnosis (Kriplani and Patel, 2013). However, no immunohistochemical marker shows high specificity or absolute sensitivity to sex cord-stromal tumors and most have limited utility in discriminating between different tumors (Lim and Oliva, 2018).

MATERIALS AND METHODS

SAMPLES COLLECTION

The study investigated ovarian tumors in 180 female single-humped camels slaughtered at Egyptian abattoirs (Toukh, Kerdasa, Warraq, and El-basateen) between January 2019 and February 2022. All information on the animal's age, location, and gross tumor lesions, such as colour, size, surface, and cut section for the presence of abnormal nodules or structures, was documented, and positive ovaries were collected for further histological analysis. During the necropsy of the animal with positive ovarian tumors, a thorough search is undertaken for primary or metastatic foci elsewhere.

HISTOPATHOLOGY AND IMMUNOHISTOCHEMISTRY EXAMINATION

After careful gross examination, specimens from the ova-

ries were fixed in 10% neutral buffered formalin, routinely processed, blocked in paraffin wax. On gelatin-coated slides, 4 µm sections were mounted, and stained with hematoxylin and eosin (HE) stain for histopathological studies (Bancroft et al., 2013).

Immunohistochemistry was performed to validate the histopathological description of specific tumor types. According to the Ramos-Vara and Beissenherz (2000) procedure, paraffin-embedded sections were subjected to immunohistochemical staining using the avidin-biotin-peroxidase complex method. The slides were incubated with primary antibodies that are summarized in Table 1. DAB (3,3-diaminobenzidine tetrahydrochloride; Sigma, St. Louis, MO) was used as a chromogen, and hematoxylin as a counter stain.

RESULTS

Based on histopathological and IHC examination, our results diagnosed 15 Sex cord-stromal tumors out of 180 dromedary she-camels (8.30 %) in the ovary including; one case each of adult granulosa cell tumor (0.55%), interstitial cell tumor (0.55%), and steroid cell tumor-NOS (0.55%), 2 cases of thecoma or fibrothecoma (1.10%) and 10 cases of Granulosa-theca cell tumor (5.55%) (Table 2).

ADULT GRANULOSA CELL TUMOR (PURE SEX CORD TUMORS)

Grossly, the left ovary was enlarged and had a firm grayish-white nodule attached to the ovary by a long stalk, with scattered small hemorrhagic areas in the cut section (Fig. 1A). Microscopically, densely cellular neoplasm with polygonal cells organized in solid sheets, supported by fine fibrovascular stroma (Fig. 1B), and surrounded by moderately thick fibrous capsule was present. Neoplastic cells had indistinct cell boundaries, scant eosinophilic cytoplasm, and round to ovoid uniform nucleus with pale chromatin and coffee-bean-like nuclear groove. Occasionally, Call-Exner bodies interspersed the neoplastic cells. Multifocally, there were areas of sarcomatous change characterized by pleomorphic round and spindle-shaped cells, with abundant eosinophilic cytoplasm and irregular, hyperchromatic, bizarre nuclei showing variable mitosis (Fig. 1C). Neoplastic cells showed cytoplasmic vimentin positivity via immunohistochemistry (Fig. 1D). The tumor mass exhibited varisized areas of hemorrhage, and low numbers of scattered inflammatory cells; whereas the capsule was markedly invaded by moderate numbers of neoplastic granulosa cells. Additionally, the normal ovarian tissue architecture was diffusely effaced by the neoplastic cells.

Table 1: Immunohistochemical antibody panel applied to ovarian tumors in dromedary camels.

Antibody	Type (Catalogue number)	Source	Dilution	Antigen retrieval
Vimentin (V9)	Mouse monoclonal antibody (M0725)	EnVision DAB system, Dako, Carpinteria, CA	1:200	Antigen retrieval was done in the pre-treatment (PT) module, PT Link (Dako, Denmark). Briefly, tissue sections were subjected to 95 °C for 40 min. in Epitope Retrieval Solution (Dako) in accordance with manufacturer's instruction for Hercep Test (Dako).
Inhibin alpha (R1)	Mouse monoclonal antibody (IR05861-2)	DAKO, Glostrup, Denmark	1:100	
Melan A (A103)	Mouse monoclonal antibody (M719629-2)	DAKO, Glostrup, Denmark	1:200	

Table 2: Sex cord-stromal tumors in the ovary of dromedary camels.

