



## NOTE

Pathology

## Uterine metastatic rhabdomyosarcoma in a scimitar-horned oryx (*Oryx dammah*)

Du-Min GO<sup>1)</sup>, Sang-Ho WOO<sup>1)</sup>, Su-Hyung LEE<sup>2)</sup>, Soo-Whan KWON<sup>3)</sup>, Dong-Hee CHUNG<sup>3)</sup>, Soong-Hee YOUN<sup>3)</sup>, Eun JUNG<sup>3)</sup> and Dae-Yong KIM<sup>1)</sup>\*<sup>1)</sup>Department of Veterinary Pathology and Research Institute for Veterinary Science, College of Veterinary Medicine, Seoul National University, Seoul 08826, Republic of Korea<sup>2)</sup>National Cancer Center, Goyang 10408, Republic of Korea<sup>3)</sup>Everland Zoological Garden, Samsung Construction and Trading, Yongin 17023, Republic of Korea*J. Vet. Med. Sci.*

80(10): 1558–1561, 2018

doi: 10.1292/jvms.18-0395

Received: 9 July 2018

Accepted: 23 July 2018

Published online in J-STAGE:  
5 September 2018

**ABSTRACT.** A 13-year-old female scimitar-horned oryx (*Oryx dammah*) died after progressive anorexia, weight loss, and depression. The necropsy showed that the retroperitoneum was compressed by a large white-to-tan uterine mass and on several sections of the mass, the uterine wall was markedly thickened because of ill-defined transmural tumor tissue. Metastatic nodules were detected in the omentum, mesentery, diaphragm, and lung. The genital tract and pulmonary and abdominal nodules exhibited highly pleomorphic sarcoma. The primary and metastatic neoplastic cells showed positive results for vimentin, desmin, and sarcomeric actin, and negative results for smooth muscle actin. Uterine metastatic rhabdomyosarcoma was diagnosed on the basis of the gross, histopathology and immunohistochemistry results.

**KEY WORDS:** immunohistochemistry, oryx, rhabdomyosarcoma, uterus

Rhabdomyosarcoma is a tumor of the skeletal muscle but can also occur in organs that lack striated muscles, such as the urinary bladder, uterus, vagina, and liver [9, 11, 14, 15]. Rhabdomyosarcoma has been rarely reported in animal species, including domestic and zoo animals. Rhabdomyosarcoma is classified into embryonal, alveolar, and pleomorphic subtypes on the basis of histopathology. In humans, the pleomorphic subtype mainly occurs in adults, whereas the alveolar and embryonal subtypes are most common in young people under 30 years of age; the most common sites are the head and neck and genitourinary tract.

The scimitar-horned oryx (*Oryx dammah*) belongs to the subfamily Hippotraginae and family Bovidae [6]. The International Union for Conservation of Nature considers this species as extinct in the wild, but it can be found captive in institutions worldwide [6]. The maximum lifespan of a captive scimitar-horned oryx is 27.5 years. Only a few cases of spontaneous tumor in oryx have been documented. Pericardial myxoid liposarcoma and Leydig cell tumor have been reported in the common eland (*Taurotragus oryx*), and uterine endometrial carcinoma and 3 cases of tumor of the fore-stomach musculature have been reported in the scimitar-horned oryx [5, 6, 12]. To the best of our knowledge, rhabdomyosarcoma has not yet been reported in the oryx. Here, we report a case of malignant metastatic rhabdomyosarcoma with primary involvement of the genital tract in the scimitar-horned oryx.