Pathological affection	Age (years)	Number of cases	Prevalence from the examined cases
Adult Granulosa cell tumor	7	1	0.55%
Interstitial cell tumor	12	1	0.55%
Thecoma or Fibrothecoma	5,11	2	1.10%
Steroid cell tumor, NOS	8	1	0.55%
Granulosa-theca cell tumor	5-11	10	5.55%
Total		15	8.30 %

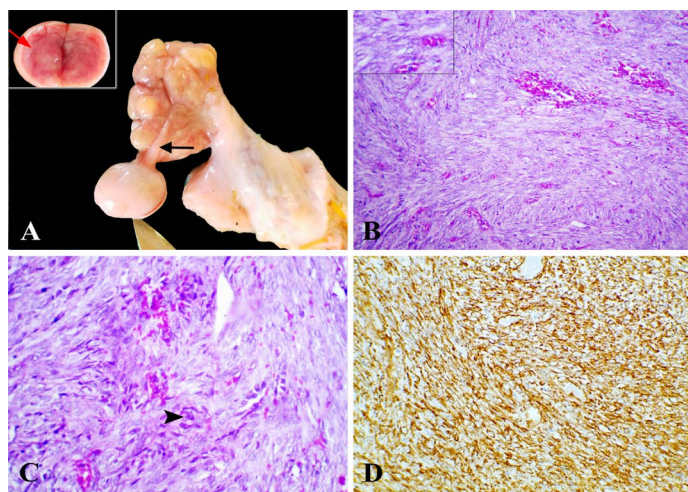


Figure 1: Adult Granulosa cell tumor, ovary, camel. (A) Firm grayish white nodule attached to the ovary by a long stalk (black arrow), Inset, hemorrhagic cut section. (B) Neoplastic cells arranged in solid sheets, supported by fine fibrovascular stroma, HE x 200. Inset, round to ovoid uniform nuclei with pale chromatin and coffee-bean-like nuclear groove, HE x 400. (C) Sarcomatous change characterized by pleomorphic cells with irregular, hyperchromatic, bizarre nuclei (arrowhead) showing variable mitosis, HE x 400. (D) Neoplastic cells expressed cytoplasmic positive reaction for vimentin, x 200.

INTERSTITIAL (LEYDIG) CELL TUMOR (PURE STROMAL TUMORS)

Grossly, the left ovary was enlarged and had a firm grayish-white nodule attached to the mesovarium (Fig. 2A). Microscopically, well-circumscribed, encapsulated, multilobulated moderately cellular neoplasm (Fig. 2B) com

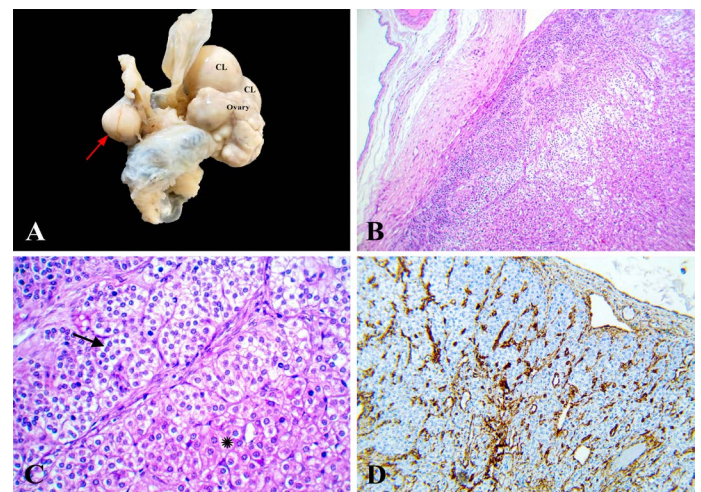


Figure 2: Interstitial cell tumor, ovary, camel. (A) Firm grayish white nodule (arrow) attached to mesovarium, CL; corpus luteum. (B) Encapsulated moderately cellular neoplasm, HE x 100. (C) Neoplastic cells arranged in solid sheets, cords (asterisk), and indistinct nests or acini (arrow) separated by fine fibrovascular stroma, HE x 400. (D) Neoplastic cells expressed cytoplasmic positive reaction for vimentin, x 200.

pressing the adjacent mesovarian structure was present. Neoplastic mass was made up of round to polygonal cells; that resemble normal interstitial cells, organized in solid sheets, cords, indistinct nests or acini separated by fine to moderate bands of fibrovascular stroma (Fig. 2C). Neoplastic cells showed clear cell boundaries, moderate to abundant eosinophilic vacuolated to finely granular cytoplasm, and spherical uniform nuclei with rare mitotic figures and indistinct nucleoli. Vimentin antibodies were

detected in the cytoplasm of the neoplastic cells using immunohistochemistry (Fig. 2D).

THECOMA AND FIBROTHERCOMA

Grossly, the left ovary was markedly enlarged and had small firm grayish-white nodules (Fig. 3A). Microscopically, there was an unencapsulated, well-demarcated, densely cellular neoplasm diffusely effacing normal ovarian tissue architecture in the cortex. The tumor is consisting of clusters of streaming oval and spindle cells with unclear cell boundaries and a round to oval nucleus (theca cells), supported by a fibrovascular stroma and often arranged in a diffuse pattern (Fig. 3B) or multiple variably sized nodular structures. Multifocally, the neoplastic cells had characteristic pale vacuolated cytoplasm (Fig. 3C). Occasionally, there was fibrothecoma characterized by mixtures of phenotypes with fibroma and thecoma (Fig. 3D).

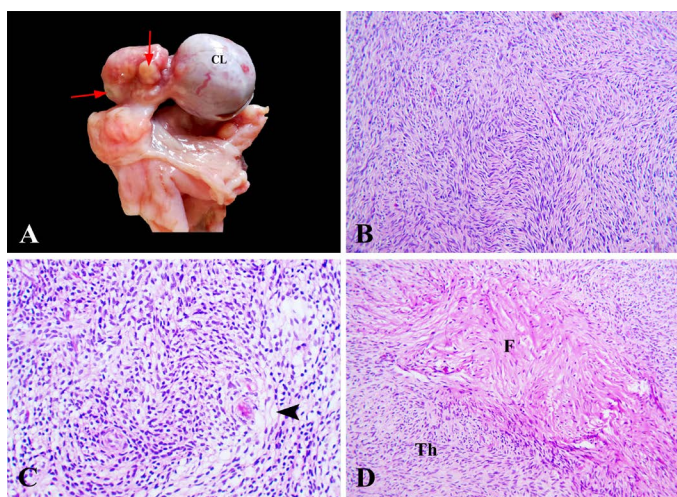


Figure 3: Thecoma, ovary, camel. (A) Small firm grayish white nodules (arrow), CL; corpus luteum. (B) Aggregates of streaming oval and spindle cells arranged in a diffuse pattern, HE x 200. (C) Neoplastic cells had pale vacuolated cytoplasm (arrowhead), HE x 400. (D) Fibrothecoma characterized by mixtures of fibroma (F) and thecoma (Th), HE x 200.

STEROID CELL TUMOR, NOS (NOT OTHERWISE SPECIFIED)

The affected left ovary was grossly enlarged and had firm grayish-white to yellow nodules embedded in the ovarian tissue (Fig. 4A). The cut section was yellow and solid. Microscopically, multiple unencapsulated and well-defined moderately cellular neoplastic foci effaced the normal architecture of the ovarian cortex. The round to polygonal neoplastic cells made arrangements in nests, sheets, or cords that were supported by a moderate fibrovascular stroma. Neoplastic cells showed varying defined cell boundaries and marked amounts of foamy (lipid-rich cells) or clear cytoplasm (Fig. 4B) to occasionally eosinophilic or pigmented with yellowish brown taint (Fig. 4C). Nuclei were

round to oval with finely granular chromatin. There was a thick layer of streaming spindle theca cells surrounding tumor cells. The neoplastic cells immunohistochemically displayed cytoplasmic positive reactivity for vimentin and melan A, while they showed a negative reaction for inhibin (Fig. 4D).

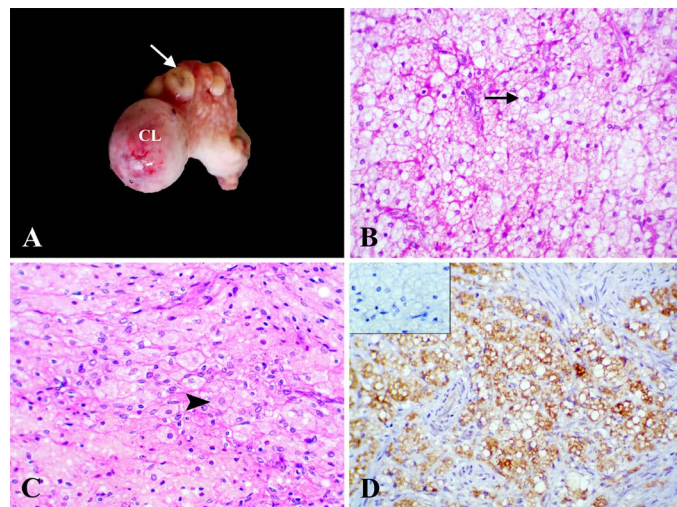


Figure 4: Steroid cell tumor, NOS, ovary, camel. (A) Firm grayish white to yellow nodules (arrow) CL; corpus luteum. (B) Neoplastic cells had marked amounts of foamy or clear cytoplasm (arrow), HE x 400. (C) Neoplastic cells had eosinophilic or yellowish-pigmented cytoplasm (arrowhead), HE x 400. (D) Neoplastic cells expressed cytoplasmic positive reaction for melan A, x 400. Inset, negative reaction for inhibin, x 400.