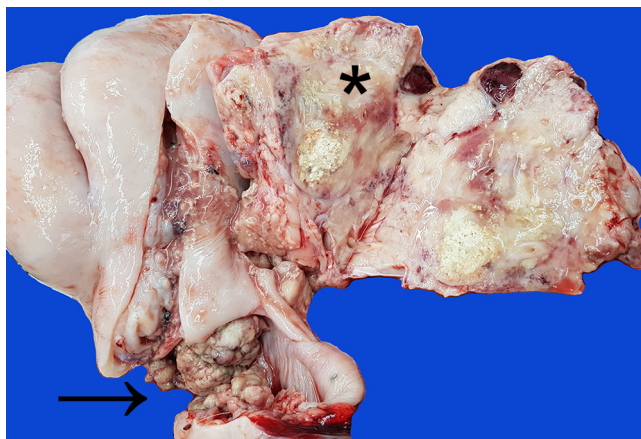
A 13-year-old, female scimitar-horned oryx showed slowly progressive anorexia, weight loss, depression, and was becoming moribund. Despite fluid treatment and other medical interventions, the oryx died and necropsy was performed after death. The necropsy showed that the retroperitoneum was compressed by a large white-to-tan mass that appeared to be the uterine horns, body of the uterus, and cervix. An ovary, the urinary bladder, and part of a kidney were incarcerated by the mass and appeared to be grossly intact. At several sections of the mass, the uterine wall was markedly thickened because of ill-defined transmural necrohemorrhagic tumor tissue involving serosa (Fig. 1). Multiple firm round nodules were also observed at the luminal side of the vagina and cervix, resulting in narrowing of the lumen. Throughout the mesentery, omentum, and diaphragm, multiple firm round nodules of varying size were scattered. The thorax was full of pleural fluid, and the lung contained multiple umbilicated nodules. Other parenchymal organs were unremarkable.

Representative tissue samples were fixed in 10% neutral phosphate-buffered formalin, processed routinely, embedded in paraffin wax, sectioned (thickness, 3  $\mu$ m), and stained with hematoxylin and eosin (H&E). Replicate serial sections of the uterine mass, diaphragm and lung nodules were prepared for immunohistochemistry (IHC). Heat-induced antigen retrieval was performed using the deparaffinized and rehydrated sections, and endogenous peroxidase was depleted by incubating the slides in 0.3% hydrogen peroxide for 1 hr. The sections were incubated overnight at 4°C with vimentin (1:200, mouse monoclonal antibody; Dako, Santa Clara, CA, U.S.A.), smooth muscle actin (SMA; 1:200, mouse monoclonal antibody; Dako), desmin (1:200, mouse monoclonal

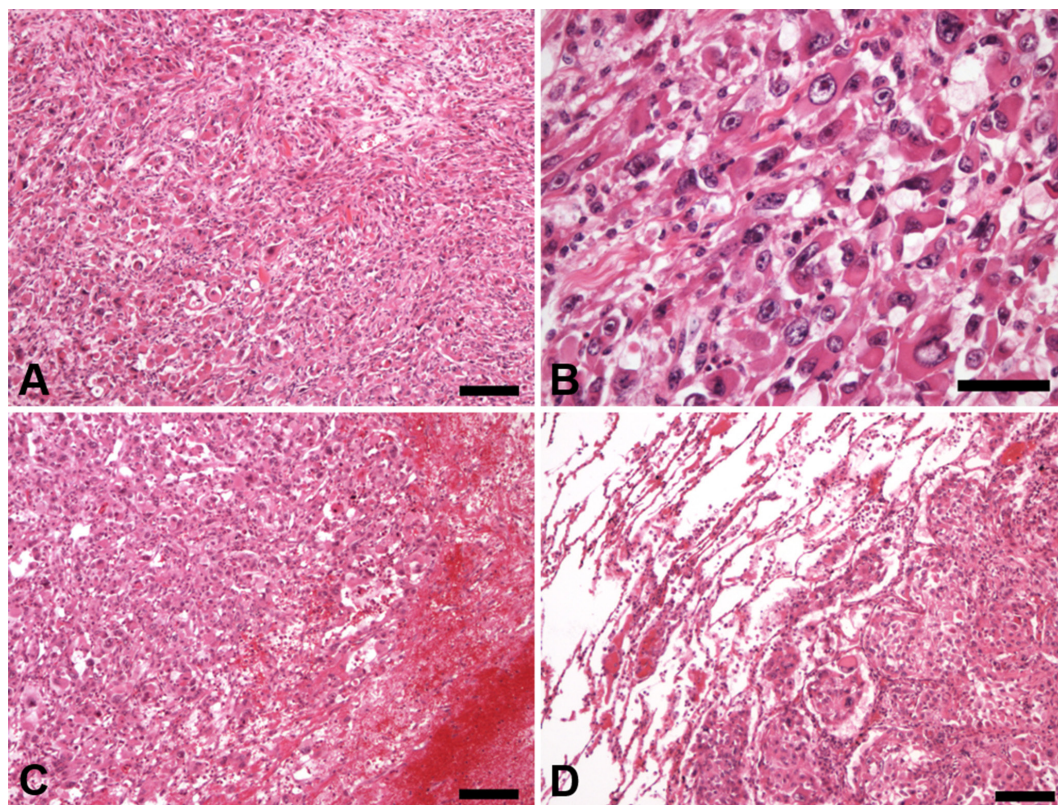
\*Correspondence to: Kim, D.-Y.: daeyong@snu.ac.kr