GRANULOSE-THECA CELL TUMOR (MIXED SEX CORD STROMAL TUMORS)

Grossly, the ovary was enlarged and had variable sizes firm grayish-white nodules, and numerous yellow cysts (Fig. 5A). Microscopically, a highly cellular, well-defined, unencapsulated tumor that was expanding and effacing the ovarian tissue architecture and extending to the submitted margins was visible. The neoplastic cells of these tumors resemble their counterparts, granulosa, and theca cells in normal follicles. Neoplastic granulosa cells had unclear cell boundaries, faint eosinophilic or vacuolated cytoplasm, and round to ovoid uniform nuclei with pale chromatin and coffee-bean-like nuclear groove. Granulosa cells were often surrounded by a variable population of streaming spindle theca cells, with unclear cell borders, scant fibrillar eosinophilic cytoplasm, and a round to oval nucleus with finely granular chromatin and indistinct nucleoli. Populations of granulosa and theca cells coexisted in a single neoplasm and exhibited a wide spectrum of histologic patterns. Numerous cystic formations of different sizes were frequently lined by neoplastic granulosa cells and organized in a macrofollicular pattern; some cysts showed significant hemorrhage or eosinophilic secretion (Fig. 5B). Multifocally, the neoplastic cells palisade in trabecular (Fig. 5C),

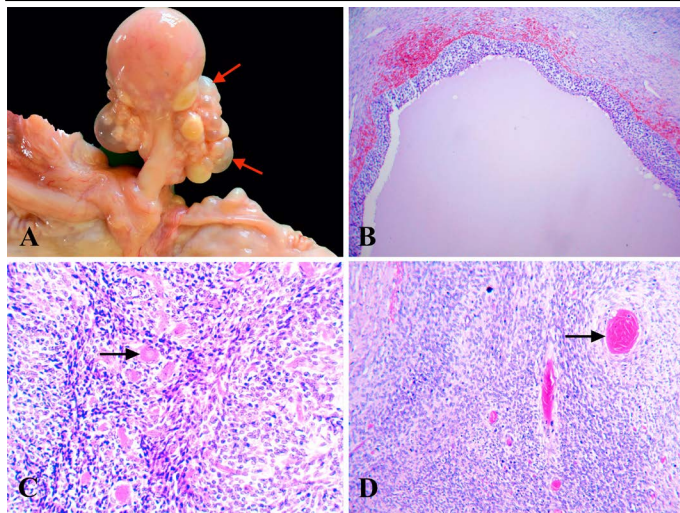


Figure 5: Granulosa-theca cell tumor, ovary, camel. (A) Firm grayish-white nodules and numerous yellow cysts (arrow). (B) Macrofollicular pattern with hemorrhage and eosinophilic secretion, HE x 100. (C) Trabecular pattern with Call-Exner bodies (arrow), HE x 400. (D) Diffuse pattern with Call-Exner bodies (arrow), HE x 200.

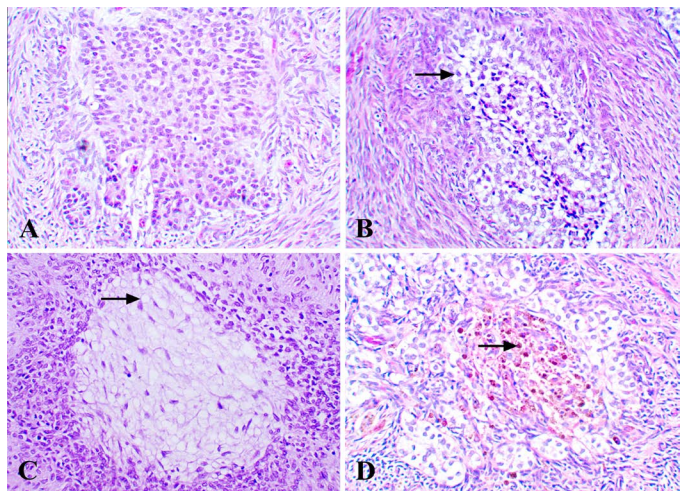


Figure 6: Granulosa-theca cell tumor, uncommon pattern, ovary, camel, HE x 400. (A) Solid follicular pattern without lumen. (B) Luteinized-granulosa (arrow) pattern. (C) Luteinized-thecoma (arrow) pattern. (D) Luteinized-pigmented pattern characterized by brownish granules (arrow).

and diffuse sheets, interspersed with Call-Exner bodies (Fig. 5D) characterized by rosette-like patterns in abortive follicles. Uncommon patterns were characterized by solid follicular (Fig. 6A), luteinized-granulosa (Fig. 6B), luteinized-thecoma (Fig. 6C), and luteinized-pigmented characterized by brownish granules (Fig. 6D), as well as insular with dense fibrous stroma (Fig. 7A), tubule-like (Fig. 7B) or Sertoli-like (Fig. 7E). Immunohistochemically, the tubule-like pattern expressed strong diffuse positive reaction for vimentin antibodies (Fig. 7C), and moderate focal positive reaction for inhibin antibodies (Fig. 7D); while the Sertoli-like pattern expressed cytoplasmic positive reaction

for vimentin or melan A antibodies (Fig. 7F), and negative reaction for inhibin.

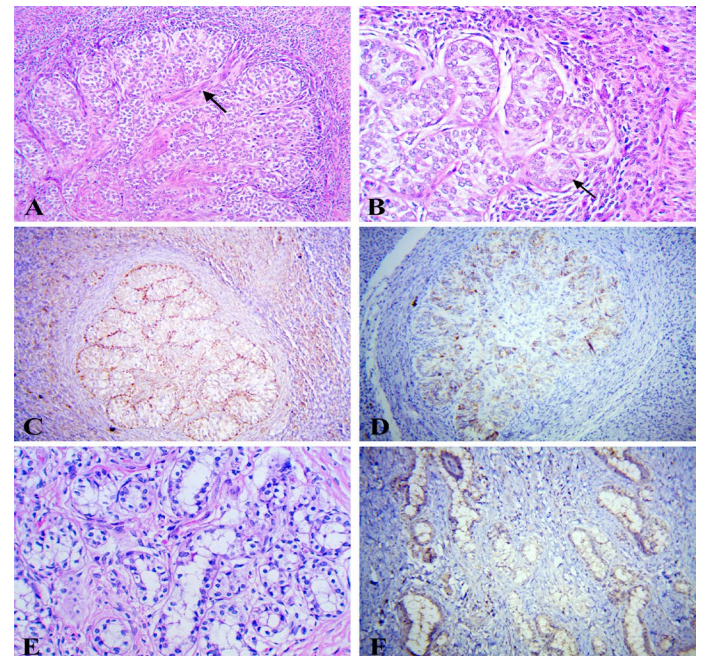


Figure 7: Granulosa-theca cell tumor, ovary, camel. (A) Insular pattern with dense fibrous stroma (arrow), HE x 200. (B) Tubule-like (arrow) pattern, HE x 400. (C) Tubule-like pattern expressed strong diffuse positive reaction for vimentin, x 200. (D) Tubule-like pattern expressed moderate focal positive reaction for inhibin, x 200. (E) Sertoli-like pattern, HE x 400. (F) Sertoli-like pattern expressed cytoplasmic positive reaction for melan A, x 200.

DISCUSSION

Sex cord-stromal tumors are categorized using the characteristics of the main cell population and their similarity to the typical components of the ovarian endocrine machinery. These tumors were classified by the World Health Organization into three types: pure sex cord tumors, pure stromal tumors, and mixed sex cord-stromal tumors (Al Harbi et al., 2021). The present study categorized the granulosa-theca cell tumor separately as a mixed sex cord-stromal tumor; regardless of the controversy in some veterinary literature that granulosa cell tumor and granulosa-theca cell tumor are synonymies and often coexist in the same tumor (Schlafer and Foster, 2016).

Adult granulosa cell tumors were diagnosed in one case in the left ovary of a 7-years old female. It is classified as a pure sex cord tumor and appeared as a firm grayish-white nodule linked to the ovary by a long stalk. The tumor was made up of polygonal cells that expressed cytoplasmic positive reaction for vimentin antibodies, arranged in solid sheets, and had round to ovoid uniform nuclei with coffee-bean-like nuclear groove. Occasionally, Call-Exner

bodies interspersed the neoplastic cells. One of the biggest challenges in histopathological diagnosis is predicting the malignancy of granulosa cell tumors, especially given our lack of information of the tumor's biological behavior and clinical characteristics. However, the detection of sarcomatous alterations with pleomorphic cells, atypical mitosis, multiple hemorrhages, capsular invasion, and infiltration of the ovarian tissue architecture by the neoplastic cells are very reliable for malignancy. Granulosa cell tumor was first reported in a female dromedary camel in Saudi Arabia (Ali et al., 2013). Another study conducted on ovarian neoplasms in dromedary camel collected from Giza abattoirs, Egypt (Elshazly et al., 2019), found 6 cases of benign Granulosa cell tumors (2 adult cases, 2 juvenile cases, and 2 cases accompanied by fibroma). There have been reports of malignant granulosa cell tumors in cows and dogs (Patnaik and Greenlee, 1987; Hostetler et al., 1997). The sarcomatous change was only observed in rare human cases of adult granulosa cell tumors (Dahoud et al., 2022). Most sarcomatous transformation cases have had an aggressive clinical history with rapid recurrence (Fashedemi et al., 2019). Based on the gross and histologic appearance, our results diagnosed a benign interstitial (Leydig) cell tumor (prevalence 1/180, 0.55%). The tumor had distinctive histomorphological features characteristic of interstitial (Leydig) cell tumors. The neoplastic mass is made up of round to polygonal cells with abundant eosinophilic vacuolated cytoplasm, and round nuclei; organized in solid sheets, cords, and acini separated by a delicate fibrovascular stroma. Additionally, the neoplastic cells showed cytoplasmic positive reaction for vimentin. Interstitial-cell tumors in testicular tissue are more common, whereas in ovarian tissue are uncommon in all species (Farjanikish and Oryan, 2017). Interstitial-cell tumor in female camels has never been described before, according to the previous literature, and just one case of Sertoli-Leydig cell tumor in a female dromedary camel has been documented (Ali et al., 2019). The cell of origin of interstitial cell tumors has yet to be determined. The testicular androgen-producing interstitial cells that migrate in from the surface of the gonadal ridge are one putative source of these tumors (Knottenbelt et al., 2015). Most documented interstitial cell tumors in various species have been linked to hyperandrogenism (Gilbert et al., 2006; Chen et al., 2018).