©2018 The Japanese Society of Veterinary Science

This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives (by-nc-nd) License. (CC-BY-NC-ND 4.0: <https://creativecommons.org/licenses/by-nc-nd/4.0/>)



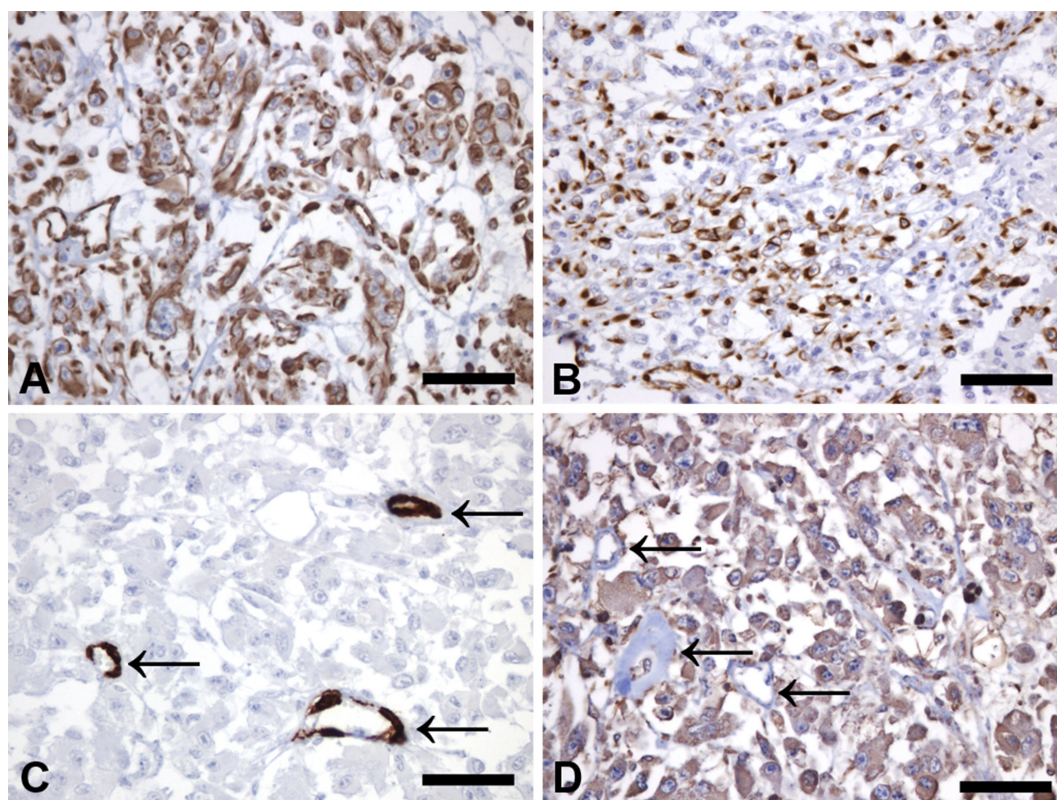
**Fig. 1.** Rhabdomyosarcoma, uterus, scimitar-horned oryx (*Oryx dammah*). On the right uterine horn mass (asterisk), the uterine wall is markedly thickened because of ill-defined transmural tumor tissue involving serosa. On the luminal side of the uterine body and cervix (arrow), a large white-to-tan mass is present.