Thecoma was detected in the present study in two cases (prevalence 1/180, 1.10%), characterized grossly by small firm grayish white nodules, composed of aggregates of streaming oval and spindle theca cells with round to oval nucleus, occasionally mixed with fibroma forming fibrothecoma. In the veterinary literature, these tumors were uncommon. Case reports of benign tumors in the ovaries of dogs and cows were frequently recorded (Soleimanzadeh et al., 2017; Iaria et al., 2019). Furthermore, the prevalence

of thecoma or fibrothecoma in dromedary camels' ovaries collected from Egypt abattoirs was 0.4% (Elshazly et al., 2019).

The preset study reported one case of steroid cell tumor (not otherwise specified) in the left ovary of 8 years old she-camel. Grossly, grayish-white to yellow nodules, with yellow solid cut sections, were embedded in the ovarian tissue. Microscopically, the tumor was composed of round to polygonal neoplastic cells, supported by moderate fibrovascular stroma and arranged in nests, sheets, or cords with the presence of lipid-rich cells and lipochrome pigment in neoplastic cells, which expressed cytoplasmic positive reaction for vimentin and melan A favor a diagnosis of steroid cell tumor. Steroid cell tumors are uncommon ovarian sex cord-stromal tumors characterized by steroid cell proliferation (Bhagat et al., 2016). In accordance with the cells from which they originate, these tumors are categorized into three subgroups: stromal luteoma, Leydig cell tumor, and steroid cell tumor, not otherwise specified (NOS). Of these subtypes, case reports of steroid cell tumors (NOS) were reported in humans (Tan et al., 2019; Faten et al., 2020; Lobaton-Ginsberg et al., 2022). Steroid cell tumor (NOS) must be differentiated from stromal luteoma and Leydig cell tumor. Stromal luteoma is found in the ovarian stroma in association with stromal hyperthecosis, whereas Leydig cell tumor is found in the hilar location and has cytoplasmic reinke crystals (Matias-Guiu, 2010). It is interesting to note that the histopathological findings of these tumors in this work did not reveal significant features suggestive of malignancy; cellular atypia or mitosis was not noted, and there was no hemorrhage or necrosis. Apart from few reports in the veterinary literature on Steroid cell tumors, the practical correlation of pathological results in these tumors with clinically malignant behavior is rarely discussed.

In this investigation, granulosa-theca cell tumors were the most often diagnosed tumors. Interestingly, our results detected 10 cases of these tumors in the ovaries (prevalence 5.5%). Importantly, these tumors were classified as mixed-sex cord-stromal tumors and diagnosed as benign; characterized grossly by numerous cysts with solid greyish white nodules, and microscopically by mixtures of granulosa cells and theca cells populations present in a single neoplasm and exhibited a wide spectrum of histologic pattern. Common patterns were micro/macrofollicular, trabecular, diffuse sheets, and Call-Exner bodies; while uncommon patterns were solid follicular, luteinized-granulosa, luteinized-thecoma, luteinized-pigmented, insular, tubule-like and Sertoli-like. Granulosa-theca cell tumors are frequently active in mares and women, producing various combinations of testosterone, inhibin and estrogen, progesterone, and anti-Mullerian hormone (Tsogtgerel et al., 2021;

Matsuoka et al., 2022). On the other hand, a granulosa cell tumor found in a dromedary camel seemed to be hormonally inert, while the ovary on the other side had developing follicles (Ali et al., 2013). However, a hormonally active granulosa cell tumor in an adult llama was recently described as producing and secreting estrogen (Carrasco et al., 2022).

Regarding the immunohistochemistry for vimentin, inhibin, and melan A in sex cord-stromal tumors, our findings revealed that vimentin expressed strong and diffuse positive reactions in the majority of these tumors. In comparison, inhibin expression was weaker, focal, and less sensitive than vimentin and negative in several phenotypes of sex cord-stromal tumors. Whereas melan A was typically positive in the steroid-secreting tumors. This finding contradicts prior findings in cows and mares in which inhibin was recently proven to be a sensitive biomarker for the detection of granulosa cell tumors (Schlafer and Foster, 2016). The interesting aspect of sex cord-stromal tumors is their ability to produce a variety of hormones and induce corresponding clinical signs. Despite this, the use of antibodies as a diagnostic marker in camelids is occasionally limited due to the lack of knowledge regarding the current species specificity and antibody cross-reactivity. As a result, future research should look at the effectiveness of using these endocrine biomarkers in camelids.

CONCLUSIONS AND RECOMMENDATIONS

The study concluded that diagnosis of sex cord-stromal tumors in camels often present a challenge, familiarity with characteristics of the different histopathologic pattern and occasionally overlapping morphology of sex cord-stromal tumors allow pathologists to narrow the differential diagnosis when facing ovarian tumors. Additionally, the use of vimentin and melan A are reliable markers in the differential diagnosis of sex cord-stromal tumors in the ovary of dromedary camels.

ACKNOWLEDGMENTS

The authors wish to express their gratitude to the Faculty of Veterinary Medicine/ Benha University for supporting this work.

CONFLICT OF INTEREST

The authors have declared no conflict of interest.

NOVELTY STATEMENT

The current study shows the use of immunohistochemical markers as a diagnostic tool for the diagnosis of ovarian tumors in dromedary camels. Our results found that vimentin expressed strong and diffuse positive reactions in the majority of these tumors whereas melan A was typically positive in the steroid-secreting tumors.

AUTHOR'S CONTRIBUTION

Conceptualization, IE, AIE, SAM, AAA; Sample collection, IE; Diagnosis, AIE, SAM, AAA; Methodology, investigation and data curation, IE, AIE, SAM, AAA; IE collected literature then drafting the manuscript in consultation with AIE, SAM, AAA; Review and editing, AIE, SAM, AAA. All authors read and approved the final manuscript.

REFERENCES

- Agnew DW, MacLachlan NJ (2017). Tumors of the Genital Systems. In: Tumors in Domestic Animals, D. J. Meuten, Ed, 5th edn, Wiley Blackwell, Ames, IA, pp. 690-701.
- Ali A, Al-Sobayil FA, Tharwat M, Mehana EE, Al-Hawas A (2013). Granulosa cell tumour in a female dromedary camel. *Comp. Clin. Pathol.* 22:1251-1254.
- Ali A, Derar D, Hassanein K, Al-Howas A, Sadan M, El-Shafayy ES, Al-Sobayil FA (2019). Sertoli-leydig cell tumour in a female dromedary camel. *J. Camel. Pract. Res.* 26:287-290. <https://doi.10.5958/2277-8934.2019.00046.8>
- Al-Afaleq AI, Homeida AGM, Barakat SEM, Moqbel MS (2021). Gross and Microscopic Lesions of the Ovaries of Camels from Abattoirs in Eastern Province of Kingdom of Saudi Arabia. *O. J. Pathol.* 12:1-11. <https://doi.10.4236/ojpathology.2022.121001>
- Al Harbi R, McNeish IA, El-Bahrawy M (2021). Ovarian sex cord-stromal tumors: an update on clinical features, molecular changes, and management: a review. *Int. J. Gynecol. Cancer.* 31:161-168. <https://doi.10.1136/ijgc-2020-002018>
- Bancroft JD, Suvarna SK, Layton C (2013). Bancroft's Theory and Practice of Histological Techniques. 7th edn. British, Churchill Livingstone Elsevier Ltd.
- Bhagat R, Bodal VK, Gupta N, Garg P (2016). Steroid cell tumour of ovary—a rare case report. *J. Clin. Diagn. Res.* 10: ED06-ED07. <https://doi.10.7860/JCDR/2016/15767.8556>
- Chen M, Zhou W, Zhang Z, Zou Y, Li C (2018). An ovarian Leydig cell tumor of ultrasound negative in a postmenopausal woman with hirsutism and hyperandrogenism: a case report. *Medicine.* 97:10. <https://doi.org/10.1097/MD.00000000000010093>
- Carrasco RA, Hutt KD, McKenzie CM, Adams GP (2022). Granulosa cell tumour in a llama (Lama glama). *Reprod. Domestic. Anim.* 00:1-6. <https://doi.org/10.1111/rda.14296>
- Dahoud W, Handler J, Parimi V, Meyer CF, Wethington SL, Eshleman JR, Vang R, Ronnett BM, Xing D (2022). Adult granulosa cell tumor with sarcomatous transformation: a case study with emphasis on molecular alterations. *Inter. J. Gynecol. Pathol.* 41:600-607. <https://doi.org/10.1097/>