**Fig. 2.** Histology of rhabdomyosarcoma in a scimitar-horned oryx (*Oryx dammah*). A. The uterine mass is composed of pleomorphic neoplastic cells arranged in haphazard or interlacing patterns. H&E. Bar=200  $\mu$ m. B. The neoplastic cells show marked pleomorphism. Note the eccentric and bizarre nuclei containing 1 or more prominent nucleoli. H&E. Bar=50  $\mu$ m. C and D. The neoplasm metastasized to the diaphragm (C) and lung (D). H&E. Bar=200  $\mu$ m.

antibody; BioGenex, Fremont, CA, U.S.A.), and sarcomeric actin (1:400, mouse monoclonal antibody; Sigma, St. Louis, MI, U.S.A.), and then incubated with horseradish peroxidase-conjugated secondary antibody for 2 hr at 18–22°C. All sections were visualized using 3,3'-diaminobenzidine (DAB) solution and then counterstained with Mayer's hematoxylin.

Sections from the uterine and metastatic nodules were examined microscopically, and they showed deletion identical changes. Microscopically, the uterus was occupied by neoplastic proliferation effacing almost the entire uterine architecture (Fig. 2A). The



**Fig. 3.** Immunohistochemistry of rhabdomyosarcoma in a scimitar-horned oryx (*Oryx dammah*). The neoplastic cells are positive for vimentin (A) and desmin (B). The neoplastic cells are negative for smooth muscle actin (C) but positive for sarcomeric actin (D). Note the positive (C) and negative (D) staining of the vascular smooth muscles (arrows). Bar=50  $\mu$ m (applies to A, B, C, and D).

neoplastic cells had spindle to round to polygonal shape with considerable pleomorphism (Fig. 2B). These cells were arranged in haphazard or interlacing patterns and had abundant eosinophilic cytoplasm and a large, round to oval nucleus containing 1 or more prominent nucleoli. Eccentric, bizarre and multiple nuclei were frequently observed. Cross-striations were not observed in the neoplastic cells. There were 1–3 mitoses per high-power field, and tumor emboli were present. Multifocal areas of necrosis and hemorrhage with heavy neutrophilic infiltration were also observed. The nodules in the diaphragm (Fig. 2C) and lung (Fig. 2D) consisted of neoplastic cells whose histological features were similar to those of the uterine mass. No remarkable microscopic changes were noted in any other examined parenchymal organs including the urinary bladder and kidney. To identify the origin of the neoplasm, IHC for vimentin, desmin, SMA, and sarcomeric actin were performed. The neoplastic cells showed strong positive signals for vimentin, indicating a mesenchymal origin (Fig. 3A). Because the site of the primary tumor was considered to be the uterus, the neoplasm was suspected to originate from the smooth muscle tissue. The neoplastic cells showed an occasional positive signal for desmin (Fig. 3B) but were negative for SMA (Fig. 3C). However, the neoplastic cells were strongly positive for sarcomeric actin, suggesting skeletal muscle origin (Fig. 3D). On the basis of the gross and histological findings and IHC results, we diagnosed uterine rhabdomyosarcoma with mesenteric and diaphragmatic implantation and pulmonary metastasis.

Primary rhabdomyosarcoma of the uterus has been rarely reported in humans and animals, and there is limited information on the characteristics of uterine rhabdomyosarcoma in animals. To the best of our knowledge, uterine rhabdomyosarcoma in animals has been reported in a filly, dog, and rat (1 case each) [1, 8, 15].