- Elshazly MO, Abd El-Rahman SS, Hamza DA, Ali ME (2019). Ovarian neoplasms in dromedary camel: Prevalence, types and pathology. *J. Camel. Pract. Res.* 26:1-9.
- Farjanikish G, Oryan A (2017). Leydig cell tumor in ovary of a German Shepherd bitch: An immunohistopathological study. *Vet. Res. Forum.* 8:81– 84.
- Fashedemi Y, Coutts M, Wise O, Bonhomme B, Baker G, Kelly PJ, Soubeyran I, Catherwood MA, Croce S, McCluggage WG (2019). Adult Granulosa Cell Tumor With High-grade Transformation: Report of a Series With FOXL2 Mutation Analysis. *Am. J. Surg. Pathol.* 43:1229–1238. <https://doi.org/10.1097/PAS.0000000000001296>
- Faten H, Dorra G, Slim C, Wajdi S, Nadia C, Kais C, Tahia B, Mohamed A (2020). Ovarian steroid cell tumor (not otherwise specified): a case report of ovarian hyperandrogenism. *Oncol. Medicine.* Article ID 6970823, 6 pages. <https://doi.org/10.1155/2020/6970823>
- Gilbert R, Kutzler M, Valentine BA, Semevolos S (2006). Hyperandrogenism from an ovarian interstitial-cell tumor in an alpaca. *J. Vet. Diagn. Invest.* 18:605–607. <https://doi.org/10.1177/104063870601800616>
- Hostetler DE, Sprecher DJ, Yamini B, Ames NK (1997). Diagnosis and management of a malignant granulosa cell tumor in a Holstein nulligravida: A case study. *Theriogenology.* 48:11–17. [https://doi.org/10.1016/S0093-691X\(97\)00188-X](https://doi.org/10.1016/S0093-691X(97)00188-X)
- Iaria C, Abbate JM, De Benedetto G, Mazzullo G, Lanteri G, Mazzullo S, Ieni A (2019). A Rare Case of Thecoma In a Dog. *Biomed. J. Sci. Technical. Res.* 19:14188-14192.
- Knottenbelt DC, Snalune K, Kane JP (2015). Clinical equine oncology. Elsevier Health Sciences, pp. 393-405.
- Kottarathil VD, Antony MA, Nair IR, Pavithran K (2013). Recent advances in granulosa cell tumor ovary: a review. *Indian. J. Surg. Oncol.* 4:37-47. <https://doi.org/10.1007/s13193-012-0201-z>
- Kriplani D, Patel MM (2013). Immunohistochemistry: A diagnostic aid in differentiating primary epithelial ovarian tumors and tumors metastatic to the ovary. *South. Asian. J. cancer.* 2:254-258. <https://doi.org/10.4103/2278-330X.119888>
- Lim D, Oliva E (2018). Ovarian sex cord-stromal tumours: an update in recent molecular advances. *Pathology.* 50:178-189.
- Lobaton-Ginsberg M, Malanco-Hernández LM, Ferreira-Hermosillo A (2022). Rare virilizing tumor: ovarian steroid cell tumor, not otherwise specified: a case report. *J. Med. Case. Reports.* 16:478. <https://doi.org/10.1186/s13256-022-03697-w>
- Matias- Guiu X (2010). Endocrine ovaries. In: *Endocrine pathology: Differential Diagnosis and Molecular Advances*, R. V. Lioyd, Ed, 2nd edn. Springer Science Business Media, LLC, pp. 307-332.
- Matsuoka A, Tate S, Nishikimi K, Kobayashi T, Otsuka S, Shozu M (2022). Serum FSH as a Useful Marker for the Differential Diagnosis of Ovarian Granulosa Cell Tumors. *Cancers.* 14:4480. <https://doi.org/10.3390/cancers14184480>
- Patnaik AK, Greenlee PG (1987). Canine Ovarian Neoplasms: A Clinicopathologic Study of 71 Cases, Including Histology of 12 Granulosa Cell Tumors. *Vet. Pathol.* 24:509-514. <https://doi.org/10.1177/030098588702400607>
- Ramos-Vara JA, Beissenherz ME (2000). Optimization of immunohistochemical methods using two different antigen retrieval methods on formalin-fixed paraffin-embedded tissues: experience with 63 Markers. *J. Vet. Diagn. Invest: official publication of the American Association of Veterinary Laboratory Diagnosticians, Inc.* 12: 307–311. <https://doi.org/10.1177/104063870001200402>
- Schlafer DH, Foster RA (2016). Female Genital System. In: *Jubb, Kennedy & Palmer's Pathology of Domestic Animals*, M. G. Maxie, Ed, Vol 3. 6th edn. St. Louis, MO: Elsevier Limited, pp. 358–464.e1. <https://doi.org/10.1016/B978-0-7020-5319-1.00015-3>
- Soleimanzadeh A, Batavani R, Nourian A, Pashaie B (2017). Ovarian Fibrothecoma in a Holstein cow: A Case report. *Iranian. J. Vet. Sci. Technol.* 9:70-74.
- Tan EC, Khong CC, Bhutia K (2019). A Rare Case of Steroid Cell Tumor, Not Otherwise Specified (NOS), of the Ovary in a Young Woman. *Case. Rep. Obstet. Gynecol.* 2019:4375839. <https://doi.org/10.1155/2019/4375839>
- Tsogtgerel M, Tagami M, Watanabe K, Murase H, Hirose Y, Kobayashi Y, Nambo Y (2021). Case report: The case of a 17 kg ovarian granulosa cell tumor in a Breton draft mare. *J. Equine. Sci.* 32:67-72. <https://doi.org/10.1294/jes.32.67>