In the human uterus, all subtypes of rhabdomyosarcoma can occur and similar to rhabdomyosarcoma in other anatomical locations, the pleomorphic subtype is the most prevalent in adults and the embryonal subtype is the most common in children [10, 13]. The incidence of the alveolar subtype in the human uterus appears to be low, regardless of patient age [10, 13]. In our case, uterine mass and other metastatic masses were considered to be the pleomorphic subtype on the basis of the histological findings and the animal's age. Rhabdomyosarcoma is considered to be the pleomorphic subtype when there are no characteristic histological findings of the embryonal or alveolar subtypes and when the tumor cells show marked pleomorphism [3]. In this case, tumor cells with abundant eosinophilic cytoplasm were proliferating haphazardly with pronounced pleomorphism, and no less-differentiated small round to oval tumor cells with scant cytoplasm of the alveolar or embryonal subtypes could be observed. In addition, no evidence of the classical or solid alveolar pattern, which are features of the alveolar subtype, or of myxomatous stroma or cambrium layer, which are features of the embryonal subtype, were detected.

In humans, classification of rhabdomyosarcoma subtypes is very important in terms of prognosis [3]. Generally, alveolar and pleomorphic subtypes have a poor prognosis, but the embryonal subtype has a relatively better prognosis. Especially the

botryoid embryonal subtype has a favorable prognosis [1, 3]. However, the prognostic relevance of the rhabdomyosarcoma subtypes in animals is unknown [2, 3]. In humans, uterine rhabdomyosarcoma generally has a poor prognosis because, in many patients, the tumor is metastasized to other organs at the time of diagnosis [13]. In humans, the pleomorphic subtype of uterine rhabdomyosarcoma is highly aggressive and associated with a high mortality rate [4]. In the 3 previously reported cases of uterine rhabdomyosarcoma in animals, widespread metastasis was observed in the dog with the alveolar subtype, and no metastasis was reported in the filly with the botryoid embryonal subtype [1, 15]. In the rat, invasion into the lymphatic vessels was observed, but there was no evidence of metastasis to other organs [8]. However, more cases need to be studied to determine the biological behavior of uterine rhabdomyosarcoma in animals.

The exact origin of rhabdomyosarcoma has not yet been elucidated, but it is presumed to originate from mesenchymal progenitor cells, which have the potential to differentiate into skeletal muscle cells [3]. Mesenchymal progenitor cells are present in various organs; thus, rhabdomyosarcoma may occur in organs without skeletal muscle [7]. Studies on the origin of tumor cells for each subtype are being performed using cultured target cells or mouse models. These studies suggest that the alveolar subtype is derived from mesenchymal progenitor cells; embryonal subtype, mesenchymal progenitor cells or the more differentiated muscle progenitor cells; and pleomorphic subtype, an unknown cell population present in adult skeletal muscle [2, 7]. In humans, risk factors for uterine rhabdomyosarcoma are hormones, tamoxifen, and radiation, but the exact association is unclear [4].

Uterine leiomyosarcoma should be considered as the principal differential diagnosis for uterine rhabdomyosarcoma. Leiomyosarcoma is more common than rhabdomyosarcoma and can be histologically similar to rhabdomyosarcoma [13]. It may be especially difficult to differentiate between pleomorphic rhabdomyosarcoma and pleomorphic leiomyosarcoma [13]. In our case, we confirmed rhabdomyosarcoma on the basis of the IHC results for SMA and sarcomeric actin. In addition, malignant mixed Müllerian tumor can be considered in the differential diagnosis; however, in this case, we excluded this possibility because neoplastic proliferation of epithelial cells was not observed histologically.

This report indicates that rhabdomyosarcoma should be considered as a differential diagnosis for uterine tumors in animals. Analysis of additional cases may help to elucidate the biological behavior, incidence, and prevalence of uterine rhabdomyosarcoma in animals.

CONFLICT OF INTEREST. The authors declare no conflicts of interest.

ACKNOWLEDGMENT. This research was supported by the Korea Mouse Phenotyping Project (NRF-2016M3A9D5A01952416) of the National Research Foundation of the Korean government.

## REFERENCES

1. Bae, I. H., Kim, Y., Pakhrin, B., You, M. H., Hwang, C. Y., Kim, J. H. and Kim, D. Y. 2007. Genitourinary rhabdomyosarcoma with systemic metastasis in a young dog. *Vet. Pathol.* **44**: 518–520. [Medline] [CrossRef]
2. Caserto, B. G. 2013. A comparative review of canine and human rhabdomyosarcoma with emphasis on classification and pathogenesis. *Vet. Pathol.* **50**: 806–826. [Medline] [CrossRef]
3. Cooper, B. J. and Valentine, B. A. 2017. Tumors of muscle, pp. 445–458. In: *Tumors in Domestic Animals*, 5th ed. (Meuten, D. J. ed.), Ames.
4. Fadare, O., Bonvicino, A., Martel, M., Renshaw, I. L., Azodi, M. and Parkash, V. 2010. Pleomorphic rhabdomyosarcoma of the uterine corpus: a clinicopathologic study of 4 cases and a review of the literature. *Int. J. Gynecol. Pathol.* **29**: 122–134. [Medline] [CrossRef]
5. Foster, A. P., Johnston, P. E., Duignan, P. J. and Schock, A. 2011. Pericardial myxoid liposarcoma in a common eland (*Taurotragus oryx*). *J. Comp. Pathol.* **145**: 103–106. [Medline] [CrossRef]
6. Harwood, D. G., Griffiths, W. H., Bradshaw, J. M. and Gilbert, T. 2009. Uterine endometrial carcinoma associated with dystocia in a captive scimitar-horned oryx (*Oryx dammah*). *Vet. Rec.* **164**: 661–662. [Medline] [CrossRef]
7. Hettmer, S. and Wagers, A. J. 2010. Muscling in: Uncovering the origins of rhabdomyosarcoma. *Nat. Med.* **16**: 171–173. [Medline] [CrossRef]
8. Kaspareit-Rittinghausen, J. and Deerberg, F. 1990. Spontaneous malignant mixed müllerian tumors and rhabdomyosarcoma of the uterus in rats. *Toxicol. Pathol.* **18**: 417–422. [Medline] [CrossRef]
9. Kim, D. Y., Hodgins, E. C., Cho, D. Y. and Varnado, J. E. 1996. Juvenile rhabdomyosarcomas in two dogs. *Vet. Pathol.* **33**: 447–450. [Medline] [CrossRef]
10. Kirsch, C. H., Goodman, M. and Esiashvili, N. 2014. Outcome of female pediatric patients diagnosed with genital tract rhabdomyosarcoma based on analysis of cases registered in SEER database between 1973 and 2006. *Am. J. Clin. Oncol.* **37**: 47–50. [Medline] [CrossRef]
11. Minkus, G. and Hillemanns, M. 1997. Botryoid-type embryonal rhabdomyosarcoma of liver in a young cat. *Vet. Pathol.* **34**: 618–621. [Medline] [CrossRef]
12. Nyska, A., Waner, T., Goldstein, J., Horowitz, Y., Harmelin, A., Orgad, U. and Jakobson, B. 1994. Interstitial cell (Leydig) tumor in an eland (*Taurotragus oryx*). *J. Wildl. Dis.* **30**: 291–294. [Medline] [CrossRef]
13. Pinto, A., Kahn, R. M., Rosenberg, A. E., Slomovitz, B., Quick, C. M., Whisman, M. K. and Huang, M. 2018. Uterine rhabdomyosarcoma in adults. *Hum. Pathol.* **74**: 122–128. [Medline] [CrossRef]
14. Suzuki, K., Nakatani, K., Shibuya, H. and Sato, T. 2006. Vaginal rhabdomyosarcoma in a dog. *Vet. Pathol.* **43**: 186–188. [Medline] [CrossRef]
15. Torbeck, R. L., Kittleson, S. L. and Leathers, C. W. 1980. Botryoid rhabdomyosarcoma of the uterus of a filly. *J. Am. Vet. Med. Assoc.* **176**: 914–916. [Medline]